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A GUIDE TO INFECTIOUS DISEASES OF MICE AND RATS

A REPORT OF THE

Committee on Laboratory Animal Diseases

INSTITUTE OF LABORATORY ANIMAL RESOURCES
NATIONAL RESEARCH COUNCIL

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PREFACE

The Institute of Laboratory Animal Resources (ILAR) was founded in 1952, within the Division of Biology and Agriculture. Its mission is to disseminate information, survey existing and required resources, establish standards, promote education, hold conferences, and generally assist in developing and improving laboratory animal resources.

This guidebook is a brief reference source for the identification of infectious diseases in laboratory mice and rats. It is intended primarily for medical investigators and animal technicians, but may also be useful to veterinarians working in the field of laboratory animal medicine. It is well recognized that naturally occurring diseases in experimental animals can interfere with both the productivity and validity of medical research. Although all types of disease occur in laboratory mice and rats, infectious diseases have a particularly high incidence and are very frequently responsible for obstructing research. Furthermore, infectious diseases in these species are often not apparent clinically and require careful pathologic or microbiologic examination to detect them.

To be entirely suitable for experimental use animals must be free of disease, but this is too often not the case. Even when professional veterinary assistance is available, the medical investigator is primarily responsible for the health of his animal colony. He must, therefore, be aware of disease problems that can exist and attempt to recognize and control them by careful selection of animal suppliers, close supervision of animal colonies, and by performing necessary clinical and pathologic examinations. We hope that this guidebook will facilitate and encourage such practices.

COMMITTEE ON LABORATORY ANIMAL DISEASES

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Unexpected or Sudden Death‡

*The number following each entry cross-refers to the respective page(s) in "Disease Outline" and "Outline of Methods for Disease Prevention and Control."

†Many infectious diseases of mice and rats may be inapparent to all but the most critical observer. This list contains those that are most likely to be overlooked.

‡Many diseases of rats and mice may cause sudden or unexpected death. This list indicates only those diseases that most often lack premonitory clinical signs.

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*Other factors must be considered, particularly husbandry.

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*Poor husbandry must be considered.

II DISEASE OUTLINES

ADENOVIRUS INFECTION

ETIOLOGY Adenovirus; 100 mμ

ANIMALS AFFECTED Mice

CLINICAL SIGNS Seen only in suckling mice; stunting, lethargy, death

PATHOLOGY Gross: white to gray spots may be seen on heart.
Microscopic: Focal necrosis of heart muscle; intranuclear inclusion bodies in heart, kidneys, adrenals

DIAGNOSIS Pathologic findings; serology (complement fixation or serum neutralization)

REFERENCES

1. Blailock, F. R., E. R. Rabin, and J. L. Melnick. 1967. Adenovirus endocarditis in mice. Science 157:69–70.

2. Hartley, J. W., and W. P. Rowe. 1960. A new mouse virus apparently related to the adenovirus group. Virology 11:645–647.

BARTONELLOSIS*

ETIOLOGY *Hemobartonella muris* (rats); *Eperythrozoon coccoides* (mice); possibly Rickettsial organisms

ANIMALS AFFECTED Mice and rats

CLINICAL SIGNS Usually inapparent infections; symptoms may in-

**Note*: Infection may be transmitted by passage of biologic materials. Simultaneous mouse hepatitis infection enhances virulence of both diseases in the mouse. Activation of disease may also result from splenectomy, immunosuppression, or other impairment to the reticuloendothelial system.

clude anemia, weakness and hemoglobinuria in rats, but only anemia in mice.

PATHOLOGY Gross: Enlarged spleen, pale tissues

Microscopic: *H. muris* appear as solid, coccoid forms and *E. coccoides* in ring and solid forms. Both measure 0.5–0.7 μ in diameter. *H. muris* tends to be on erythrocytes, whereas *E. coccoides* occurs on erythrocytes and free in plasma.

DIAGNOSIS Clinical and pathologic findings; inapparent infection may be detected by splenectomy and daily examination of Giemsa stained blood smears; incubation period is 4–6 days and organisms may not appear until 12–24 hr prior to hemolytic crisis

REFERENCES

1. Baker, H. J., and J. R. Lindsey. 1967. Latent bartonellosis: A complicating factor in animal experimentation. Exp. Hematol. 14:53–65.

2. Ott, K. J. and L. A. Stauber. 1967. *Eperythrozoon coccoides*: Influence on course of infection of *Plasmodium chabaudi* in mouse. Science 155:1546–1548.

Bordetella bronchiseptica* INFECTION

ETIOLOGY *Bordetella bronchiseptica* (gram-negative bacillus)

ANIMALS AFFECTED Mice and rats

CLINICAL SIGNS May be inapparent. Rats may show head tilt or circling. Mice may show purulent conjunctivitis and labored breathing.

PATHOLOGY Gross: Lung consolidation in rats and mice with pus in bronchi; pus in middle ear of rat

Microscopic: Purulent bronchopneumonia; purulent otitis media

DIAGNOSIS Isolation of organism

REFERENCES

1. Winsser, J. 1960. A study of *Bordetella bronchiseptica*. Proc. Anim. Care Panel 10:87–101.

COCCIDIOSIS

ETIOLOGY Protozoan parasites

a. Intestinal coccidiosis—at least four species of coccidia in labora-

*Note: *Bordetella bronchiseptica* is a normal inhabitant of respiratory tract in rats and is associated with pneumonia in rats and mice. Its role as a primary pathogen in murine pneumonia is uncertain.

tory rat (*Rattus norvegicus*), three species in black rats (*Rattus rattus*), and eight species in mice

b. Gastric and intestinal coccidiosis (cryptosporidiosis)—two species in mice: *Cryptosporidium muris* and *C. parvum.*

c. Renal coccidiosis—*Klossiella muris* in mice

ANIMALS AFFECTED Mice and rats

CLINICAL SIGNS Usually none

PATHOLOGY No lesions; incidental finding of organisms in epithelial cells of alimentary tract or renal tubules

DIAGNOSIS Pathologic findings; gastric and intestinal species—fecal examination and identification of oocysts. *K. muris* sporocysts can be recovered from urine.

REFERENCES

1. Levine, N. D., and V. Ivens. 1965. The coccidian parasites (protozoa, sporozoa) of rodents. The University of Illinois Press, Urbana, Illinois.

Corynebacterium kutscheri* INFECTION (Pseudotuberculosis)

ETIOLOGY *Corynebacterium kutscheri* (gram-positive, diphtheroid bacillus)

ANIMALS AFFECTED Mice and rats

CLINICAL SIGNS May be inapparent; nasal and ocular discharge, difficult respiration, enlarged joints, skin abscesses

PATHOLOGY Gross: Variable, may include consolidation of lungs or caseous lesions of lungs, liver, kidneys, lymph nodes; purulent polyarthritis

Microscopic: Acute to caseous pneumonia; abscesses in viscera, purulent arthritis

DIAGNOSIS Isolation of organism; serology (agglutination)

REFERENCES

1. Fauve, R. M., C. H. Pierce-Chase, and R. Dubos. 1964. Corynebacterial pseudotuberculosis in mice. II. Activation of natural and experimental latent infections. J. Exp. Med. 120:283–304.

2. Giddens, W. E., Jr., K. K. Keakey, G. R. Carter, and C. K. Whitehair. 1968. Pneumonia in rats due to infection with *Corynebacterium kutscheri*. Path. Vet. 5:227–237.

3. Weisbroth, S. W., and S. Scher. 1968. *Corynebacterium kutscheri* infection in the mouse. I & II. Lab. Anim. Care 18:451–468.

**Note*: Apparently widespread as inapparent infection in mice and rats. Acute disease may follow radiation, administration of cortisone, or occur in absence of known "stress."

ECTROMELIA (Mouse Pox)

ETIOLOGY Pox virus; 170 X 230 mμ

ANIMALS AFFECTED Mice (latent infection occurs in rats)

CLINICAL SIGNS Often latent. Variable signs include dermal papules or pustules, necrosis and sloughing of digits or limbs; sudden death.

PATHOLOGY Gross: Minimal changes to pale or red spots on liver; enlarged spleen initially (shrunken spleen in later stages); reddening of intestines

Microscopic: Minimal to severe necrosis of liver, pancreas and spleen; intestinal hemorrhage; lymphoid necrosis; cytoplasmic inclusion bodies may occur in skin and elsewhere

DIAGNOSIS Pathologic findings; serology (hemagglutination inhibition using vaccinia antigen, serum neutralization, indirect immunofluorescence)

REFERENCES

1. Briody, B. A. 1959. Response of mice to ectromelia and vaccinia viruses. Bact. Rev. 23:61–95.

2. Fenner, F. 1949. Mouse pox (infectious ectromelia of mice); A review. J. Immunol. 63:341–373.

3. Marchal, J. 1930. Infectious ectromelia. J. Path. Bacteriol. 33:713–728.

ENZOOTIC BRONCHIECTASIS

ETIOLOGY Uncertain; presently considered a virus

ANIMALS AFFECTED Mice and rats

CLINICAL SIGNS Chattering in mice and snuffling or rales in rats; labored respiration; sporadic deaths

PATHOLOGY Gross: Red to gray consolidation of lungs, often with abscesses; mucopurulent exudate in nasal passage; purulent exudate in middle ears of mice

Microscopic: suppurative bronchitis, bronchiectasis and bronchopneumonia; peribronchiolar lymphoid cuffs and nodules

DIAGNOSIS Pathologic findings and negative cultures for *M. pulmonis*

REFERENCES

1. Nelson, J. B. 1967. Respiratory infections of rats and mice with emphasis on indigenous mycoplasmas, p. 259–289. *In* E. C. Cotchin and F. J. C. Roe (ed.), Pathology of laboratory rats and mice. Blackwell Scientific Publications, Oxford and Edinburgh.

2. Ebbesen, P. 1968. Chronic respiratory disease in BALB/c mice. I. Pathology and relation to other murine lung infections. II. Characteristics of the disease. Amer. J. Path. 53:219–243.

EPIZOOTIC DIARRHEA OF INFANT MICE (EDIM)

ETIOLOGY Unclassified virus; 65–75 mμ

ANIMALS AFFECTED Mice

CLINICAL SIGNS High morbidity; soiling about the tail from about 5–15 days of age. Soiling may last longer in severe cases and may be ephemeral in mild ones. Death occurs only late in the disease and is due to constipation and/or secondary bacteremia. Animals may be stunted through weaning and postweaning period.

PATHOLOGY Gross: distention of colon with light mustard-colored feces. Stomach is often distended.

Microscopic: vacuolation of epithelial cells at tips of villi of small intestine, particularly in ileum. With proper stains, small acidophilic intracytoplasmic inclusions can be seen.

DIAGNOSIS Clinical and pathologic findings

REFERENCES

1. Blackwell, J. H., R. W. Tennant, and T. G. Ward. 1966. Serological studies with an agent of epizootic diarrhea of infant mice, p. 63–66. *In* Viruses of laboratory rodents. Nat. Cancer Inst. Monograph 20. U.S. Government Printing Office, Washington, D.C.

2. Kraft, L. M. 1966. Epizootic diarrhea of infant mice and lethal intestinal virus infections of infant mice, p. 55–61. *In* Viruses of laboratory rodents. Nat. Cancer Inst. Monograph 20. U.S. Government Printing Office, Washington, D.C.

GREY LUNG PNEUMONIA*

ETIOLOGY Uncertain; a virus and a noncultivable mycoplasma-like agent reported

ANIMALS AFFECTED Rats; natural occurrence uncertain in mice

CLINICAL SIGNS Often inapparent; labored respiration with sporadic deaths

PATHOLOGY Gross: Patchy or diffuse gray to red consolidation of lungs; frothy fluid in trachea

Microscopic: Pulmonary edema; leukocytes and later mono-

*Note: This appears to be a pathologic entity, but no specific etiology has been determined.

nuclear cells in alveoli and around blood vessels with thickening of alveolar septa

DIAGNOSIS Pathologic findings

REFERENCES

1. Andrewes, C. H., and R. E. Glover. 1945. Grey lung virus. An agent pathogenic for mice and other rodents. Brit. J. Exp. Path. 26:379–386.

2. Gay, F. W. 1967. Fine structure and location of the mycoplasma-like grey lung and rat pneumonia agents in infected mouse lung. J. Bacteriol. 94:2048–2061.

3. Niven, J. S. F. 1950. The histology of "grey lung virus" lesions in mice and cotton rats. Brit. J. Exp. Path. 31:759–766.

HEXAMITIASIS

ETIOLOGY *Hexamita muris**; flagellated protozoan measuring about 2 × 5 μ

ANIMALS AFFECTED Mice

CLINICAL SIGNS May be inapparent; acute infection causes diarrhea; loss of weight and sporadic deaths occurring in all age groups but particularly in young (2–3 weeks old). Weight loss and lethargy seen in chronic infections.

PATHOLOGY Gross: Marked dilatation of duodenum containing yellowish-brown liquid

Microscopic: Acute to chronic duodenitis with crypt abscesses and crypts dilated by numerous *Hexamita*

DIAGNOSIS Pathologic findings; also demonstrate *Hexamita* sp. in duodenum by fresh saline mounts and fixed smears

REFERENCES

1. Levine, N. D. 1957. Protozoan diseases of laboratory animals. Proc. Anim. Care Panel 7:98–126.

2. Meshorer, A. 1969. Hexamitiasis in laboratory mice. Lab. Anim. Care 19:33–37.

INFECTIOUS CATARRH

ETIOLOGY *Mycoplasma pulmonis*

ANIMALS AFFECTED Mice and rats

**Note*: It is uncertain whether this protozoan is truly pathogenic; the lesions which have been observed may not have been due to *Hexamita* alone. Other protozoa, such as *Entamoeba muris, Giardia* spp. and *Trichomonas* spp., occur in intestine of mice and rats but are not known to be pathogenic.

CLINICAL SIGNS Chattering in mice; snuffling and rales in rats; labored respiration; rarely head tilt, incoordination and circling; sporadic deaths

PATHOLOGY Gross: Red to gray consolidation of lungs, often with abscesses; mucopurulent nasal exudate; purulent to caseous exudate in middle ears

Microscopic: Suppurative bronchitis and bronchopneumonia; peribronchiolar lymphoid cuffs and nodules; suppurative otitis media and sometimes labyrinthitis; mucopurulent rhinitis; occasional oophoritis and salpingitis in rat

DIAGNOSIS Pathologic findings and isolation of organism

REFERENCES

1. Nelson, J. B. 1967. Respiratory infections of rats and mice with emphasis on indigenous mycoplasmas, p. 259–289. *In* E. C. Cotchin and F. J. C. Roe (ed.), Pathology of laboratory rats and mice. Blackwell Scientific Publications, Oxford and Edinburgh.

2. Sabin, A. B. 1941. The filterable microorganisms of the pleuropneumonia group. Bacteriol. Reviews 5:1–66.

3. Tully, J. C. 1965. Biochemical, morphological, and serological characterization of mycoplasma of murine origin. J. Infect. Dis. 115:171–185.

K VIRUS INFECTION

ETIOLOGY Papovavirus; 40–58 mμ

ANIMALS AFFECTED Mice

CLINICAL SIGNS None in adults; labored breathing and death in suckling mice

PATHOLOGY Gross: Lung consolidation

Microscopic: Interstitial pneumonia with proliferation of endothelial cells which may contain intranuclear inclusion bodies

DIAGNOSIS Pathologic findings; serology (hemagglutination inhibition, serum neutralization)

REFERENCES

1. Fisher, E. R., and L. Kilham. 1953. Pathology of a pneumotropic virus recovered from C_3H mice carrying the bittner milk agent. AMA Arch. Path. 55:14–19.

2. Kilham, L., and H. W. Murphy. 1953. A pneumotropic virus isolated from C_3H mice carrying the Bittner milk agent. Proc. Soc. Exp. Biol. Med. 82:133–137.

3. Tennant, R. W., J. C. Parker, and T. G. Ward. 1966. Respiratory virus infections of mice, p. 92–104. *In* Viruses of laboratory rodents. Nat. Cancer Inst. Monograph 20. U.S. Government Printing Office, Washington, D.C.

KLEBSIELLA INFECTION

ETIOLOGY *Klebsiella pneumoniae* (Friedlander's bacillus)
ANIMALS AFFECTED Mice
CLINICAL SIGNS Usually inapparent; labored breathing, cyanosis, and death
PATHOLOGY Gross: lung consolidation; subpleural hemorrhages; hydrothorax; abscesses may occur in any tissue
Microscopic: bronchopneumonia; pleuritis, abscesses in various organs
DIAGNOSIS Isolation of organism
REFERENCES

1. Webster, L. T. 1930. The role of microbic virulence, dosage, and host resistance in determining the spread of bacterial infections among mice. II. *B. Friedlaenderi*-like infection. J. Exp. Med. 52:909–929.

LACTIC DEHYDROGENASE (LDH)* VIRUS INFECTION

ETIOLOGY Unclassified virus; 40–60 mμ
ANIMALS AFFECTED Mice
CLINICAL SIGNS A latent infection; no clinical signs except elevated plasma enzyme levels, including lactic dehydrogenase, isocitric dehydrogenase, malic dehydrogenase, phosphohexose isomerase, glutamic oxalacetic transaminase
PATHOLOGY Gross: None
Microscopic: None
DIAGNOSIS Elevation of plasma LDH levels following animal inoculation with suspect plasma. (Test animals must have normal preinoculation enzyme levels.)
REFERENCES

1. Howard, R. J., A. L. Notkins, and S. E. Mergenhagen. 1969. Inhibition of cellular immune reactions in mice infected with lactic dehydrogenase virus. Nature 221:873–874.
2. Riley, V. 1968. Role of the LDH-elevating virus in leukemia therapy by asparaginase. Nature 220:1245–1246.
3. Riley, V. 1968. Lactate dehydrogenase in the normal and malignant state

**Note*: This agent is a common contaminant of transplantable tumors and other passaged materials. Infection leads to serious effects, including elevated globulin levels, enhanced antibody formation, delay in rejection of allografts, reduction in turnover of plasma proteins, enhanced growth rate of certain transplantable tumors, and some protection against whole body irradiation.

in mice and the influence of a benign enzyme-elevating virus, Vol. IV, p. 493–618. *In* H. Busch (ed.), Methods in Cancer research. Academic Press, New York.

LEPTOSPIROSIS*

ETIOLOGY Gram-negative spirochetes, members of genus *Leptospira*: *L. ballum, L. sejroe, L. soxkoebing, L. hebdomadis, L. icterohemorrhagiea*

ANIMALS AFFECTED Rats and mice

CLINICAL SIGNS Generally absent; rarely, icterus in rat

PATHOLOGY Gross: Usually none; rarely icterus and serosal hemorrhages

Microscopic: Variable; possibly hepatic necrosis and interstitial nephritis

DIAGNOSIS Microscopic demonstration of organisms in tubules of kidney with silver impregnation techniques; isolation in specialized media; animal inoculation (baby hamsters or guinea-pigs); serology (agglutination-lysis)

REFERENCES

1. Alston, J. M., and J. C. Broom. 1958. Leptospirosis in man and animals. E. & S. Livingstone Ltd., London.

2. Van Thiel, P. H. 1948. The leptospiroses. University of Leiden, Netherlands.

3. Van DerHoeden, J. 1964. The zoonoses. Elsevier Publishing Company, New York.

LETHAL INTESTINAL VIRUS OF INFANT MICE (LIVIM)

ETIOLOGY Unclassified virus

ANIMALS AFFECTED Mice

CLINICAL SIGNS High mortality; emaciation and death in animals usually before 10 days old. Some soiling may occur about the tail.

PATHOLOGY Gross: Small intestine greatly distended by gas and fluid; colon usually empty but may contain small amount of colorless watery to mucoid material

Microscopic: blunting of villi; epithelial multinucleate giant cells in intestine; intracytoplasmic inclusions

**Note*: Transmissible to man–a laboratory hazard.

DIAGNOSIS Pathologic findings

REFERENCES

1. Kraft, L. M. 1962. An apparently new lethal virus disease of infant mice. Science 137:282–283.

2. Kraft, L. M. 1966. Epizootic diarrhea of infant mice and lethal intestinal virus infection of infant mice, p. 55–61. *In* Viruses of laboratory rodents. Nat. Cancer Inst. Monograph 20. U.S. Government Printing Office, Washington, D.C.

LYMPHOCYTIC CHORIOMENINGITIS (LCM)*

ETIOLOGY RNA virus; 50 mμ

ANIMALS AFFECTED Mice

CLINICAL SIGNS Usually none. Characterized by immunologic tolerance and absence of symptoms; photophobia, conjunctivitis, spasticity and convulsions may be seen. Congenital or transplacental infections are most frequent and result in retarded growth and shortened life-spans.

PATHOLOGY Gross: Clear fluid in pleural cavity; enlarged spleen
Microscopic: Variable; lesions may include lymphocytic infiltration of meninges, necrosis of liver and lymphoid tissue; glomerulonephritis occurs in aged animals.

DIAGNOSIS Extremely difficult; pathologic findings; animal inoculation (intracerebral in LCM-free mice and by any route into guinea pigs); serology (immunofluorescence)

REFERENCES

1. Hotchin, J. 1965. Chronic disease following lymphocytic choriomeningitis inoculation and possible mechanisms of slow virus pathogenesis. *In* D. C. Gajdusek, C. J. Gibbs, Jr., and M. Alpers (ed.), Nat. Inst. Neurol. Dis. Blindness Monogr. 2. Slow, latent and temperate virus infections. U.S. Public Health Service Publication No. 1378. U.S. Government Printing Office, Washington, D.C.

2. Traub, E. 1936. An epidemic in a mouse colony due to the virus of acute lymphocytic choriomeningitis. J. Exp. Med. 63:533–546.

3. Wilsnack, R. E., and W. P. Rowe. 1964. Immunofluorescent studies of the histopathogenesis of lymphocytic choriomeningitis virus infection. J. Exp. Med. 120:829–841.

4. Oldstone, M. B. A., and F. J. Dixon. 1969. Pathogenesis of chronic disease associated with persistent lymphocytic choriomeningitis viral infection. I. Relationship of antibody production to disease in neonatally infected mice. J. Exp. Med. 129:483–505.

**Note*: Transmissible to man—a laboratory hazard.

MAMMARY CARCINOMA

ETIOLOGY Mammary tumor virus* (Bittner agent; MTV); RNA virus

ANIMALS AFFECTED Mice

CLINICAL SIGNS Mammary tumors in female (rarely male) animals. Tumors may be located anywhere from cervical to pelvic, and ventral or lateral surfaces of body.

PATHOLOGY Gross: Circumscribed, round to nodular gray-white masses in subcutaneous tissue. The tumors may become very large, ulcerated and hemorrhagic.

Microscopic: Adenocarcinomas (Types A,B,C), adenoacanthomas or carcinosarcomas

DIAGNOSIS Pathologic findings

REFERENCES

1. Bittner, J. J. 1948. Some enigmas associated with the genesis of mammary cancer in mice. Cancer Res. 8:625–639.

2. Dunn, T. B. 1959. Morphology of mammary tumors in mice. *In* F. Homburger (ed.), The physiopathology of cancer, 2nd ed. Hoeber-Harper, New York.

3. De Ome, K. B. 1962. The mouse mammary tumor virus. Fed. Proc. 21:15–18.

MINUTE VIRUS OF MICE (MVN) INFECTION†

ETIOLOGY Parvovirus; 26 mμ

ANIMALS AFFECTED Mice and rats

CLINICAL SIGNS Usually a latent infection; runting may occur in neonatal animals following experimental inoculation

PATHOLOGY Gross: None

Microscopic: In experimental infections, necrosis of the external germinal layer of the cerebellum reported in mice; necrosis of ependyma and choroid plexus may be seen in rats; intranuclear inclusions may be present in affected areas

**Note*: Virus is transmitted to offspring via mother's milk; it may be transmitted also to adults by contact, but this usually does not produce tumors. Mammary tumors also occur in Bittner virus-free mice and rats; the incidence may be quite high in certain strains but the relationship to the MTV agent is unclear. Hormonal factors are involved.

†*Note*: This is a highly prevalent inapparent infection in mouse colonies and also occurs as a contaminant of transplanted tumors.

DIAGNOSIS Animal inoculation (neonatal hamsters); serology (neutralization, hemagglutination inhibition)

REFERENCES

1. Crawford, L. V. 1966. A minute virus of mice. Virology 29:605–612.

2. Kilham, L., and G. Margolis. 1970. Pathogenicity of minute virus of mice (MVM) for rats, mice, and hamsters. Proc. Soc. Exp. Biol. Med. 133:1447–1551.

3. Parker, J. C., M. J. Collins, Jr., S. S. Cross, and W. P. Rowe. 1970. Minute virus of mice. II. Prevalence, epidemiology, and occurrence as a contaminant of transplanted tumors. J. Nat. Cancer Inst. 45:305–310.

MOUSE ENCEPHALOMYELITIS (Theiler's Disease; Mouse Polio)

ETIOLOGY Picornavirus (several strains); 25 mμ

ANIMALS AFFECTED Mice

CLINICAL SIGNS Usually none; this is an inapparent infection (virus present in intestine). About 1 in 1000 mature animals develop spontaneous flaccid paralysis, usually of the hind limbs. It is not always fatal, but may be once paralysis occurs.

PATHOLOGY Gross: None

Microscopic: Neuronal degeneration, perivascular cuffing and gliosis in brain stem and spinal cord, none in inapparent infections

DIAGNOSIS Clinical signs; pathologic findings; viral isolation; serology (hemagglutination inhibition)

REFERENCES

1. Andrewes, C. H., and H. G. Pereira. 1967. Viruses of vertebrates, 2nd ed. p. 34. Williams & Wilkins, Co., Baltimore, Maryland.

2. Theiler, M. 1937. Spontaneous encephalomyelitis of mice; A new virus disease. J. Exp. Med. 65:705–719.

MOUSE HEPATITIS*

ETIOLOGY Unclassified RNA virus; 70–90 mμ; several strains described

ANIMALS AFFECTED Mice

CLINICAL SIGNS Usually a latent infection; occasionally jaundice and neurologic signs including spasticity, incoordination, tremors, and death

**Note*: Simultaneous *Eperythrozoon coccoides* infection may enhance the severity of mouse hepatitis.

PATHOLOGY Gross: Usually none; pale to red spots in liver which may coalesce to large areas of mottling; enlarged spleen

Microscopic: Variable according to strain of virus; necrosis of liver parenchyma with minimal inflammation; lymphoid necrosis; neuronal degeneration, nonsuppurative encephalitis, and demyelination with neurotropic strains.

DIAGNOSIS Pathologic findings; serology (complement fixation with polyvalent antigen); mouse inoculation

REFERENCES

1. Gledhill, A. W., and C. H. Andrewes. 1951. A hepatitis virus of mice. Brit. J. Exp. Path. 32:559–568.

2. Nelson, J. B. 1957. Mouse hepatitis in relation to leukemia (abstr.). Bull. N.Y. Acad. Med. 2nd Ser. 33:811–813.

3. Piazza, M. 1969. Experimental viral hepatitis. Charles C Thomas, Springfield, Illinois.

MOUSE PAPULE DISEASE

ETIOLOGY Unclassified virus

ANIMALS AFFECTED Mice

CLINICAL SIGNS Papular lesions in the skin of any part of the body; especially noticeable in nursing animals having short or no hair

PATHOLOGY Gross: Raised papule anywhere on skin of body

Microscopic: Intracytoplasmic acidophilic inclusions in epidermis at various stages of infection; subcutis infiltrated with mononuclear cells

DIAGNOSIS Pathologic findings; agent does not cross react with ectromelia virus from which it must be differentiated.

REFERENCES

1. Kraft, L. M., and A. E. Moore. 1961. A papular skin lesion of mice caused by a transmissible agent. Zschr. Versuchstierk 1:66–73.

MOUSE PNEUMONITIS (Nigg Virus Infection)

ETIOLOGY "Nigg virus," a Miyagawanella agent

ANIMALS AFFECTED Mice

CLINICAL SIGNS None, a latent infection requiring activation by intranasal instillations. Respiratory distress then occurs in 24–48 hr, followed by death.

PATHOLOGY Gross: Pulmonary consolidation
Microscopic: Interstitial and bronchopneumonia. Etiologic agent can be seen in bronchial epithelium.
DIAGNOSIS Pathologic findings; elementary bodies stained by Macchiavello or Castaneda stains; Serology (complement fixation)
REFERENCES

1. Andrewes, C. H. 1964. Viruses of vertebrates, 1st ed. p. 375. Williams & Wilkins Co., Baltimore, Maryland.
2. Nigg, C., and M. D. Eaton. 1944. Isolation from normal mice of a pneumotropic virus which forms elementary bodies. J. Exp. Med. 79:497–510.
3. Gogolak, F. M. 1953. The histopathology of murine pneumonitis infection and the growth of the virus in the mouse lung. J. Infect. Dis. 92:254–272.

MOUSE THYMIC AGENT INFECTION

ETIOLOGY Unclassified virus; 75–100 mμ
ANIMALS AFFECTED Mice (newborns only)
CLINICAL SIGNS None
PATHOLOGY Gross: None
Microscopic: Focal necrosis of thymus in newborn mice
DIAGNOSIS Based on histopathologic findings and inoculation of newborn mice
REFERENCES

1. Rowe, W. P., and W. I. Capps. 1961. A new mouse virus causing necrosis of the thymus in newborn mice. J. Exp. Med. 113:831–844.

MURINE LEUKEMIA

ETIOLOGY RNA viruses; 90–100 mμ. There are several closely related strains causing different types of tumors. Some are thymic dependent and others spleen dependent. Strain susceptibility varies. Major identified viruses and associated tumors are listed:

Gross (passage A) virus	lymphocytic leukemia
Moloney virus	lymphocytic leukemia
Kaplan virus	lymphocytic leukemia
AKR virus	lymphocytic leukemia
Friend virus	erythrocytic leukemia
Rauscher virus	erythrocytic leukemia
Graffi virus	granulocytic leukemia

ANIMALS AFFECTED Mice; neonatal rats susceptible experimentally

CLINICAL SIGNS High incidence in certain strains, e.g., AK and C58; onset usually at 6–8 months of age. Symptoms include anemia weakness, labored breathing, swollen abdomen, swollen lumph nodes, and death.

PATHOLOGY Gross: Enlarged thymus, liver, spleen, and lymph nodes

Microscopic: Tumor cell infiltrates in various tissues

DIAGNOSIS Pathologic findings; latent infection* detected by COMuL and XC tests

REFERENCES

1. Dunn, T. B. 1954. Normal and pathologic anatomy of the reticular tissue in laboratory mice with a classification and discussion of neoplasms. J. Nat. Cancer Inst. 14:1281–1433.

2. Rich, M. A. (ed.). 1968. Experimental leukemia. Appleton-Century-Crofts, New York.

3. Rich, M. A. (ed.). 1966. Conference on murine leukemia. Nat. Cancer Inst. Monograph 22. U.S. Government Printing Office, Washington, D.C.

4. Hartley, J. W., W. P. Rowe, W. I. Capps, and R. J. Huebner. 1969. Isolation of naturally occurring viruses of the murine leukemia virus group in tissue culture. J. Virol. 3:126–132.

5. Klement, V., W. P. Rowe, J. W. Hartley, and W. E. Pugh. 1969. Mixed culture cytopathogenicity: A new test for growth of murine leukemia viruses in tissue culture. Proc. Nat. Acad. Sci. 63:753–758.

Mycoplasma neurolyticum INFECTION†

ETIOLOGY *Mycoplasma neurolyticum*

ANIMALS AFFECTED Mice

CLINICAL SIGNS Usually inapparent; occasionally encrustation of eyelids

PATHOLOGY Gross: Eyelids may be swollen and coated with a sticky exudate

Microscopic: Conjunctivitis

DIAGNOSIS Isolation of organism

**Note*: Latent infections occur in *all strains* examined to date including "germfree" mice; infections may be activated by radiation, certain chemicals, hormones, and so on.

†*Note*: Experimental infection causes "rolling disease" due to exotoxin produced by this mycoplasma.

REFERENCES

1. Nelson, J. B. 1950. Association of a special strain of pleuropneumonia-like organisms with conjunctivitis in a mouse colony. J. Exp. Med. 91:309–320.

2. Tully, J. G., and I. Ruchman. 1964. Recovery, identification, and neurotoxicity of Sabin's type A and C mouse mycoplasma (PPLO) from lyophilized cultures. Proc. Soc. Exp. Biol. Med. 115:554–558.

MYCOPLASMAL POLYARTHRITIS*

ETIOLOGY *Mycoplasma arthritidis*

ANIMALS AFFECTED Mice and rats

CLINICAL SIGNS Usually inapparent; migratory swelling of joints and toes may occur.

PATHOLOGY Gross: Swelling of joints and toes with eventual ankylosis

Microscopic: Early leukocytic infiltration; later fibrous proliferation, necrosis of cartilage

DIAGNOSIS Pathologic findings; isolation of organism

REFERENCES

1. Barden, J. A., and J. G. Tully. 1969. Experimental arthritis in mice with *Mycoplasma pulmonis*. J. Bacteriol. 100:5–10.

2. Findlay, G. M., R. D. Mackenzie, F. O. MacCallum, and E. Klieneberger. 1939. The aetiology of polyarthritis in the rat. Lancet 237:7–10.

3. Sabin, A. B. 1939. Experimental proliferative arthritis in mice produced by filterable, pleuropneumonia-like microorganisms. Science 89:228–229.

NOSEMATOSIS† (Encephalitozoonosis)

ETIOLOGY *Nosema cuniculi* (*Encephalitozoon cuniculi, Nosema muris*); protozoan, a microsporidian

ANIMALS AFFECTED Mice and rats

CLINICAL SIGNS None; inapparent infection

PATHOLOGY Gross: None

Microscopic: Nonsuppurative meningoencephalitis with glial nodules

DIAGNOSIS Pathologic findings; identification of organisms individually or in groups in brain tissue, particularly in glial nodules;

*Note: Some strains of *Mycoplasma pulmonis* reported to cause polyarthritis following intravenous inoculation.

†*Note*: Must be differentiated from *Toxoplasma* in tissue sections.

organisms selectively stain with methenamine silver, carbol-fuchsin, and gram (positive); animal inoculation

REFERENCES

1. Innes, J. R. M., W. Zeman, J. K. Frenkel, and G. Borner. 1962. Occult endemic encephalitozoonosis of the central nervous system of mice (Swiss-Bagg-O'Grady strain). J. Neuropath. Exp. Neurol. 21:519–533.

2. Nelson, J. B. 1967. Experimental transmission of a murine microsporidian in Swiss mice. J. Bacteriol. 94:1340–1345.

3. Perrin, T. L. 1943. Spontaneous and experimental encephalitozoon infection of laboratory animals. Arch. Pathol. 36:559–567.

4. Petri, M. 1969. Studies on *Nosema cuniculi* found in transplantable ascites tumors with a survey of microsporidiosis in mammals. Acta Pathol. Microbiol. Scand. Suppl. 204:1–91.

PASTEURELLOSIS*

ETIOLOGY *Pasteurella pneumotropica*; small gram-negative bacillus. (*P. pseudotuberculosis* and *P. multocida* are questionable pathogens in mice and rats.)

ANIMALS AFFECTED Mice and rats

CLINICAL SIGNS Usually inapparent; has been associated with signs of pneumonia, conjunctivitis, metritis, cystitis, and dermatitis

PATHOLOGY Gross: Variable; lung consolidation and fibrinous pleuritis

Microscopic: Fibrinopurulent bronchopneumonia and pleuritis; perhaps metritis, cystitis, conjunctivitis

DIAGNOSIS Isolation of organism

REFERENCES

1. Brennan, P. C., T. E. Fritz, and R. J. Flynn. 1969. Murine pneumonia: A review of the etiologic agents. Lab. Anim. Care 19:360–371.

PNEUMOCOCCAL INFECTION

ETIOLOGY *Diplococcus pneumoniae*† (gram-positive diplococcus)

ANIMALS AFFECTED Rats

**Note*: This is considered a widespread inapparent infection. Pathogenecity is enhanced by factors which reduce host defense mechanisms; the role of *P. pneumotropica* as a primary pathogen is uncertain.

†*Note*: Common indigenous pathogen in conventional stocks of rats.

CLINICAL SIGNS Inapparent infection common; snuffling, nasal exudate, labored breathing, weight loss or sudden onset, and death; variable mortality

PATHOLOGY Gross: variable; may include consolidation of lungs; fibrinous pleuritis, pericarditis, peritonitis, meningitis; also, splenic infarcts

Microscopic: Purulent bronchopneumonia; fibrinopurulent pleuritis, pericarditis, peritonitis; meningitis; splenic infarcts

DIAGNOSIS Isolation of organism

REFERENCES

1. Baer, H. 1967. Diplococcus pneumonia type 16 in laboratory rats. Canad. J. Comp. Med. Vet. Sci. 31:216–218.

2. Ford, T. 1965. An outbreak of pneumonia in laboratory rats associated with *Diplococcus pneumoniae*, type 8. Lab. Anim. Care 15:448–451.

3. Weisbroth, S. H., and E. H. Freimer. 1969. Laboratory rats from commercial breeders as carriers of pathogenic pneumococci. Lab. Anim. Care. 19:473–478.

PNEUMOCYSTOSIS*

ETIOLOGY *Pneumocystis carinii*; uncertain whether protozoan or fungus

ANIMALS AFFECTED Rats

CLINICAL SIGNS Usually an inapparent infection. Activation may result from debility or immunosuppression and respiratory signs may be noted.

PATHOLOGY Gross: Redness and consolidation of lungs. Cut surface may appear gelatinous.

Microscopic: Alveoli contain foamy material and causative organisms. Organisms appear as nests of ring forms approximately 1.0 mμ diameter containing minute nuclei 0.2–0.5 μ diameter. Outer rims stain with methenamine silver, the nuclei with Giemsa. Inflammatory cells are minimal, although an interstitial plasma cell infiltrate may be present.

DIAGNOSIS Pathologic findings, including identification of organisms in Giemsa stained touch preparations of lungs. Inapparent infection may be activated by prolonged administration of corticosteroids.

**Note*: A common inapparent infection in rats. May be transmissible to man.

REFERENCES

1. Barton, E. G., and W. G. Campbell, Jr. 1969. *Pneumocystis carinii* in lungs of rats treated with cortisone acetate. Ultrastructural observations relating to the life cycle. Amer. J. Path. 54:209–236.

2. Frenkel, J. K., J. T. Good, and J. A. Schultz. 1966. Latent pneumocystis infection of rats, relapse and chemotherapy. Lab. Invest. 15:1559–1577.

3. Vavra, J., and K. Kučera. 1970. *Pneumocystis carinii* Delanoë, its ultrastructure and ultrastructural affinities. J. Protozool. 17:463–483.

PNEUMONIA VIRUS OF MICE (PVM) INFECTION*

ETIOLOGY Unclassified RNA virus; 80–120 mμ

ANIMALS AFFECTED Mice and rats

CLINICAL SIGNS Usually latent; serial passage activates infection and produces labored respiration; variable death rate

PATHOLOGY Gross: Partial or complete consolidation of lungs which are dark red or plum colored

Microscopic: Patchy interstitial pneumonia with mononuclear infiltration and bronchitis; pulmonary edema

DIAGNOSIS Animal inoculation (nasal instillation using PVM-free animals); serology (hemagglutination inhibition and serum neutralization)

REFERENCES

1. Harter, D., P. Choppin, and R. W. Compans. 1967. Studies on pneumonia virus of mice. II. Structure and morphogenesis of the virus particle. J. Exp. Med. 126:267–274.

2. Horsfall, F. L., Jr., and R. G. Hahn. 1940. A latent virus in normal mice capable of producing pneumonia in its natural host. J. Exp. Med. 71:391–408.

POLYOMA VIRUS INFECTION

ETIOLOGY Papovavirus; 45 mμ

ANIMALS AFFECTED Mice

CLINICAL SIGNS Usually inapparent; natural or experimental infection of neonatal mice causes stunted growth and tumor development after 1–6 months

PATHOLOGY Gross: Usually none. Neonatal infections cause tumors in various sites, particularly parotid salivary gland

**Note*: This is a widespread inapparent infection.

Microscopic: Variable. Tumors are most often pleomorphic sarcomas

DIAGNOSIS Serology (hemagglutination inhibition; serum neutralization)

REFERENCES

1. Eddy, B. 1960. The polyoma virus. Adv. Virus Res. 7:91–102.

PSEUDOMONAS INFECTION

ETIOLOGY *Pseudomonas* (*Pyocyaneus*) *aeruginosa*; small gram-negative bacillus

ANIMALS AFFECTED Mice and rats

CLINICAL SIGNS Usually an inapparent infection* which may be activated by irradiation, stress, and immunosuppression. Signs include lethargy, sudden death, and occasionally incoordination, head tilt, or circling.

PATHOLOGY Gross: No consistent or specific lesions. Suppurative otitis media may occur in some outbreaks

Microscopic: Not specific

DIAGNOSIS Isolation of organism from blood or tissues

REFERENCES

1. Flynn, R. J. (ed.). 1963. Conference on *Pseudomonas aeruginosa* infection and its effects on biological and medical research. Lab. Anim. Care 13(1) part 2:1–69.

2. Hightower, D. 1966. *Pseudomonas aeruginosa* infection in rats used in radiobiology research. Lab. Anim. Care 16:96–104.

RAT VIRUS INFECTION (Kilham Rat Virus; Hemorrhagic Encephalopathy)

ETIOLOGY Parvovirus; 20 mμ

ANIMALS AFFECTED Rats

CLINICAL SIGNS A latent infection; runting and sometimes paralysis of nursling rats, with possible death following experimental inoculation

PATHOLOGY Gross: Stunted growth and dental deformities; hemorrhagic lesions in brain and spinal cord

**Note*: Often an inapparent infection in mouse colonies and may be activated by experimental or husbandry procedures which reduce host resistance.

Microscopic: Intranuclear inclusion bodies in reticuloendothelial cells reported; hemorrhagic necrosis in brain and spinal cord

DIAGNOSIS Animal inoculation (newborn rats, nursling hamsters) produces cerebellar hypoplasia, "mongolism," and dental deformities. Serology (hemagglutination)

REFERENCES

1. Kilham, L. 1961. Mongolism associated with rat virus (RV) infection in hamsters. Virology 13:141–143.

2. Kilham, L. 1966. Viruses of laboratory and wild rats, p. 117–140. *In* Viruses of laboratory rodents. Nat. Cancer Inst. Monograph 20. U.S. Government Printing Office, Washington, D.C.

3. Toolan, H. W. 1960. Experimental production of mongoloid hamsters. Science 131:1446–1448.

4. El Dadah, A. H., N. Nathanson, K. O. Smith, R. A. Squire, G. W. Santos, and E. C. Melby. 1967. Viral hemorrhagic encephalopathy of rats. Science 156:392–394.

REOVIRUS INFECTION (Hepatoencephalomyelitis)

ETIOLOGY Reovirus type 3; 70 mμ

ANIMALS AFFECTED Mice

CLINICAL SIGNS Usually latent in weaned mice. Newborn mice show oily appearance of skin, yellowish fatty feces, jaundice, stunting, incoordination, tremors, paralysis, conjunctivitis, loss of hair, sporadic deaths

PATHOLOGY Gross: White or yellow spots in liver, pancreas, and heart muscle

Microscopic: Focal or widespread necrosis of liver with cellular infiltration; parenchymal necrosis of pancreas; necrosis of heart muscle; malacia and neuronal degeneration; nonsuppurative encephalitis

DIAGNOSIS Pathologic findings; serology (hemagglutination inhibition and indirect immunofluorescence)

REFERENCES

1. Stanley, N. F., D. C. Dorman, and J. Ponsford. 1954. Studies on the hepato-encephalomyelitis virus (HEV). Aust. J. Exp. Biol. Med. 32:543–561.

2. Stanley, N. F., P. J. Leak, M. N. Walter, and R. A. Joske. 1964. Murine infection with reovirus. II. The chronic disease following reovirus type 3 infection. Brit. J. Exp. Med. 45:142–149.

RINGWORM (Favus)

ETIOLOGY *Trichophyton* spp., *Miscrosporum* spp., as well as other dermatophytic fungi

ANIMALS AFFECTED Mice and rats

CLINICAL SIGNS Bald spots with or without scaliness anywhere on the body; inapparent infections may occur

PATHOLOGY Gross: Focal hair loss

Microscopic: Organisms present in hair follicles and hair shafts; hyperkeratosis

DIAGNOSIS Skin scrapings for microscopy of hair root sheaths; culture on suitable medium; some lesions fluoresce under Wood's light

REFERENCES

1. Davies, R. R., and J. Shewell. 1965. Ringworm carriage and its control in mice. J. Hyg. (Camb.) 63:507–515.

2. Povar, M. 1965. Ringworm infection in a colony of albino Norway rats. Lab. Anim. Care 15:264–265.

3. Snell, G. D. (ed.). The biology of the laboratory mouse, 2nd ed. Dover Publications, New York.

SALIVARY GLAND VIRUS INFECTION (Cytomegalovirus Infection)

ETIOLOGY Herpes virus; 120–180 mμ

ANIMALS AFFECTED Mice and rats, each with a host-specific virus

CLINICAL SIGNS None, a latent infection. Experimental transmission to young mice may cause generalized infection and death

PATHOLOGY Gross: None

Microscopic: Intranuclear inclusions in salivary gland duct epithelium

DIAGNOSIS Pathologic findings

REFERENCES

1. Andrewes, C. H., and H. G. Pereiera. 1967. Viruses of vertebrates. 2nd ed., p. 311. Williams & Wilkins Co., Baltimore, Maryland.

SALMONELLOSIS*

ETIOLOGY Most *Salmonella* species can cause disease, especially *S. typhimurium* or *S. enteriditis*; aerobic, non-lactose-fermenting, gram-negative bacilli

ANIMALS AFFECTED Mice and rats

CLINICAL SIGNS Adult carriers often asymptomatic; acute infections may cause diarrhea, anorexia, cachexia and sudden death. Poor growth, weight loss, and diarrhea occur in chronic infection

PATHOLOGY Gross: Enlarged spleen; pale spots on liver

Microscopic: Focal necrosis of liver and spleen with accumulations of macrophages and lymphocytes; thrombosis of portal veins; enteritis; mesenteric lymphadenitis

DIAGNOSIS Pathologic findings; bacterial culture of liver, spleen and feces on differential media; serologic confirmation with group specific antisera

REFERENCES

1. Habermann, R. T., and F. P. Williams, Jr. 1958. Salmonellosis in laboratory animals. J. Nat. Cancer Inst. 20:933–947.

2. Hoag, W. G., and H. Meir. 1966. Infectious diseases, 589–600. *In* E. L. Green (ed.), Biology of the laboratory mouse. The Blakiston Division, McGraw-Hill, New York.

SENDAI VIRUS INFECTION

ETIOLOGY Myxovirus, parainfluenza type I; RNA, 130–250 mμ

ANIMALS AFFECTED Mice and rats

CLINICAL SIGNS Usually none; a latent infection which may be activated by intranasal instillations; labored respiration, chattering, and variable mortality

PATHOLOGY Gross: Partial or complete consolidation of lungs with red color

Microscopic: Interstitial pneumonia reported

DIAGNOSIS Serology (hemagglutination inhibition)

REFERENCES

1. Grunert, R. R. 1967. Isolation of Sendai virus as a latent respiratory virus of mice. Lab. Anim. Care 17:164–171.

2. Parker, J. C., and R. K. Reynolds. 1968. Natural history of Sendai virus infection in mice. Amer. J. Epidemiol. 88:112–125.

**Note*: Transmissible to man.

3. Tennant, R. W., J. C. Parker, and T. G. Ward. 1966. Respiratory virus infections of mice, p. 93–104. *In* Viruses of laboratory animals. Nat. Cancer Inst. Monograph 20. U.S. Government Printing Office, Washington, D.C.

SIALODACRYOADENITIS* (Salivary and Harderian Gland Infection)

ETIOLOGY Unclassified virus

ANIMALS AFFECTED Rats

CLINICAL SIGNS May be inapparent. Neck may be swollen and appear shortened; eyes may be bulging and red

PATHOLOGY Gross: Enlarged submaxillary salivary glands; exophthalmos

Microscopic: Necrosis of ductular epithelium and inflammation of submaxillary and parotid salivary glands. Harderian glands undergo severe necrosis of tubuloalveolar epithelium followed by squamous metaplasia and inflammation

DIAGNOSIS Pathologic findings; animal inoculation (susceptible rats) (must exclude cytomegalovirus infection)

REFERENCES

1. Innes, J. R. M., and M. F. Stanton. 1961. Acute disease of the submaxillary and Harderian glands (sialo-dacryoadenitis) of rats with cytomegaly and no inclusion bodies. Amer. J. Path. 38:455–468.

2. Jonas, A. M., J. Craft, L. Black, P. N. Bhatt, and D. Hilding. 1969. Sialodacryoadenitis in the rat. A light and electron microscopic study. Arch. Path. 88:613–622.

Streptobacillus moniformis INFECTION†

ETIOLOGY *Streptobacillus moniliformis*; gram-negative, highly pleomorphic bacillus

ANIMALS AFFECTED Mice and rats

CLINICAL SIGNS Usually latent in rats; mice show swelling of joints, toes and tails, and watering of eyes. Joint stiffness may follow recovery

PATHOLOGY Gross: Swelling of joints; enlarged liver and spleen

*Note: Apparently present in many conventional rat stocks and even in some "germfree" lines.

†*Note*: Transmissible to man (Rat-bite fever, Haverhill fever).

Microscopic: Suppurative arthritis followed by fibrous ankylosis; focal necrosis of liver and spleen; sometimes pericarditis

DIAGNOSIS Pathologic findings and isolation of organism

REFERENCES

1. Brown, T. McP., and J. C. Nunemaker. 1942. Rat-bite fever. Bull. Johns Hopk. Hosp. 70:201–328.

2. Von Rooyen, C. R. 1936. The biology, pathogenesis and classification of *Streptobacillus moniliformis*. J. Path. Bacteriol. 43:455–472.

STREPTOCOCCAL INFECTIONS

ETIOLOGY Group A*, type 50 streptococcus or type D enterococcus; gram-positive coccii

ANIMALS AFFECTED Mice

CLINICAL SIGNS Enlargement of cervical lymph nodes; labored breathing; mortality reaching 50% over 3 months (group A, type 50 streptococci); diarrhea, melena, nonspecific signs of illness and death in 48 hr from onset (type D enterococci)

PATHOLOGY Gross: Consolidation of lungs; abscesses in cervical nodes, fibrinous exudate on pleura, pericardium, and perhaps peritoneum with Group A infection; irregular white foci throughout liver and discrete red spots in wall of intestine with type D infection

Microscopic: Fibrinopurulent pneumonia, pleuritis, pericarditis, peritonitis, and cervical lymphadenitis (Group A); focal necrosis of liver and focal enteritis (type D)

DIAGNOSIS Isolation of organisms

REFERENCES

1. Gledhill, A. W., and R. J. W. Rees. 1952. A spontaneous enterococcal disease of mice and its enhancement by cortisone. Brit. J. Exp. Path. 32:183–189.

2. Hook, E. W., R. R. Wagner, and R. C. Lancefield. 1960. An epizootic of Swiss mice caused by a group A streptococcus, newly designated type 50. Amer. J. Hyg. 72:111–119.

3. Nelson, J. B. 1954. Association of group A streptococci with an outbreak of cervical lymphadenitis in mice. Proc. Soc. Exp. Biol. Med. 86:542–545.

**Note*: Stocks infected with group A streptococci may carry organisms in throats for prolonged periods without clinical signs.

TYZZER'S DISEASE

ETIOLOGY *Bacillus piliformis*; long, slender, gram-negative bacillus
ANIMALS AFFECTED Mice and rats
CLINICAL SIGNS May be inapparent; sudden death may occur, especially in young mice; diarrhea may be seen
PATHOLOGY Gross: Multiple gray-white spots throughout liver
Microscopic: Focal necrosis of liver; enteritis
DIAGNOSIS Histologic demonstration of organisms in liver sections; organism not cultured by conventional methods
REFERENCES

1. Fujiwara, K., Y. Takaki, M. Naiki, K. Maejima, and Y.Tajima. 1964. Tyzzer's disease in mice. Jap. J. Exp. Med. 34:59–75.
2. Hoag, W. G., and H. Meir. 1966. Infectious diseases. 589–600. *In* E. L. Green (ed.), Biology of the laboratory mouse. The Blakiston Division, McGraw-Hill, New York.
3. Saunders, L. Z. Tyzzer's disease. 1958. J. Nat. Cancer Inst. 20:893–897.
4. Stedham, M. A., and T. J. Bucci. 1970. Spontaneous Tyzzer's disease in a rat. Lab. Anim. Care 20(4):743–746.

WILD RAT PNEUMONIA

ETIOLOGY Equivocal, regarded as a virus but noncultivable mycoplasma-like bodies have been described in lungs
ANIMALS AFFECTED Wild and laboratory rats
CLINICAL SIGNS Usually latent but activation by nasal instillation in mice results in illness with labored respiration and sporadic deaths
PATHOLOGY Gross: Firm pink areas in lungs; fluid in trachea and bronchi
Microscopic: Interstitial pneumonia and pulmonary edema
DIAGNOSIS Pathology and animal inoculation (intranasal in mice)
REFERENCES

1. Gay, F. W. 1967. Fine structure and location of the mycoplasma-like gray lung and rat pneumonia agents in infected mouse lung. J. Bacteriol. 94:2048–2061.
2. Nelson, J. B. 1949. Observation on a pneumotropic virus obtained from wild rats. J. Infect. Dis. 84:21–31.

ECTOPARASITES

Acariasis (Mite Infestation)

ETIOLOGY *Radfordia ensifera* (rat mite)
ANIMALS AFFECTED Rats only
CLINICAL AND PATHOLOGIC SIGNS Scratching around head, nose, and neck: small, dry scabs on head, ears, and upper neck

ETIOLOGY *Psorergates simplex* (mouse mite)
ANIMALS AFFECTED Mice only
CLINICAL AND PATHOLOGIC SIGNS White nodules visible on inner surface of skin, anywhere on body, but primarily face and forehead

Microscopic: Invaginations of skin filled with mites and debris; epidermal lining intact; no inflammatory cells at first; later a cyst lined with connective tissue and with numerous inflammatory cells

ETIOLOGY *Bdellonyssus bacoti* (tropical rat mite)
ANIMALS AFFECTED Rats only
CLINICAL AND PATHOLOGIC SIGNS Poor general condition; rough hair coat; scabby skin

ETIOLOGY *Myocoptes musculinus*; *Myocoptes romboustí* (mouse mites)
ANIMALS AFFECTED Mice only
CLINICAL AND PATHOLOGIC SIGNS Loss of hair and reddened skin primarily on abdomen and thorax; peculiar irregular brown ring around neck; usually affects lactating females and unweaned mice; spontaneous loss of lesions after weaning

ETIOLOGY *Myobia musculi; Radfordia affinis* (mouse mites)
ANIMALS AFFECTED Mice only
CLINICAL AND PATHOLOGIC SIGNS Loss of hair; scab formation; lesions usually confined to head, neck, and shoulders; usually seen only in breeding males, 5 months of age or older

ETIOLOGY *Notoedres muris* (rat mange mite)
ANIMALS AFFECTED Rats only
CLINICAL AND PATHOLOGIC SIGNS Red vesicles or papules and wartlike projections on ears, nose, tail, feet, external genitalia

DIAGNOSIS OF ACARIASIS Examine skin scrapings for mites, use 5% KOH. Place dead animal on black paper; mites will crawl off as body cools.

Pediculosis (Louse Infestation)

ETIOLOGY *Polyplax spinulosa* (rat louse)
ANIMALS AFFECTED Rats only
CLINICAL SIGNS Loss of hair; pruritis

ETIOLOGY *Polyplax serrata* (mouse louse)
ANIMALS AFFECTED Mice only
CLINICAL SIGNS Loss of hair; pruritis

DIAGNOSIS OF PEDICULOSIS Examine hair and skin for the organisms

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HELMINTH INFECTIONS

Nematodes (Roundworms)

ETIOLOGY *Heterakis spumosa*
ANIMALS AFFECTED Mice and rats
PARASITE LOCATION Colon and cecum
PATHOLOGY None

ETIOLOGY *Aspiculuris tetraptera*
ANIMALS AFFECTED Mice and rats
PARASITE LOCATION Colon and cecum
PATHOLOGY None

ETIOLOGY *Syphacia obvelata*
ANIMALS AFFECTED Mice and rats
PARASITE LOCATION Colon and cecum
PATHOLOGY Occasional impaction by worms, intestinal intussusception, possible rectal prolapse

ETIOLOGY *Trichinella spiralis*
ANIMALS AFFECTED Rats
PARASITE LOCATION Adults in duodenum; larvae in muscle
PATHOLOGY Muscle degeneration, fibrosis, and cyst formation

ETIOLOGY *Capillaria hepatica*
ANIMALS AFFECTED Mice and rats
PARASITE LOCATION Liver
PATHOLOGY Yellow streaks and patches in liver due to eggs. Microscopically, there is focal inflammation around eggs

ETIOLOGY *Trichosomoides crassicauda*
ANIMALS AFFECTED Rats
PARASITE LOCATION Bladder, ureters, and renal pelvis (males live within uterus of female worm)
PATHOLOGY Focal granulomas in lungs due to larvae

ETIOLOGY *Nippostrongylus muris*
ANIMALS AFFECTED Mice and rats
PARASITE LOCATION Small intestine
PATHOLOGY Unthriftiness, diarrhea, pulmonary hemorrhage, and possible pneumonia due to larval migration

ETIOLOGY *Angiostrongylus cantonensis*
ANIMALS AFFECTED Rats
PARASITE LOCATION Adults in pulmonary arteries; larvae in brain and pulmonary arteries
PATHOLOGY None in rats

ETIOLOGY *Gongylonema neoplasticum*
ANIMALS AFFECTED Mice and rats

PARASITE LOCATION Tongue, esophagus, stomach
PATHOLOGY None

Acanthocephala

ETIOLOGY *Moniliformis moniliformis*
ANIMALS AFFECTED Mice and rats
PARASITE LOCATION Small intestine
PATHOLOGY Enteritis, ulceration, occasionally penetration, and peritonitis

Cestodes (Tapeworms)

ETIOLOGY *Hymenolepis diminuta*
ANIMALS AFFECTED Mice and rats
PARASITE LOCATION Ileum
PATHOLOGY None

ETIOLOGY *Hymenolepis nana**
ANIMALS AFFECTED Mice and rats
PARASITE LOCATION Small intestine
PATHOLOGY None

ETIOLOGY *Oochoristica ratti*
ANIMALS AFFECTED Mice and rats
PARASITE LOCATION Small intestine
PATHOLOGY None

ETIOLOGY *Cysticercus fasciolaris*
ANIMALS AFFECTED Mice and rats
PARASITE LOCATION Adult (*Taenia taeniaformis*) in small intestine of cats; bladder worm (cysticercus) in liver of rats and mice
PATHOLOGY White cysts in liver

ETIOLOGY *Coenurus serialis*
ANIMALS AFFECTED Mice
PARASITE LOCATION Adult (*Taenia serialis*) in intestine of dogs

**Note*: Transmissable to man–a laboratory hazard.

and foxes; bladder worm (coenurus) in intermuscular connective tissue of mice

PATHOLOGY Ovoid cysts 4 cm long in connective tissue

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APPENDIX

Chronic Murine Pneumonia

This is apparently not a specific disease entity, but rather a disease complex characterized by varying degrees of chronic inflammation of the upper and lower respiratory tracts in mice and rats. There probably are several etiologies including one or more of the following: viruses, mycoplasma, streptococci, pneumococci, *Corynebacterium kutscheri, Pasteurella pneumotropica,* and *Bordetella bronchiseptica.* The reader should refer to specific etiologic agents and to the disease entities *Enzootic Bronchiectasis* (p. 10) and *Infectious Catarrh* (p. 12) in this section.

Staphylococcal Infection

Staphylococcus aureus, a gram-positive coccus, is pathogenic for many species under appropriate circumstances. It is often associated with suppurative lesions of the skin, but may be a contaminant of any debilitated tissue. Bacteremia may also occur. Diagnosis must be confirmed by bacterial isolation.

Systemic Mycosis

Mice and rats are variably susceptible to experimental infection with several fungi including *Histoplasma capsulatum, Coccidioides immitis, Cryptococcus neoformans, Candida albicans, Sporotrichum schenckii,* and *Aspergillus fumigatus.* Naturally occurring diseases due to these agents have rarely been reported or, in several cases, followed the administration of corticosteroids.

Toxoplasmosis

Toxoplasma gondii is an ubiquitous protozoan parasite which readily produces disease in mice and rats following experimental inoculation. The disease occurs in wild mice, although its natural occurrence in laboratory mice or rats is not well documented. The pathologic changes produced are widespread and consist of nonsuppurative encephalitis with malacia, interstitial pneumonia, and focal necrosis in many organs. Toxoplasma cysts and organisms may be identified in tissue sections. Diagnosis may also require serologic procedures (Sabin-Feldman dye test, complement fixation, passive hemagglutination).

Citrobacter freundii Infection

This gram-negative bacillus has been reported to be associated with diarrhea and enterocolitis in mouse colonies. The prevalence is uncertain. Diagnosis depends upon bacterial isolation.

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III OUTLINE OF METHODS FOR DISEASE PREVENTION AND CONTROL

There are many useful practices for preventing or controlling infectious diseases in mice and rats. In general, they are best applied according to the peculiar needs of each animal facility and research project. Ideally, such programs should be developed in consultation with a veterinary specialist in laboratory animal medicine. However, such standard practices as those outlined below usually can be applied with great benefit.

A. *Procurement of Animals*

1. Select suppliers who maintain strict animal health programs that include monitoring for infectious agents by serologic and other screening procedures. One may initially order a few animals of varying ages and subject these to diagnostic procedures in order to determine the health status of production colonies.

2. When possible, it is recommended that stocks be used that are known to be free of infectious diseases by virtue of having been derived by cesarean techniques and maintained in strict isolation or by exhaustive testing for evidence of infectious diseases. It may be worthwile to ask the supplier to protect the air vents of shipping containers with bacterial filter media to reduce danger of contamination en route.

B. *Examination of Newly Purchased Animals*

1. Isolate and quarantine new arrivals, observing them closely for clinical signs of illness.

2. Sacrifice a few random animals, or those showing clinical signs of illness, and perform pathologic and microbiologic examinations as indicated before introducing them to an established animal colony. Similar precautions should be observed before placing new animals on experiment.

3. Notify supplier within a reasonable time after arrival if any animals show signs of disease; do not accept such animals.

C. *Maintenance of Disease-Free Stocks*

1. Care of laboratory mice and rats should be in accordance with established standards. These standards may be obtained by requesting the following documents from the *Institute of Laboratory Animal Resources, National Research Council, 2101 Constitution Avenue, N.W., Washington, D.C. 20418*:

"Guide for Laboratory Animal Facilities and Care"
"Standards for the Breeding, Care, and Management of Laboratory Mice"
"Standards for the Breeding, Care, and Management of Laboratory Rats"

2. If possible, use a physical barrier system at entrances to animal rooms, and maintain positive air pressure within rooms. Attendants and investigators should wash their hands and cover their street clothes with gowns before entering. Avoid all unnecessary visits into the animal rooms.

3. Limit each animal room to one animal species.

4. As an added precaution against infectious diseases, use filter tops on rodent cages to prevent aerosol transmission of agents. If possible, transfer cages to exhaust hood before removing tops for cleaning, feeding, etc.

5. Use automatic washing to sanitize cages and other equipment.

6. Observe animals daily for clinical signs of illness or ectoparasites. Remove and isolate or kill affected animals.

7. Perform pathologic and microbiologic examinations on any animals that die or are killed.

8. Perform routine bacteriologic and parasitologic screening examinations of fecal samples, and serologic surveys for virus infections.

9. In some instances, such as radiation research, it will be found helpful to acidify animals' drinking water to pH 2.5 for control of *Pseudomonas* spp. in mice.

D. *Care of Colonies Found to be Diseased*

1. Remove sick animals immediately.
2. Insure that diseased colonies are isolated from disease-free stocks.
3. Use filter top caging system to prevent aerosol transmission within the affected colony.
4. Do not add or remove animals from the colony until investigation is complete.
5. Consider cesarean derivation and establishment of disease-free stock. By this procedure it appears that most agents can be eliminated, with exception of the causal agents of lymphocytic choriomeningitis and sialodacryoadenitis, the leukemia viruses, and rat virus.
6. In some instances it is best to eliminate the entire colony.
7. Specific antimicrobial therapy is not generally recommended since it usually only reduces the severity of the problem and does not eliminate the infection from the colony. However, in some cases, in order to salvage an experiment, it may be necessary to treat individual animals or the entire colony. Such procedures should be supervised by a veterinarian experienced in laboratory animal medicine.

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