RICKETSSIAL DISEASES

Rickettsiae are minute, Gram-negative, obligate intracellular parasites. The rickettsiae and chlamydiae, in contrast to other bacteria, only multiply within cells.

Species comprising the genus Rickettsia are divided into three groups based on their effect in humans: 1. Typhus group, 2. Spotted fever group, and 3. Scrub typhus group. These organisms are spread by arthropods, and although mice, rats, squirrels, and rabbits are susceptible. Rickettsiae are transmitted from One vertebrate species to another by arthropod vectors in which transovarian transmission is common.

Rickettsia species have a predilection (affinity) for growth in **endothelial cells** and **vascular smooth muscle cells**, which accounts for most lesions. They cause a **vasculitis** which may be complicated by **thrombi and haemorrhages.**

Pathologically, the main lesion is a **vasculitis of capillaries, arterioles, and venules**. The changes comprise endothelial hypertrophy and hyperplasia, cuffing with leukocytes, and thrombosis. This may lead to necrotic foci in the skin, and in visceral organs as well.

Genus / Specie	Disease Caused	In HOST	Through VECTOR	Imp Sign & Lesions	
I. Typhus Group					
Ricketssia prowazekii	Typhus Fever (Epidemic Typhus)	Humans	Louse	--	
II. Typhus Group					
R. rickettsii	Rocky Mountain Spotted fever	Dogs (rarely)	Ticks		
R. conorii	Boutonneuse Fever	Dogs (rarely)	Ticks		
III. Scrub Typhus Group					
R. tsutsugamushi	Tsutsugamushi Fever	Monkeys	Mites		
Rochalimaea quintana	Trench Fever	Monkeys	Louse		
Neorickettsia helminthoeca	Salmon Disease of Dogs (Neorickettsiosis)	Dogs, foxes, bears	Fluke		
Coxiella humetii	Q - Fever	Cattle, Sheep, Goat, Birds	Ticks, Aerosol Transmission		
Cowdria ruminantium	"Heartwater" or Cowdriosis	Cattle, Sheep, Goat	Ticks		
Ehrlichia phagocytophila	Tick Borne Fever	Cattle, Sheep, Goat	Ticks		
Ehrlichia risticii	Potomac Horse Fever	Horses	Unknown		
Ehrlichia equi	Equine Ehrlichiosis	Horses	Ticks		
Ehrlichia bovis	Bovine Ehrlichiosis	Cattle	Ticks		
Ehrlichia canis	Canine Ehrlichiosis	Dogs	Ticks		
Cytoecetes ondiri	Bovine Petechial Fever (Ondiri Disease)	Cattle	Unknown		

HEARTWATER (COWDRIOSIS)

This disease is important in the ruminant population (cattle, sheep and goats) of the African continent. It is named after its Characteristic Lesion: **Hydropericardium**.

The causative agent, ***Cowdria ruminantium*** (previously *Rickettsia ruminantium),* is an intracellular parasite transmitted by ticks. Cattle, sheep, goats, and wild ruminants are susceptible, The disease may be peracute and fatal, or inapparent.

Usually, there is FEVER characterized by signs of Central Nervous Dysfunction, such as unsteady gait, twitching of muscles, circling, aggressive ebehaviour, convulsions, and coma.

The characteristic lesions include Hydropericardium, Pulmonary Oedema, Hydrothorax, Ascites, And Lymphadenopathy. Microscopically, tissues are oedematous, and there is generalized perivascular leukocytic infiltration.

The rickettsia, a tiny, rod-shaped, often diplococcoid organism, can be demonstrated with Giemsa's stain in endothelial cells of the jugular vein, vena cava, renal glomerular capillaries as well as in reticulo-endothelial cells and neutrophils.

EHRLICHIOSIS

Ovine and Bovine Ehrlichiosis ("Tick-borne Fever")

The disease is caused by a rickettsial organism called ***Ehrlichia phagocytophila*** *(Cytoecetes phagocytophila, Rickettsia phagocytophila).* It is transmitted by Tick *Ixodes ricinus.* The main clinical finding is fever of several days duration associated with **Lymphopaenia, Neutropaenia and Thrombocytopaenia**.

Potomac Horse Fever (Equine Monocytic Ehrlichiosis)

This disease is caused by *Ehrlichia risticii.* The signs are initially characterized by fever, followed by anorexia, colic, and diarrhoea. The fever can be biphasic. There is Leukopaenia and thrombocytopaenia. The organisms are visible in **circulating Monocytes**.

There are no diagnostic lesions. Usually, the caecum and colon are haemorrhagic, and often eroded or ulcerated & Mesenteric lymph nodes are enlarged & haemorrhage. Organisms occur in the **colonic epithelium, and macrophages** in the lamina propria.

Equine Ehrlichiosis

The disease is caused by *Ehrlichia equi*. The infection is more serious in horses over 3 years of age. The clinical signs include fever, anorexia, oedema of the legs, and ataxia.

Clinical laboratory findings include leukopaenia (Lymphopaenia), thrombocytopaenia, increased plasma icterus index, decreased PCV.

Gross lesions include petechiae, ecchymoses, and Oedema in muscles, fascia, and subcutis. Jaundice and Orchitis are common. The microscopic lesions consist of arteritis and phlebitis, particularly in muscles and fascia. The blood vessels undergo necrosis as well as swelling of endothelium and smooth muscle cells.

The organisms appear as granular bodies (spherical, single or multiple) in **NEUTROPHILS** and **EOSINOPHILS**.

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Canine Ehrlichiosis (Canine Rickettsiosis)

This disease is caused by *Ehrlichia canis* and is seen in India. The disease is transmitted by the tick *Rhipicephalus sanguineus.* The organism multiplies in reticulo-endothelial cells, lymphocytes, and monocytes, and may be seen in stained smears of peripheral blood or tissue impressions.

The life cycle of the parasite is not yet completely understood. However, three intracellular forms are recognized:

- Initial bodies are small, spherical structures. These develop into larger bodies described as Mulberry bodies or morulae.
- Mulberry bodies or morulae: The morula is thought to dissociate into small granules called Elementary bodies
- Elementary bodies

The disease is usually mild, except in young puppies or when complicated by another disease, such as infection with *Babesia canis.* In Concurrent infections, the signs of babesiosis usually overshadow those of ehrlichiosis. In Asia, the disease has been called, "**Canine Tropical Pancytopaenia**".

Signs

- Clinical signs include recurrent fever, serous nasal discharge, photophobia (intolerance to light), vomiting, splenomegaly, and signs of central nervous system derangement.
- Leukopaenia, thrombocytopaenia and anaemia, with increased levels of gamma globulin in the serum, are clinical features observed late in the disease.

Lesions

Haemorrhage in the mucosae of the gastrointestinal and urogenital tracts and kidneys, oedematous and haemorrhagic enlargement of most lymph nodes, and oedema of the Limbs.

Microscopically, widespread perivascular accumulations of lymphoreticular and plasma cells, particularly in the meninges, kidneys, liver, and lymphopoietic tissues. The bone marrow is usually hypoplastic. Degeneration and acute necrosis are common in the centre of lobules of the liver. In the central nervous system, haemorrhages and plasma cell accumulations occur in the meninges.

Ehrlichia platys has also been identified recently as a cause of disease in dogs. It causes severe but transient thrombocytopaenia.

Diagnosis

- Inclusions are found in Monocytes, with associated Leukopenia & Thrombocytopenia.
- Confirmed by identifying the organisms in sections of tissues in fatal cases.
- Serological identification by an indirect immunofluorescence test.

Diseases caused by Anaplasmataceae

The Family Anaplasmataceae (order Rickettsiales) now contains organisms grouped in five genera. Of these only three are important, namely, Anaplasma, Haemobartonella, and Eperythrozoon.

These organisms are obligate parasites found on or within erythrocytes, or free in the plasma of domestic and wild animals. The organisms may occur in short chains or irregular groups within erythrocytes or in plasma. They are Gram-negative, multiply by binary fission, and are transmitted by arthropods. ANAEMIA is the usual clinical sign in infected animals.

ANAPLASMOSIS

The organisms which cause anaplasmosis are at present grouped into a single genus - Anaplasma. Three species are of pathogenic importance:

1. *Anaplasma marginale (cattle & buffalo)*
2. *A. centrale,* and
3. *A. ovis (Sheep & Goat)*

With Giemsa stain, these organisms appear as dense, bluish-purple, homogeneous round structures within erythrocytes near the margin or near the centre of the cell.

A. marginale parasitizes the red cells of **cattle and buffaloes**, and causes disease of worldwide distribution. The infection results in overt (visible) disease only in **Adult Animals** (similar to babesiosis). *A. centrale* also affects cattle but causes mild anaplasmosis.

A marginale, which causes severe anaplasmosis, is a tiny, spherical body, found within the cytoplasm of erythrocytes, near the periphery of the cell. It is best demonstrated in blood smears with Giemsa's stain.

Four developmental stages of Anaplasma are recognized in infected erythrocytes:

1. Early stage, consisting of "**initial bodies**", the infective form,
2. Mixed population with marginal and initial bodies,
3. Vigorous growth and transfer, and
4. Massive multiplication with a predominance of **marginal bodies**.

The organisms reproduce by binary fission and pass through the four stages of development after penetration of the erythrocyte by initial bodies. Then, they are transferred to other mature erythrocytes by direct contact between cells. The initial body is spherical and surrounded by a double membrane. The marginal body contains up to six subunits (initial bodies), and is surrounded by a single membrane.

Transmission

The infection can be transmitted to a normal animal by carrying over a minute amount of blood. It can occur by the use of improperly sterilized phlebotomy (opening of a vein, venesection) needles, or by dehorning or castration without previous aseptic precautions. Bites of Ticks *(Boophilus annulatus etc)* are the most important vectors and sometimes Biting flies (Tabanus species).

Pathogenesis

Anaplasma are **obligate intra-erythrocytic** bacteria-like protozoa-like organism. They infect mature erythrocytes by an endocytic process called "endocytosis" ('endocytosis' is uptake of extracellular substances by cells), and reproduce by binary fission to produce 2-8 infective initial bodies which leave by exocytosis (opposite of endocytosis) to infect other erythrocytes. The number of infected erythrocytes doubles every 24-48 hours, and the infection becomes patent (visible) 2-6 weeks after infection. At least 15 % have to be parasitized before there is clinical disease.

Parasitized erythrocytes are removed by phagocytosis in the reticulo-endothelial system with release of acute-phase inflammatory reactants and associated Anemia. The first appearance of organisms in the blood coincides with a fall in the haematocrit and erythrocyte levels, and the appearance of immature erythrocytes in blood smears and the development of Fever. The degree of anaemia varies widely in young cattle up to 3 years of age, but is always severe in adults. Cattle that survive the disease become carriers, and serve as reservoirs of infection.

Signs

- Fever & Anemia manifested by weakness, pallor (paleness) of mucosae, increased respiration, jaundice, decreased red cell count and decreased haemoglobin.
- Anaemia results from increased destruction of parasitized erythrocytes by the reticulo-endothelial system and not by haemolysis. Therefore, haemoglobinuria is not seen.
- Sometimes, muscular trembling, anorexia, and excessive salivation.

Gross Lesions

- ✓ Severe anaemia, with pallor (paleness) of the tissues and sometimes with Jaundice.
- ✓ The spleen Enlarged; Liver is also enlarged, has round edges, and is yellowish in cases with jaundice. Grossly enlarged distended Gallbladder.
- ✓ Petechiae may be seen on the pericardium, and catarrhal inflammation in the gastrointestinal tract.

Microscopic Lesion:

- ✓ Hyperplasia of the bone marrow, and extramedullary haematopoiesis in the spleen and other organs.
- ✓ Anaplasma organisms can be demonstrated with difficulty in erythrocytes in tissue sections.
- ✓ Demonstration of the organisms in the blood smears is highly variable. Before the onset of anaemia, majority of erythrocytes may harbour organisms, but with sudden removal from the circulation, their numbers decrease. Immature erythrocytes (reticulocytes) which enter into the circulation in response to anaemia, are resistant to the parasites.

Diagnosis

- ✓ Diagnosis is made on the basis of clinical signs, and demonstration of Anaplasma organisms in erythrocytes. In Giemsa stained blood-films, Anaplasma are seen as small, round, dark red 'inclusion bodies' within Red cells which characteristically lies at 'Outer Margin' mostly.
- ✓ The Agglutination Tests, Complement-fixation test can be used for the detection of clinically silent carriers.

Feline Infectious Anaemia

(Feline Haemobartonellosis)

Disease of domestic and wild cats is caused by *Haemobartonella felis.* Iinfection occurs only as concurrent infection with feline leukaemia virus or under immune-supression.

They are best seen in blood smears stained with Giemsa or Wright stain. The organisms are seen as small coccoid, ring-shaped, or rod-shaped bodies on erythrocytes of affected cats.

Clinical Signs

- ✓ Fever, Anorexia, Depression
- ✓ Macrocytic, Haemolytic Anaemia - revealed by pale, sometimes icteric, mucous membranes, weakness, and characteristic blood picture in which haemoglobin and packed cell volumes are severely decreased.

- ✓ Macrocytosis (having large erythrocytes) and Anisocytosis (having erythrocytes of varying size) are usually prominent features. In the early stages, Nucleated Erythrocytes are present in large numbers. Reticulocytes (immature erythrocytes) are also increased in number, and some of them may contain *H. felis.*

Gross Lesions:

- ➢ The lesions are those of haemolytic anaemia.
- ➢ Jaundice is a feature in acute cases.
- ➢ The spleenomegaly - is enlarged many times, and its cut surface bulges.

Microscopic Lesions:

- ➢ Congestion and extramedullary haematopoiesis; bone marrow is usually solidly red in the long bones; Lymph Nodes Swollen.
- ➢ Haemoglobin stains the urine in bladder, and haemorrhages on serous surfaces.
- ➢ Liver reveals fatty change, and also central or paracentral necrosis.

Eperythrozoonosis

The genus Eperythrozoon is at present grouped in the family Anaplasmataceae. The organisms are similar to Haemobartonella species and are often difficult to differentiate from them. The main features which differentiate Haemobartonella from Eperythrozoon are that Eperythrozoa occur both in the erythrocytes and plasma & mostly in ring-form, whereas Haemobartonella organisms are rarely found in the plasma and also rarely in the ring forms.

Eperythrozoon suis is associated with disease in PIGS, and when parasitaemia is high, produces clinical signs of Anaemia - a disease known as **"ictero-anaemia".** *Eperythrozoon ovis* causes infection in Sheep (associated with haemolytic anaemia).

Signs

- ✓ Clinical disease occurs only in sheep and pigs. Infection is in **Young Animals**. The natural disease in pigs is called "**ictero-anaemia**", and somewhat resembles anaplasmosis of herbivora.
- ✓ In SHEEP, the symptoms begin with FEVER (104°-107° F), accompanied by depression and weakness. The total red cell count drops suddenly to 1-2 million/mm3, haemoglobin is decreased to 2-4 g/dL, and the packed red blood cell volume falls between 4-7%. Haemoglobinuria has been noticed in sheep, which indicates that anaemia is haemolytic.

- ✓ In cattle, the most common sign of eperythrozoonosis is oedema of the hind limbs and teats.

Gross Lesions:

- ➢ Haemolytic anaemia, Blood is thin and watery.
- ➢ Jaundice - Liver is yellowish brown- & Gallbladder contains thick gelatinous bile. Hydropericardium and Ascites in some cases.
- ➢ Petechiae may be seen in the mucosa of the urinary bladder.

Microscopic Lesions:

- ➢ In Bone marrow which is hyperplastic.
- ➢ Liver shows some fatty change and central and paracentral necrosis of lobules.

Diagnosis

Eperythrozoonosis must be differentiated from Anaplasmosis, Haemobartonellosis, Babesiosis, and other haemolytic anaemias.

Eperythrozoon organisms in blood smears stained with Giemsa are seen as tiny pleomorphic structures (i) within the erythrocytes, (ii) lying on their surface or (iii) free in the plasma. The organisms are pale purple to pinkish-purple and are **mostly ring-shaped.** One to a dozen organisms may be present in a single red blood cell.