

Pathology of Bacterial Diseases of Lab Animals

1. 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 Enteritidis and Typhimurium

Salmonella enterica var Typhimurium

Salmonella enterica var Enteritides

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

Transmission: The disease is spread by Faecal-oral transmission. Food, water, and bedding may be contaminated by infected feces from wild mice or rats.

Pathogenesis: Following the oral infection by Sal. typhimurium, moderate inflammation occurs in the mucosa of small intestine & by the 3rd day, this organism passes through the portal vein to the liver which causes necrosis of hepatocytes & proliferation of macrophages occurs. After such lesions develop in liver, the organism reaches to gall bladder & returns 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.

Clinical Signs: Disease in susceptible colonies may be manifest only as acute death with no clinical signs of infection. 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.

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 and Hepatitis is characteristic. In Liver, multiple necrotic foci, lymphoid histiocyte monocyte 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 polymorphs & clumps of bacteria may be seen in these lesions. Spleen is usually enlarged & engorged with blood. Area of focal necrosis is similar to those in liver.

2. TULAREMIA

Also known as **Rabbit Fever**, it is a bacterial plague-like disease caused by *Francisella tularensis* which was earlier called *Pasteurella tularensis*. This disease has a zoonotic importance too.

Animals Affected: Disease mainly affects Rabbit, Guinea pig, Wild Rat/Mice and Monkey.

Transmission:

Tularemia can be transmitted by aerosol, direct contact, ingestion, or arthropods. Inhalation of aerosolized organisms can produce a Pneumonic Form.

Direct contact with, or ingestion of, infected carcasses of wild animals (eg, cottontail rabbit) can produce the ulceroglandular, oculoglandular, oropharyngeal (local lesion with regional lymphadenitis), or typhoidal form.

Ticks are the most important vectors of *F. tularensis*, transferring the bacterium between rabbits, hares, and rodents and serving as an interepizootic reservoir. They can maintain infection transstadially and transovarially, making them efficient reservoirs and vectors.

Grossly:

Diseases is usually recognized by presence of multiple, chalky focal lesion scattered on liver, spleen & lymph nodes. These focal lesion vary from pin point size to large irregular shape foci on the surface.

Microscopic Lesions:

The most consistent lesions are **miliary, white to off-white foci of necrosis in the liver** and sometimes in the spleen, lung, and lymph nodes. In Liver, central mass of caseous necrosis surrounded by a zone of lymphocytes along with few polymorph nuclear cells & macrophages is observed. Early lesions may have purulent area but it is replaced by necrotic tissue debris & there is thrombosis of small blood vessels which is frequently noticed.

Organisms can be readily isolated from necropsy specimens by use of special media. The infective dose required to transmit this pathogen is extremely low; thus, risk of infection during necropsy or to laboratory personnel is significant, and special procedures and facilities are essential.

Diagnosis:

Tularemia must be differentiated from other septicemic diseases (especially plague and pseudotuberculosis) or acute pneumonia.

Diagnosis of acute infection is confirmed by culture and identification of the bacterium, direct or indirect fluorescent antibody test. Causative organism being Gram -ve are difficult to demonstrate into tissue sections but are present in large number. particularly in phagocytes at the margins of lesion.

3. TYZZER'S DISEASE

It is the disease of Mice, Rat & Hamster mainly.

Etiology

Clostridium piliforme / *Bacillus piliformis*, which is a Gram –ve, curved rod shaped organism. It is obligatory intracellular organism & organism also inhabit as saprophyte in the mouse colonies.

Hosts (some evidence of partial species-specificity of strains)

Rodents (virtually all, Mongolian gerbil very susceptible), Rabbits, Carnivores (cat, dog), Non-human primates. Zoonotic cases have also been reported.

Prevalence: Tyzzer's Disease is infrequent, although the organism may be widespread

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

Transmission: Horizontal transmission by ingestion of spores in Feces, Contaminated feed and bedding or Carcasses (cannibalism)

Pathogenesis

Vegetative form survives only inside Cells of Epithelium (small and large intestine, gall bladder, bile duct), Hepatocytes, Myocardial fibers, smooth muscle of small and large intestine

Proposed sequence of infection

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

Vegetative form infects and multiplies 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.

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 **megaloileitis** (rat), greatly dilated, fairly flaccid, hyperemic small intestines (ileum). Hyperemia, edema, hemorrhage, and *possibly* ulceration of any part of the intestines, but especially the 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. It is Pale, circumscribed, sometimes raised foci may be present on the surface. Pale linear streaks near the apex of the heart

Microscopic Lesions:

In Liver, **Coagulative necrosis** (frequently periportal) with or without Inflammation (neutrophils, mononuclear cells, histiocytes, and rare multinucleated giant cells. 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. Numerous organisms are present around the necrotic foci in inflammatory zone and in intact zone. They usually cannot be seen in H&E stained tissue but can be seen in giemsa stained tissue.

In Heart, myocardial degeneration with or without necrosis. Mixed inflammatory cells & Dystrophic calcification is seen.

Intestines may show nothing even if lesions in liver and heart are there. Necrotizing enteritis, typhlitis, and colitis with or without Edema (common). Blunted and fused villi with Crypt epithelial hyperplasia. Ulceration, Haemorrhage & Cellular debris in crypts and lymphatics. The organisms are also found in the intestinal epithelial cells resulting in necrotising enteritis the mesentric lymph nodes may contain small abscess.

4. Cilia-associated bacillus (CAR bacilli) Infection

ETIOLOGY – Gliding bacterium, similar to Flavobacterium and Flexibacter

Natural lab animal **HOST** range of CAR bacillus are Rats, Mice, Rabbits, Goats

Clinical signs of CAR bacillus infection: sometimes nonspecific respiratory signs (dyspnea) AND weight loss

Gross lesions: Resemble those of the primary infections, e.g., Mycoplasmosis, Sendai ETC. 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. Cilia prominent, not lost as with M. pulmonis.

Histopathology of CAR bacillus infection

Cilia on respiratory epithelium may appear slightly basophilic with H&E

Long, slender bacilli among the cilia at any level of respiratory epithelium (nasal cavity to bronchioles) - observed in silver stained sections

Hyperplastic BALT

Rarely, there may also be suppurative bronchopneumonia

5. Pseudotuberculosis in Rodents

Etiology: *Corynebacterium kutscheri*

Hosts: include 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 or tissues with either a large capillary network (lung, liver, and kidney) and/or responsible for filtering blood (synovia and glomeruli). This accounts 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 are usually 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 and immunosuppressive conditions like Stress (poor husbandry, overcrowding, shipping, etc.), Concurrent infections, Irradiation, Immunosuppressive drugs (steroids, cyclophosphamide, etc.), Malnutrition (e.g., pantothenic acid and biotin deficiencies)

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 Pathology:

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

Histopathology: In Lungs, 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.

Lesions may be noticed in any other tissues too (e.g., brain, skin, joints)

Differential Diagnosis

- Localized or disseminated opportunistic bacterial infections: *Staphylococcus* spp., *Streptococcus* spp. (mice), *Salmonella* spp., etc.
- *Streptobacillus moniliformis* (mice) and Tyzzer's Disease.
- Mycoplasmal diseases
- Mycotic pneumonia (Aspergillosis, Mucormycosis, etc.)
- Viral Pneumonia

Pseudotuberculosis in Rabbits

It is common in rabbit and mice.

Naturally acquired latent infections of mice by **Corynebacterium** may be activated by experimental procedure to produce generalized infections which may cause high mortality or result in lesion formation.

Etiology- *Corynebacterium pseudotuberculosis*

This organism produces infection in mice following administration of cortisone or sub lethal dose of X- irradiation. This infection is of considerable importance as this is an in apparent disease.

Resistant mice with avirulent strain are usually naturally affected, this doesn't result into any lesions until a dose of continuous administered following the cortisone treatment

Virulent organism are isolated from the joints, from kidney abscess, myocardium & liver.

Lesions in LIVER consists of sharply circumscribe granuloma in which *Corynebacterium* are found.

5. Yersiniosis (Bubonic Plague)

Causative agent:

Yersinia pastis, *Y. enterocolitica*, *Y. pestis* (*Pasturella pestis*) is the cause of bubonic plague in man, rat & rodents.

It is transmitted by **rat flea**. *Y. pseudotuberculosis* & *Y. enterocolitica* produce enteric & systemic disease which are similar but not identical. Both the disease are described as pseudotuberculosis or Yersiniosis because of gross appearance of visceral lesions

Y. pseudotuberculosis principally causes disease rodents & birds, rabbit & mice.

Cause of Disease –

infection of *Y. pseudotuberculosis* occur as fatal acute septicaemia with few gross specific lesions or a chronic infection.

Gross Lesions-

Discrete white or gray nodules in the liver, spleen & lymph nodes.

Microscopically-

Lesion consist of necrotic coat of pus & bacteria surrounded by a zone of macrophages (epithelioid cells) & fibrous capsule present. Giant cells are absent in the intestine, necrotic lesions are seen.

6. Tuberculosis

It is one of the most prevalent Wasting diseases of man & animal. The causative agent is an acid-fast bacilli of genus *Mycobacterium*. There are three strains: Human strain, Bovine strain, Avian strain (more dangerous).

These are classified as *Mycobacterium tuberculosis* (Human strain), *Mycobacterium bovis* (Bovine strain) and *Mycobacterium avium* (Avian strain).

These organism produces similar lesions closely resembles to each other morphologically but vary in cultural characteristics, Antigen, compliment & pathogenesis to various species, Among the most susceptible animal to tuberculosis are monkey, guinea pig, rabbits.

Monkeys are exposed when captured & placed in contact with infected animals. Guinea pig & rabbit are not usually infected in nature but are very susceptible to tuberculosis include dog, cat, rat & mice. Natural infection is cause in these species & large number of organisms are required to produce experimental infection. A typical mycobacterial species can be distinguished by the culture.

SN	Name of organism	Host	Name of disease
1	M. tuberculosis	Man, cattle, dogs, experimentally G.pig	Tuberculosis
2	M. bovis	Cattle, man, swine, experimentally in G. pig, mice	Tuberculosis
3	M. avium	Birds, swine, fowl, man, experimentally rabbit, mice, G. pig	Avian tuberculosis
4	M. ulcerasis	Man, experimentally in rat & mice	Ulceration of spleen
5	M. fortuitum	Cattle& man experimentally in G. pig, rabbit,& mice	Mastitis, pulmonary disease, local abscess

Grossly- There is white nodular structure with hard consistency .When it is cut it gives gritty sound because of calcification.

Microscopically-

A central calcified & caseated tissue is found. The calcified area stain bluish with H&E stain. While caseous area is faintly bluish or colourless. A zone of necrosis containing the nuclear mass of cell. Surrounding this a zone of epithelioid cells & sometimes mingling with them are Langhan's Giant cells. Surrounding the above is a narrow zone of lymphocytes. Finally zone of young fibroblast which merge with the surrounding tissues.

Material collected- Urine, faeces, lymph node in 10% formalin

Diagnosis- Tuberculin test

7. Botulism

Etiology- *Clostridium botulinum*

It occurs by consuming canned & preserved food& decomposing food materials

Pathogenesis → organism → ingestion → digestive tract → bacteria grows on Bone & decomposing organic matter

→ produce exotoxins in warm & moist condition → ingestion → intoxication & paralysis of muscles → DEATH.

In cattle, due to PICA.

Toxins prevents the formation of Acetyl choline → Paralysis

Incubation period → 5 days

Symptoms: Paralysis of muscles (neck, legs, pharynx); Death due to asphyxia.

P.M. changes→

- 1) Congestion & haemorrhage of mucous membrane.

2) Presence of Gastroenteritis in rat & mice .

Diagnosis →

1. symptoms
2. Differential diagnosis from milk fever & equine encephalomalacia.
3. presence of toxins in feed & tissue
4. Biological test by inoculation of extract in mice & death.
5. Fluorescent antibody test
6. Neutralization test.

8. Mastitis

Inflammation of mammary gland is called as mastitis. Occasionally encountered in bitches or cat. It may be acute or chronic.

Etiology→ it is mostly caused by staphylococcus & occasionally by streptococcus.

Predisposing factors → Trauma to the teat. Infection reaches to mammary gland then to the Lymphatics & rarely by hematogenous route from the distant foci.

Disease generally occur in bitches & cats during lactation & in pseudo pregnancy.

Clinical finding of mastitis → pain, dullness, fever, anorexia, leucocytosis, vomiting, diarrhoea, congestion of visible mucous membrane.

Gangrenous Type → these signs are prominent & animal may die within a few days if surgical operation is not done.

Gross→ Acute mastitis→ mostly affects one mammary gland, sometimes several mammary glands may be affected. Mammary gland is swollen, oedematous, painful, overlying skin become red in colour & tense. In many cases localized softening of gland leads to formation of abscess.

Chronic mastitis→ regional lymph node may be enlarged.

Microscopically→ Acute- Diffused infiltration of polymorph nuclear cells, oedema, hyperemia, in latter stages histopathological appearance is that of an acute abscess.

Gangrenous form→ It shows necrosis with complete loss of parenchymatous structure.

Chronic mastitis- lactating ducts are dilated & lining epithelium is proliferated.

In chronic suppurative mastitis –there is fibrosis, abscess formation, presence of polymorph nuclear cell, plasma cell, lymphocyte and there is disappearance of the gland tissue at the site.

9. Canine Distemper

(Carre's disease or Hard pad disease)

It is a viral disease caused by pantropic virus. It is characterised by **diphasic fever**, acute catarrhal inflammation of various mucous membranes, pneumonia & in some cases skin lesion. In some cases involvement of central nervous system is also seen. Antigenically viruses resemble to that of measles & Rinderpest viruses.

Animal affected – Dog, fox, jackals, & other canines.

Route of infection → Ingestion & some time by inhalation. All excretion & secretions contain the virus. This disease is always complicated by secondary invader.

eg. *Bordetella bronchiseptica* causing pneumonia & *Salmonella* species producing GIT lesions.

Incubation period → 5 days

10. Suppurative Dermatitis

Suppurative inflammation of skin occur when principal constituent of exudate is pus.

Etiology- streptococcus, staphylococcus, *Corynebacterium pyogenes*

Certain chemical can infected into dermis

Route of infection-

1. Incision, laceration, microorganism get entry into the skin.
2. when the defence mechanism impaired by malnutrition.
3. Vascular disturbance and septicemia lesions

Macroscopically- suppurative inflammation may be diffuse or focal or circumscribed.

Diffused inflammation occurs due to deep penetration of pathogen up to dermis and subcutaneous tissue and accumulation of pus occurs.

Focal suppurative inflammation of skin occur when the organism surround the immediate vicinity of wound. And the circumscribed focal lesions appear as abscess. Pustules are seen when the pus is contained within epidermis.

Furuncle/ boil are seen when pus is accumulated in hair follicles or sebaceous gland.

Microscopically-

There is hyperemia and exudation into the area.

There is liquefactive necrosis and presence of pus in area.

Proliferation of connective tissue when the focal suppurative inflammation occurs. Serous tract in also visible to some extent.

11. Streptococcal Infection

(In guinea pig)

Streptococcal infections are frequently encountered in G. pigs. Abscess occur in the lymph nodes of head, neck, and may lead to generalized dissemination of organism to pleura, lungs peritoneum, pericardium or the lymph nodes generally.

Etiology-

Organism most frequently isolated are

Streptococcus epidermicus; *Streptococcus pyogens animalis*

Lesion –

In lymph node the lesion in localized form as usually described as gross abscess of lymph node filled with cream coloured pus.

Lung –reaction in plural and peritoneal surface is fibrinopurulent with thrombosis and necrotic zone in the lungs differential diagnosis from pneumococci infection by identification.

12. Cannibalism (metabolic disease)

It is common vices of poultry.

It is common behavioral problem in poultry. It can be serious problem in the raised up poultry when large population are kept in close confinement.

Cannibalism can occur as toe picking, head or tail, occur in older flocks. The lack of some nutrient may result in cannibalism.

When chicks are fed diet low in protein or deficient in an essential amino acid, some picking often occurs and other factors implicated have been overcrowded, housing condition, insufficient feed and water spaces or too much light in house.

It is controlled by Debeaking, at hatching or at 6 week of age. The upper 2/3 part of beak and lower 1/3 part of beak is removed with the help of debeaker.

13. LISTERIOSIS

Etiology- *Listeria monocytogenes*

A gram positive, rod shaped bacteria. It causes disease in rabbit. In certain rodents, it causes liver infection. Systemic or Septicemic form of Listeriosis is described in rodents also.

Pathogenesis- *Listeria* has the ability to penetrate the epithelial cells (conjunctiva, urinary bladder, intestine) where they multiply & destroy the cells & their, these are phagocytized by macrophages. Transport of the organisms by macrophages and resulting in septicemia.

Lesions – Generalized Listeriosis is most frequently observed in newborn and infants. Most characteristic lesion in this form is **focal necrosis of liver**, less frequently of spleen, lymph node, lung, adrenal gland, myocardium & brain.

Microscopically- Lesions consists of focal necrosis infiltrated with mononuclear cells and some polymorph nuclear cells.

14. Mycoplasmal Infection in Lab Animals

1. Murine Chronic respiratory disease (MCRD) Or Chronic Murine Pneumonia (CMP)

It is a bronchiectasis of rats, **infection catarrh** of rats or rodent pulmonary mycoplasmosis.

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

Clinical signs-

some rats severely 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.

Macroscopically-

Lungs have 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.

15. Trichobezores (hair balls)

Animals having itching skin condition or young ones when kept together may lick each other's ear/tail hairs, that are swallowed & rolled into balls during the intestinal contractions.

Mucous forms a smooth coat over such balls.

Sometimes these balls obstruct the passage of regurgitation of a food balls into the oesophagus and which may be choked.

Often these are found only at PM examination.