PATHOLOGY of Important Diseases of Rats, Mice and Guinea Pigs

Infectious Diseases of Rat, Mice, Guinea Pigs & Hamsters						
S. No.	**Disease**	**Etiology**	**Host**	**Important manifestations in Animal / Age**	**Important manifestations in Tissue / Organ**	**Remarks**
VIRAL Diseases						
1.	Mouse Pox / Ectromelia	Orthopox virus (mouse **pox** virus)	Mice	Mice	Skin rashes; 'Marchai body' in epithelial cells of skin & mm ; necrosis of lymphoid tissue, Liver and Intestinal hemorrhage	
2.	Murine Hepatitis Virus (MHV) Infection	Murine Hepatitis Virus (Mouse **Corona** virus)	Mice	Young Mice > Suckling Mice	' Syncytium formation'; with or without necrosis in Liver /Intestine ; Hepatic necrosis, jaundice etc (Liver); Neurotropic variants induce flaccid paralysis of the hindlimbs, Conjunctivitis, convulsions, and circling	
3.	Minute Virus of Mice (MVM) Infection	Minute Virus of Mice (MVM) (**Mouse Parvovirus)**	Mice, Hamsters	Neonatal Hamsters	Teratogenic effects; Mongoloid deformities: Cerebellar lesions like Cerebellar Hypoplasia	
4.	Mouse Encephalomyelitis Virus (MEV) Infection	Mouse Encephalomyelitis Virus (MEV), (enterovirus- **Picorna virus**)	Mice	Young Mice	poliomyelitis-like demyelinating disease; flaccid paralysis of the rear legs, while the tail remains mobile	
5.	Sendai Viral Pneumonia	*Sendai virus* (paramyxovirus)	Mice, Rat, G. pig & Hamsters	Suckling Mice; Young adults	Lungs / Pleuritis	
BACTERIAL Diseases						
6.	Tyzzer's Disease	*Clostridium piliforme / Bacillus piliformis*	Rat, Mice, Guinea Pigs, Hamsters	Rats	circular grey-white foci on Liver; Megalo-Ileitis; Apex of heart; lymph nodes	

7.	PseudoTuberculosis	*Corynebacterium kutscheri*	Mice, Rats, Guinea pig & Hamster	Adults **Mice** (hepatic & renal) & **Rats** (pulmonary involvement)	Porphyrin and mucopurulent ocular and nasal discharges; Lameness; Casous necrosis with soltayr / multiple abcesses in Lungs (& pleuritis); Liver; Kidneys; Prepucial glands; Middle Ear; Joints and Skin (ulcers; fistulous tract)
8.	Salmonellosis	Salmonella enterica var. Typhimurium Salmonella enterica var. Enteritides	Mice & Rats	Young & Adults Mice & Rats	Portal vein of liver; Multiple **white to yellow necrotic foci** occur on the liver; Multifocal necrotizing Splenitis and Hepatitis; Spleenomegaly
9.	CAR bacilli infection	Cilia-associated bacillus; Gliding bacterium, similar to Flavobacterium	Mice, Rats and Rabbits	Mice, Rats	Attack Cilia on respiratory epithelium; Bronchiectasis, Mucus accumulation in bronchioles; Hyperplastic BALT; rare suppurative bronchopneumonia
10.	Murine Chronic Respiratory Disease (MCRD) Or Chronic Murine Pneumonia (CMP)	*Mycoplasma pulmonis*	Mice & Rats	Rats	involves the nasal passage, middle ear, larynx, trachea, bronchi & lungs; Bronchiectasis ; infection catarrh of rats; dilated & thick walled bronchi; Squamous metaplasia of bronchial epithelium; purulent rhinitis; cobble stone like appearance of Lungs
11.	Bubonic Plague (Yersiniosis)	*Yersinia pestis* (Pasturella pestis); Y. pseudotuberculosis & Y. enterocolitica (transmitted by rat flea)	Mice & Rats	Mice & Rats	Fatal acute septicaemia; Discrete white or gray nodules in the liver, spleen & lymph nodes
PARASITIC Diseases					
12.	Pin Worm Infection	*Syphacia obvelata* & *Aspiculuris tetraptera* *(*Pinworms are nematode parasites of family	Mice	Adult Mice	Perianal itching; rectal prolapsed, fecal impaction; Live in the cecum or proximal colon. Females migrate to the anus, where they lay adhesive -coated

		Oxyuridae)			eggs, from which larvae hatch and become infective 5-20 hours later
	Dwarf Tapeworm of Mice	*Hymenolepis nana*			
	Mouse mite	*Myobia musculi*			
	Mouse louse	*Polyplex serrate*			

MOUSE POX / ECTROMELIA

Etiology:

Mousepox is a devastating disease of mice caused by **Ectromelia virus (ECTV)**, an **orthopoxvirus**. Mousepox was first reported by Marchai in England, and the causative virus was detected soon after by Barnard and Elford. Field strains of ectromelia virus have been isolated in many countries, but two strains, **Hampstead** (low virulence) and **Moscow** (high virulence), have been extensively known.

Mousepox usually takes one of three clinical courses: acute infection with high mortality, chronic infection with variable mortality, or asymptomatic infection. The expression of clinical signs reflects an interplay between virus-related factors, such as virulence, and dose- and host-related factors, such as age, genotype, immunological competence, and portal of entry.

Affected Specie / Transmission:

The laboratory mouse is the primary host for ectromelia virus and poxlike viruses have also been found in rats. Highly susceptible mice die from visceral infections before a skin rash develops; therefore they are a relatively small hazard for dissemination of virus. Resistant mouse strains are dangerous because they can develop enzootic asymptomatic infections.

Transmitted by direct contact or by Fomites. **Natural exposure** is thought to occur through small abrasions of skin, but experimentally, oral exposure can cause **chronic** inapparent infection of Peyer's patches, prolonged excretion of virus in feces, and occasional chronic tail lesions. Mice with chronic intestinal infection appear not to readily transmit infection by contact, but carrier mice can be a source of contaminated tissue suspensions. Arthropod transmission is importantfor some pox viruses, but this appears not to apply to ectromeliavirus, although the blood-sucking rat mite ***Ornithonyssus bacoti*** may be a passive vector.

Pathogenesis:

The pathogenesis of infection following skin invasion begins with viral multiplication in the draining lymph node and a primary viremia. Splenic and hepatic involvement begins within 3 to 4 days, whereupon larger quantities of virus are disseminated in blood to the skin. This sequence takes approximately1 week and, unless mice die of acute hepato-splenic infection, ends with the development of a primary skin lesion at the original site of viral invasion. The primary lesion is due ostensibly to the development of antiviral cellular immunity.

Signs:

Acute lethal infection may produce clinical signs, such as ruffled fur or prostration, for only a few hours before death. The rapidly fatal form of mousepox is associated with extensive necrosis of lymphoid tissue and liver and with intestinal hemorrhage.

Mice that survive acute infection often develop a skin rash whose severity depends on the extent of secondary viremia after infection of parenchymal organs. The pox rash can develop anywhere on the body and may be solitary or generalized. In some mice, conjunctivitis also occurs.

Severe viral infection of the feet and tail can lead to amputation; hence the name infectious ectromelia.

Lesions:

External lesions during the acute phase of infection in susceptible surviving mice include conjunctivitis, alopecia, cutaneous erythema and erosions (rash), cutaneous pustules, ulceration of muzzle, lips, ears& tails, and swelling and dry gangrene of extremities. The lesion that gives its name ECTROMELIA, is partial amputation of Limbs and Tail.

Internally, livers may be swollen, friable, and mottled with multiple pinpoint white to coalescing hemorrhagic foci. Spleens, lymph nodes, and Peyer's patches are enlarged, with patchy pale or hemorrhagic areas. Intestinal hemorrhage, particularly in the upper small intestine, is common.

Microscopic lesions consist of focal coagulative necrosis in the liver, spleen, lymph nodes, Peyer's patches, and thymus, as well as other organs. The complex of liver, spleen, and epithelial lesions bearing typical inclusions is pathognomonic. Splenic fibrosis in recovered mice is also a unique feature of this disease.

Multiple basophilic to eosinophilic intracytoplasmic inclusion bodies (1.5–6 μm) are evident in infected cells, especially hepatocytes at the periphery of necrotic foci. Ectromelia virus multiplies in the cytoplasm and produces two types of inclusion bodies. The A-type (**Marchal bodies**) is acidophilic and is found primarily in epithelial cells of skin or mucous membranes. The B-type inclusion is basophilic and can be found in all ectromelia-infected cells.

Focal or confluent hepatocellular necrosis occurs in susceptible mice during acute stages of mousepox. White spots indicative of necrosis are seen grossly throughout the liver. In nonfatal cases, regeneration begins at the margins of necrotic areas, but inflammation is variable.

Splenic necrosis in acute disease commonly precedes hepatic necrosis but is at least equally severe. Necrosis and scarring of red and white pulp can produce a gross "mosaic" pattern of white and red-brown.

Necrosis of the thymus, lymph nodes, Peyer's patches, intestinal mucosa,and genital tract also have been observed during acute infection,whereas resistant or convalescent mice can develop lymphoid hyperplasia.

The primary skin lesion, which occurs 6-10 days after exposure, is a localized swelling that enlarges from inflammatory edema. Necrosis of dermal epithelium provokes a surface scab and heals as a deep, hairless scar. Secondary skin lesions (rash) develop 2 to 3 days later, are often multiple and widespread, and can be associated with

conjunctivitis, blepharitis, and, in severe cases, with buccal and lingual ulcers. Secondary skin lesions also ulcerate and scab before scarring.

Diagnosis:

- Mousepox can be diagnosed from clinical signs, lesions, serological tests, and demonstration of virus or viral antigen in tissues.
- Characteristic intracytoplasmic eosinophilic inclusions aid histological confirmation, and typical poxvirus particles can be found in tissues by electron microscopy.
- Serological Test including ELISA / IFA
- PCR Testing
- Mousepox must be **differentiated** from other infectious diseases that cause hepatitis in adult mice, such as MHV, Tyzzer's disease and salmonellosis. The skin lesions of chronic mousepox must be differentiated from bite wounds, alopecia, hypersensitivity, and other forms of dermatitis. gangrene and amputation of digits or tail can also occur due to trauma or "ringtail."

Murine Hepatitis Virus (MHV) Infection

(Mouse Hepatitis Virus / Mouse Coronavirus Infection)

Etiology:

MHV belongs to the order Nidovirales, family Coronaviridae, genus Coronavirus. Its official name is *Murine Hepatitis Virus* (*MHV*), but mouse hepatitis virus / mouse Coronavirus infection is more generally accepted. Despite "hepatitis" in its name, MHV is not always hepatotropic.

Species affected / Transmission:

Natural transmission can occur mainly through Oral or Respiratory Routes. The respiratory tract is a major portal of entry for MHV and primary lesions (syncytia) are in pulmonary vascular endothelium.

Pathogenesis:

Those strains with respiratory tropism initially replicate in nasal mucosa and disseminate to a variety of other organs because of their polytropic nature.

Dissemination of MHV from the nose occurs via the blood and lymphatics to pulmonary vascular endothelium and draining lymph nodes, respectively. Secondary viremia disseminates virus to multiple organs, with virus replication and cytolytic lesions in central nervous system, liver, lymphoid tissues, bone marrow, and other sites.

Infection of central nervous system by viremic dissemination occurs primarily in neonatal or immunodeficient mice but not older, immunocompetent mice. Direct infection of adult mouse brain can also occur by extension of the virus along olfactory neural pathways, even in the absence of dissemination to other organs.

Enterotropic MHV strains tend to selectively infect intestinal mucosal epithelium, with minimal or no dissemination to other organs.

Signs:

Clinical signs of MHV infection depend on a number of factors, including age and strain of mouse, virus strain and tropism. Acute MHV is most prevalent in young mice. Suckling mice can develop diarrhoea, inappetance, dehydration, weight loss, lassitude, and ruffled hair. These signs are seen in various combinations and often terminate in death

Lesions:

Hepatotropic strains of MHV cause damage to liver. Neurotropic variants induce flaccid paralysis of the hindlimbs. Conjunctivitis, convulsions, and circling may be seen occasionally. Mouse hepatitis is, for all practical purposes, an infection of mice.

In susceptible weanlings and adults, yellow-gray foci of hepatic necrosis are seen with varying frequency. Icterus, sanguinous peritoneal exudates, or intestinal hemorrhage may accompany hepatic lesions. In suckling mice, focal spotting of the liver may occur, but intestinal lesions are more common.

The stomach is often empty, and the intestine is filled with watery to mucoid, yellowish, sometimes gaseous contents. Hemorrhage or rupture of the intestine can occur. Enterotropic strains can produce syncytia and necrosis in the intestine after oral exposure and can contaminate the hepatic portal system to produce lesions in the liver and elsewhere.

Morphologically, **syncytium formation with or without necrosis** is highly characteristic of MHV infection. **Histologically**, hepatic necrosis can be focal or confluent and may be infiltrated by inflammatory cells. Syncytia commonly form at the margin of necrotic areas and, in mild infections, may develop in the absence of frank necrosis. Intestinal lesions can be found at all levels and range from syncytium formation to necrosis and inflammation with severe blunting of surviving villi.

Syncytia can often be found in asymptomatic adults on careful examination of intestinal mucosa. Necrosis and syncytia have also been detected in spleen, stomach, lymph nodes, and pancreas. In athymic mice, syncytia occur in many tissues, and hepatic necrosis can be extensive.

Neurotropic variants, produce central nervous system lesions after invasion of the nasal passages. Necrosis predominates in the hippocampus and olfactory lobes, whereas demyelination, secondary to viral invasion of oligodendroglia, occurs in brainstem and in peri-epdendymal areas. Neurotropic strains can also penetrate the cribiform plate to the olfactory bulbs after initial replication in nasal mucosa.

Diagnosis:

- In acute cases, visualization of characteristic lesions with syncytia in target tissues.
- Immunohistochemistry; PCR Test
- *Differential Diagnosis* from other infectious diseases that cause diarrheal illness, runting, or death in suckling mice. These include EDIM, mousepox, Tyzzer's disease, and salmonellosis and reovirus infections. Neurological signs must be differentiated from mouse encephalomyelitis virus.

INFANTILE DIARRHOEA

Introduction

Diarrheal disease of unweaned mice is a complex syndrome caused by a number of viral / bacterial agents.

Etiology

Ubiquitous viral or bacterial organisms may be incriminated as producing diarrheal or septicemic signs in unweaned mice

Signs

The clinical signs of the syndrome are: slight-to-severe diarrhea in which fecal material ranges from bright yellow to light brown in color. Nursing mothers will sometimes very efficiently clean up the anal region of the affected animal so that only a slight "pasting up" condition is noted. Animals affected by diarrhea (usually 4 to 10 days of age) usually recover, but many are discarded as runts at weaning time.

Lesions

At necropsy, the only common finding is the presence of light colored and watery fecal material in the intestinal tract, with occasional bubbles of gas. Histologically the tissues demonstrate a mild catarrhal inflammation.

EPIZOOTIC DIARRHEA OF INFANT MICE (EDIM)

Etiology: EDIM virus is a non-enveloped RNA virus of the **rotavirus group A**.

Affected Specie / Transmission: Affects laboratory mice. This virus is highly contagious and is transmitted via contaminated bedding, airborne dust, aerosol, and through direct contact with infected mice. Route of entry is **oral–fecal route**. Animals are most susceptible between 0 and 14 days of age. Adult mice are unapparent viral carriers and shed the virus to their susceptible young.

In Infant mice less than 2 wks age, selectively infect terminally differentiated enterocytes of villi and surface mucosa of small and large intestine respectively. Causes Hydrophic degeneration and vacuolation of terminally differentiated enterocytes. This causes functional disturbances of intestine (fluid accumulation & dilation). Diarrhoea further causes loss of absorptive epithelial cells and secretion.

Clinical Signs: Clinical signs are generally limited to mice under 14 days of age. These animals present with watery, mustard-colored stools, lethargy, and distended abdomens. The cardinal signs are **bloated abdomens with fecal soiling of the perineum**, which may extend to the entire pelage in severe cases. Rectal impaction may occur at 12 to 16 days of age.

Lesions:

Grossly, the intestines contain scant, yellow, gaseous contents. The **intestine is often distended, flaccid, and filled with gray–green gaseous liquid or mucoid fecal material that soils the pelage**. **Stomach contains curdled milk**, except in terminal cases with anal impaction due to caking of dried feces. If a dried perianal fecal plug is present, the intestinal tract may be distended.

Microscopically, causes **hydropic change and vacuolation** of terminally differentiated enterocytes at the "tips of villi" which give **villi a clubbed appearance** (arrowhead, B.). Degenerative virus-induced vacuoles vary in size and are associated enterocyte nuclear pyknosis. Lesions induced with EDIM infection must be distinguished from the normal lipoprotein vacuoles seen in suckling mice, which are uniform and often contain a pink proteinaceous droplet, with unremarkable nuclei.

Acidophilic intracytoplasmic inclusions have been described but are not diagnostic. **Lamina propria edematous and lymphatics dilated**, although inflammation is minimal.

Diagnosis

Serological Tests like ELISA , IFA

PCR Test

LYMPHOCYTIC CHORIOMENINGITIS

Etiology

Causative agent is *lymphocytic* ***choriomeningitis*** *mammarenavirus* (LCMV), a member of the family Arenaviridae; a RNA virus

Affected species / Transmission:

The lab mice and hamsters are commonly affected. Rats are naturally resistant.

It is a Zoonotic infection.

Spread through contact with saliva, nasal secretions or urine. Entry is through Oro-nasal route or skin abrations.

Signs

Depend on age, virus strain and route of infection. Naturally infected mice do not show symptoms. In-utero infected ones are often runted (undersized).

Lesions

Grossly, chronic wasting is observed or runting in new borns.

Microscopic lesions includes characteristic lymphocytic choriomeningitis (membranes surrounding brain /spinal cord); heavy lymphocytic infiltrates in Liver, Adrenals, Kidney, Spleen and Lung; immune-complex Glomerulonephritis, Lymphadenopathy and Vasculitis.

Diagnosis

Serological Tests like ELISA , IFA

PCR Test

Minute Virus of Mice (MVM) Infection

Minute virus of mice is a **Parvovirus**. It is highly contagious and highly prevalent in wild and lab mice and hamsters too.

Minute virus of mice is antigenically distinct from rat parvoviruses. Transmission occurs by oro-nasal exposure Natural MVM infection is essentially asymptomatic in Mice or is very moderately pathogenic BUT it is more important in HAMSTERS.

In hamsters, MVM infection is **teratogenic** in **neonatal hamsters** and produces **Mongoloid deformities**. Virus also can replicate in fetal tissues without inducing lesions. Contact exposed neonates occasionally **develop cerebellar lesions including Cerebellar Hypoplasia**.

Mouse Encephalomyelitis Virus (MEV) Infection

Etiology: The causative agent, mouse encephalomyelitis virus (MEV), is a small RNA-containing enterovirus of the family **Picornaviridae**.

Signs & Lesions:

The characteristic observed sign of natural infection is **flaccid paralysis of the rear legs**, while the **tail remains mobile**. Paralysis may be preceded by weakness in the forelimbs or hindlimbs. This poliomyelitis-like disease is characterized morphologically by acute necrosis of ganglion cells, neurophagia and perivascular inflammation, particularly in the ventral horn of the spinal cord gray matter. In demyelinating disease, mononuclear cell inflammation develops in the leptomeninges and white matter of the spinal cord.

Some mice may recover from paralysis, but death frequently ensues. The course of disease may be exacerbated by a failure to obtain food or water and by urinary incontinence. Mice that recover from the paralytic syndrome are disposed to a **chronic demyelinating phase**, which is expressed clinically as a **mild gait disturbance.**

Sendai Viral Pneumonia

Etiology: ***Sendai virus,*** which is a paramyxovirus.

Species affected / Transmission: Natural infections occur in mice, rats, hamsters, and guinea pigs, but the latter three species rarely show clinical signs. Sendai virus is transmitted by aerosol or by contact.

Signs: Acute epizootics are Most Common in previously uninfected mouse colonies and are characterizedby respiratory distress, neonatal mortality, retarded growth, and prolonged gestation. Weaning rates can decrease dramatically until infection subsides. Susceptible adult mice typically sit in a hunched position and have an erect haircoat. Rapid weight loss and dyspnea occur, and there may be crusting of the eyes and chattering. Infection is commonly more lethal in **suckling mice** and, to some extent, is more severe in aged mice than in young adults.

Lesions:

Gross lesions are characterized by partial to complete consolidation of the lungs. Individual lobes are meaty and plum-colored, and the cut surface may exude a frothy serosanguinous fluid. Demarcation between normal and pneumonic zones is usually distinct. Pleural adhesions or lung abscesses caused by secondary bacterial infection are seen occasionally, and fluid may accumulate in the pleural and pericardial cavities.

Histologically, typical changes begin with inflammatory **edema of bronchial lamina propria**, which may extend to alveolar ducts, alveoli, and perivascular spaces. Necrosis and exfoliation of bronchial epithelium ensues, frequently in a segmental pattern. Alveolar epithelium also may desquamate, especially in severe disease, and necrotic cell debris and inflammatory cells can accumulate in airways and alveolar spaces.

Alveolar septae are usually infiltrated by leukocytes to produce **Interstitial Pneumonia**. Lymphoid cells also invade epibronchial and perivascular spaces. Regeneration and repair begin shortly after the lytic phase and are characterized by hyperplasia and squamous metaplasia of bronchial epithelium,which may extend into alveolar septae. Proliferation of cuboidal epithelium may give terminal bronchioles an **Adenomatoid Appearance**.

Diagnosis:

Because only one serotype is known, sero-diagnosis (ELISA / IFA) is an effective means to detect exposure to infection.

Differential diagnosis with Bacterial pneumonias, murine respiratory mycoplasmosis.

TYZZER'S DISEASE

Tyzzer's disease is typically an enterohepatic disease, with secondary involvement of the heart.

Etiology: caused by *Clostridium piliforme / Bacillus piliformis*, and characterized by segmental necrosis of cecal mucosa and focal necrotic lesions on the liver and heart. Bacterium is Gram –ve, filamentous, curved rod shaped organism and it is an obligatory intracellular organism.

Affected Species / Transmission:

Mice, Rats, Gerbils, Rabbits, Carnivores (cat, dog) and Non-human primates. Virtually all Mongolian GERBILS are very susceptible. This disease is also of Zoonotic importance.

Transmission is through ingestion of spores from environment or in faeces of infected animals. Contaminated feed / bedding or carcasses (cannibalism) are also an important source. Infection occurs through oro-fecal route.

Pathogenesis

Infection occurs by **ingestion** of spores from environment or feces of infected animals. After ingestion of the spores, the bacterium is phagocytosed by intestinal epithelial cells. Inside the cell, the vegetative form escapes the phagosome and begins replication in the cytoplasm. Produce exotoxin, lead to necrosis of intestinal epithelium. Bacteria are either deposited back into the lumen, or sometimes find their way deeper into the intestinal wall, where they may infect smooth muscle cells or gain access to the portal circulation. From the portal vein bacteria may infect the liver and/or heart. Hepatitis and occasionally myocarditis.

Proposed sequence of infection

Spores ingested >> produce the vegetative form, actively phagocytosed by epithelial cells overlying the GALT >> vegetative form escapes phagosome >> multiples in intestinal mucosal epithelial cells and possibly RE cells in Peyer's patches.

Vegetative form infects and multiples in the hepatocytes and then may (depending on host survival) enter into the blood stream or lymphatics to colonize the myocardium and MAY possibly enter into epithelium of biliary tree to multiply and eventually be shed into bile to re-infect intestine and liver (Auto-infection).

Most infections appear to be cleared at this point, and animals stop shedding spores within about 2 weeks. If infection extends past GI tract - Vegetative form reaches liver by one or more routes that includes Portal circulation (most likely) or Lymphatics or Common bile duct (the vegetative form is motile). In Rabbits, *Escherichia coli* reportedly potentiates *C. piliforme* infections.

Signs: Are usually absent. Overt disease mostly in young recently weaned animals. Anorexia, lethargy, emaciation, distended abdomen (rats), ruffled fur (rabbit) is noticed. Diarrhea with or without mucus and blood and distended abdomen (rat) also seen.

Gross Lesions-

Consists of circular grey-white foci 1-2 mm in diameter on the capsule & cut surface of the liver. Perianal fecal staining may be present

In Liver, multiple, disseminated, pinpoint or larger, pale foci (necrosis) within and on the surface of the liver. The liver may only be swollen and mottled

Intestines show marked dilation of the terminal small intestine [**megalo**ileitis (rat)], greatly dilated, fairly flaccid, hyperemic small intestines (ileum). Hyperemia, edema, hemorrhage, and *possibly* ulceration of terminal ileum, cecum, and colon is also seen.

Usually not ulcerative (helps distinguish from other diseases). Enlarged, hyperemic and edematous mesenteric lymph nodes

Heart is less often involved. Pale, circumscribed, sometimes raised foci may be present on the surface, like Pale linear streaks near the apex of the heart.

Microscopic Lesions:

Most characteristic lesions are of **Necrotizing Hepatitis.** In Liver, coagulative necrosis (frequently periportal) with or without Inflammation is noticed. Hemorrhages, Dystrophic calcification and Fibrosis also observed. The necrotic foci consists of focal area of hepatic necrosis surrounded by a zone of polymorphnuclear cells & lesser number of lymphocyte & macrophages.

In Heart, pale streaks or areas over myocardial or epicardium with or without necrosis. Mixed inflammatory cells & Dystrophic calcification is seen.

In Intestines, Necrotizing enteritis, typhlitis, and colitis with or without Edema (common) is seen. Blunted and fused villi with Crypt epithelial hyperplasia, ulceration, haemorrhage & cellular debris in crypts and lymphatics. Mesentric lymph nodes may be enlarged and contain small abscess.

Diagnosis:

Demonstrating the bacteria in smears.

PCR Testing

PSEUODTUBERCULOSIS

Etiology: *Corynebacterium kutscheri, a Gram-positive diphtheroid bacillus*

Affected Specie / Transmission: seen in Rats, Mice, Guinea pig and hamster (culture evidence, no disease). Transmission is probably through direct contact and/or oronasal exposure. Septic emboli become trapped in organs ortissues with either a large capillary network(lung, liver, and kidney) and/or responsible forfiltering blood (synovia and glomeruli). Thisaccounts for the distribution of the lesions.

Clinical Signs

Nonspecific (sick rat) clinical signs may be observed with death in 1 to 7 days. Porphyrin and mucopurulent ocular and nasal discharges, Respiratory rales and dyspnea and Lameness are common. Low morbidity (high mortality in affected)

Latent infections are currently rare in laboratory rats and mice. However, infected animals areusually clinically normal. In these, the organism may be found in Submaxillary (cervical) lymph nodes, Oral cavity, Nasal cavity, Middle ears and Preputial gland abscesses (reported, but really rare)

Latent infections may advance with age andimmunosuppressive conditions like Stress (poor husbandry, overcrowding, shipping, etc.), Concurrent infections, Irradiation, Immunosuppressive drugs (steroids, cyclophosphamide, etc.), Malnutrition (e.g., pantothenic acid and biotindeficiencies)

Pathogenesis:

Although any or all organs and tissues may be involved, the frequency of lesion distribution varies with the species

In Rat: pulmonary involvement

In Mouse: hepatic and renal involvement

Gross Lesions:

Cervical lymph nodes of carrier animals may be enlarged (reactive) but without abscessation. Raised, graywhite nodules up to 1 cm in diameter may be present in liver, kidney, and lungs and, to a lesser extent, in other tissues, including subcutis. Suppurative and erosive arthritis may also be present, particularly in the carpal/ metacarpal or tarsal/metatarsal joints, with marked swelling and erythema. Conjunctivitis is another manifestation that has been described

Lung: 1 or more randomly distributed abscesses +/- hemorrhage and pleuritis (fibrinous or fibrous)

Liver: Solitary or multiple abscesses and/or necrosis

Kidney: Solitary or multiple abscesses and/or pyelonephritis

Preputial gland: Abscess

Joints: Suppurative arthritis

Skin: Abscess(es), ulcerations, fistulous tracts, pododermatitis

Middle Ear: Suppurative otitis media

Microscopically, Lungs show caseous necrosis, Abscesses mostly in the interstitium due to hematogenous dissemination. Epithelioid macrophages and multinucleated giant cells may be present in the abscesses. Bronchi and bronchioles may contain suppurative Exudate.

Liver having caseous necrosis, Kidney show Septic embolic glomerulitis, Abscesses with or without pyelonephritis.

Suppurative thrombosis and embolization involving the pulmonary or mesenteric and portal vessels may be evident. Lesions may be noticed in any other tissues too (e.g., brain, skin, joints)

Diagnosis

Characteristic bacterial colonies, with "**Chinese letter configurations**" of less dense colonies, are readily evident within suppurative lesions, mainly in tissue sections.

Bacterial culture, isolation and identification

Differential Diagnoses include other disseminated chronic bacterial infections that induce abscesses, including *Staphylococcus* and *Streptococcus*, and arthritis associated with *Mycoplasma* or *Streptobacillus*.

SALMONELLOSIS

Etiology:

Salmonella is a Gram-negative, toxin-producing, invasive, enteric bacterium. The most common serotypes of ***Salmonella enterica*** to infect rats & mice are serovars ***enteriditis*** and ***typhimurium***

Salmonella enterica var Typhimurium (most common)

Salmonella enterica var Enteritides

These are important enteric pathogens which spread from the interstinal tract to the liver.

Affected Specie / Transmission:

Syrian Hamsters are mostly affected.

The disease is spread by Faecal-oral transmission. Food, water, and bedding may be contaminated by infected feces from wild mice or rats. It is also of Zoonotic importance.

Pathogenesis:

Infection is initiated by ingestion of contaminated feed or bedding. Organisms gain entry to mucosa via fimbrial attachment to M cells in gastric mucosa. Initial replication in enterocytes is followed by multiplication in gut-associated lymphoid tissue (GALT).

In the liver, bacteria replicate intracellularly within macrophages, Producing focal histiocytic granulomata as the hallmark lesion. By the 3rd day, this organism passes through the portal vein to the liver which cause necrosis of hepatocytes & proliferation of macrophages occurs. Then organism reaches to gall bladder & return to intestine, where further infection of mucosa may occur via lymphatics. Invasion occurs in the mesenteric lymph nodes & less frequently from tracheal, bronchial & cervical lymph nodes.

Signs: Disease in susceptible colonies may manifest only as acute death with no clinical signs. Moderate morbidity characterized by hunched posture, anorexia, lethargy, and high to sporadic mortality may be observed in weanlings and in females in late gestation showing acute deaths, fetal reabsorption, or abortion.

Lesions:

At necropsy, there may be multifocal, pinpoint-size, pale areas in the liver, with patchy pulmonary hemorrhage and reddened hilar lymph nodes. Lesions are mainly noticed in the spleen, liver and intestinal tract.

Gross findings may include splenomegaly, with multifocal pale miliary foci present on the liver.

Grossly Liver is enlarged, deep brown to yellowish brown in colour & often friable. Multiple **white to yellow foci** occur on the liver. Splenomegaly with spleen enlarged 2 to 3 times normal size. Lesions in the small intestine consist of mucosal congestion and edema with thrombosis of the mesenteric vasculature. Mesenteric lymph nodes may be enlarged and edematous.

Microscopically, Multifocal necrotizing Splenitis (SPLEEN) and Focal necrotizing Hepatitis (LIVER) with leucocytic infiltration and venous thrombosis are typical characteristic. In Liver, multiple necrotic foci, lymphoid, histiocyte monocytic nodules,

swelling of kupffer cell & **widespread thrombosis** of branches of portal vein are found. These veins are often surrounded by zones of necrosis in the adjacent part of liver. Periphery of necrotic foci is often invaded by polymorph & clumps of bacteria may be seen in these lesions.

Microscopic changes in the LUNG are characterized by multifocal interstitial pneumonitis, with intra-alveolar hemorrhage. In the pulmonary veins and venules, there may be a **septic thrombophlebitis**, with thrombi containing leukocytes, and erosion of venous walls. In KIDNEYS, Embolic glomerular lesions also noticed.

Diagnosis:

Bacterial Culture, isolation and Identification

Differential diagnoses include Tyzzer's disease, pathogenic *E. coli* infections, and other acute bacterial infections, such as pseudomoniasis

Cilia-Associated Respiratory Bacillus (CAR-B) Infection

Etiology – Still Unclassified and is a Gliding bacterium, similar to Flavobacterium and Flexibacter. It is Gram negative, motile, fusiform, non-spore forming bacterium.

Host / Transmission: Natural lab animal **HOST** range includes Rats (most common), Mice, Rabbits, Goats and transmission is by Direct Contact

Signs: nonspecific respiratory signs (dyspnoea) AND weight loss, ruffled fur, snuffling (breath noisily) and chromodacrorrhea (blood-tinged / red lacrimal secretion; red tears) in rats, etc.

Lesions: Resemble those of the primary infections, e.g., Mycoplasmosis, Sendai virus pneumonia. Grossly animals have mucopurulent Bronchopneumonia. Rarely, uncomplicated infections may produce bronchiectasis, mucus accumulation in bronchioles, and lymphoid hyperplasia. Inflammation can be neutrophilic, but less suppurative than with mycoplasmosis.

Bronchial epithelium is preserved, or hyperplastic. The Cilia is prominent, **not lost** as with M. pulmonis.

Histopathology of CAR bacillus infection

Chronic bronchitis, organism seen amongst and parallel to the cilia of respiratory epithelium at any level (nasal cavity to bronchioles) - observed in silver stained sections

Hyperplastic BALT

Diagnosis:

Identification and Isolation Bacterial Culture,

Warthin-Starry Silver Staining - of Respiratory epithelium for demonstration of CAR bacilli amongst Cilia.

Serology / ELISA

Murine Chronic Respiratory Disease (MCRD)
Or Chronic Murine Pneumonia (CMP)

Introduction: It is a **bronchiectasis** of rats, infection catarrh of rats or rodent pulmonary mycoplasmas.

Etiology: *Mycoplasma pulmonis* is the cause of specific syndrome and involves the nasal passage, nasal sinuses, middle ear, larynx, trachea, bronchi & lungs of lab animals. Rats are most commonly affected.

Signs- some rats severly affected. Other show **purulent rhinitis** with nasal and ocular discharges, coughing, sneezing and involvement of middle ear result in loss of equilibrium, show inactivity, roughened hair coat, loss of body wt., polypnoea.

Lesion:

Grossly, Lungs having pale grey color & characteristically have a **cobble stone like appearance** on the surface due to dilated thick walled bronchi.

Microscopically- In early stage the wall of the bronchi are thick due to the aggregate of lymphocyte & plasma cells. In prolonged cases the bronchi becomes dilated & also contain pus. **Squamous metaplasia** of bronchial epithelium is frequent findings.

PIN WORM of MICE

Etiology:

The pinworms, are nematode parasites (of family Oxyuridae) and two species of pinworms commonly infect laboratory mice: *Syphacia obvelata* and *Aspiculuris tetraptera*.

Syphacia obvelata, the common mouse pin worm, is a ubiquitous parasite of wild and laboratory mice. Infestation is diagnosed by demonstrating eggs in the perianal area or adult worms in the cecum or large intestine.

Affected Specie / Transmission:

Pin worms are transmitted by fecal-oral contact or also via fomites. The eggs of pinworms are sticky and long-lived and so may persist in environment for long.

Sign / Lesions:

In immunocompetent animals, Infection is usually asymptomatic, and gross lesions are not prevalent aside from the presence of adult pinworms in lumen of intestine. Heavily infected mice can occasionally sustain various intestinal lesions including rectal prolapse, intussusception, enteritis, and fecal impaction, weight loss and poor hair coat.

Diagnosis:

Since most eggs are deposited outside the gastrointestinal tract, fecal examination is not much reliable. Eggs are usually detected by pressing “Perianal cellophane Tape Test” and then to a glass slide that is examined by microscopy. Eggs are flattened on one side and have pointed ends. Anal Swabbing or Centrifugation techniques can also be used.

Examining Caelic and Colonic contents to detect adult worms. Female worms range from 3.4 to 5.8 mm in length, and male worms are smaller (1.1-1.5 mm).

Hymenolepis nana	- the Dwarf Tapeworm
Mouse mite	Myobia musculi
Mouse louse	Polyplex serrate