Haematopoietic System

Anemia of blood cell parasitism

- **Babesiosis**
- **Cytauxzoonosis**
- **Hepatozoonosis**
- **Anaplasmosis**
- ***Mycoplasma (Eperythrozoon) suis***
- **Hemotrophic *Mycoplasma* infection (hemobartonellosis)**
- **Ehrlichiosis**

Babesiosis

- The protozoan Babesia parasitizes the erythrocytes ~a wide range ~mamreals including humans, and there is normally quite strict host specificity.
- The agent is transmitted by ticks.
- Natural transmission is largely transovarial, that is, the adult female becomes infected, and, depending on the babesial and tick species, the ensuing larval or nymphal generation then transmits the infection to a susceptible host.
- Transtadial transmission occurs in three-host ticks, infection being carried through a molt off the host, permitting transmission to the next host encountered.
- There is no evidence for transmission by biting insects or contaminated instruments (in contrast to the situation with Anaplasma infection), but infection is transmitted by experimental blood inoculation.

Babesiosis

- Cattle➔ B bovis (B. argentina, B. berbera, B. Colchia)
- B. divergens B. bigemine, B. mojor.
- B. occultans, B. ovata, B. jakimavi
- Small ruminant➔B. ovis, B. motosi, B. crossa (goat)
- Dog➔ B. canis
- Cat➔ B. felis
- Schwein➔ B. trautmanni
- Mouse, rat➔ B. microti, B. Hylomysci, B. Rodhaini, B. microti

Babesiosis

- Pathogenic effects are, in most infections, related directly to lysis of red cells by emerging parasites but other mechanisms, including sludging of infected red cells, hemoglobinuric nephrosis, and release of vasoactive peptides, contribute to the signs and are responsible for death.
- The severity of many of the anemias caused by parasites of blood cells is enhanced by splenectomy.

Bovine Babesiosis- Babesia bovis

- ***Babesia*** *bovis (= B. argentina, B. berbera, B. colchica) is probably the most important cause of the* ***"tick fevers"*** *of cattle.*
- Young cattle have pronounced resistance to severe infection.
- Immunity passively acquired from colostrum by very young calves may persist for up to 9 months of age.
- *Strong acquired immunity follows overt infection*, and may persist indefinitely in the absence of latent infection, although the latter is usual. or in areas of greatly fluctuating tick populations.
- Infection by B. boris causes severe febrile illness which begins about 2 weeks after exposure to ticks.

Bovine Babesiosis- Babesia bovis

- The animal may become extremely ill before severe anemia, parasitemia or hemoglobinuria are apparent, and sometimes the clinical picture is dominated by nervous derangement, likely associated with the tendency for parasitized red cells to sludge in cerebral capillaries as well as in the microvasculature of the adrenal and kidney of splenectomized animals.
- **The clinical picture** is characterized by weakness, fever, hemoglobinuria, and anemia; the latter is more severe in animals surviving more than a week.
- The parasite is never numerous in circulating blood, rarely being seen in more than 5% of circulating erythrocytes.

Bovine Babesiosis- Babesia bovis

- Parasitized erythrocytes are much more likely to be found in smears of blood squeezed from cut skin capillaries than in routine blood samples from large veins.
- Photosensitization may occur in the convalescent phase, probably due to overload of the phylloerythrin-conjugating sequence by bilirubin derived from hemolysis.
- ***The most typical* postmortem findings *are those to be expected of an acute intravascular hemolytic crisis.***
- There **is anemia, variably severe jaundice and hemoglobinuria**.
- **The kidneys** are deep red-brown throughout as a result of hemoglobin staining and intense congestion of capillaries.

Bovine Babesiosis- Babesia bovis

- There is capillary congestion of most organs, **the spleen** is always grossly swollen, soft and dark.
- **The liver** is also acutely congested and may be heavily stained with bile pigment.
- **The gallbladder** is distended with thick, dark viscous bile.
- **In some acute case**s, **the lungs** are congested and edematous and the larger airways contain stable foam. Recent hemorrhages are common in the thoracic serosal membranes.

Bovine Babesiosis- Babesia bovis

- **The most characteristic macroscopic feature of B. bovis infections is striking, uniform congestion of the gray matter throughout the brain, imparting to it a dramatic, deep pink color (the cerebral flush), which contrasts strongly with the white matter**; the latter is often stained a faint yellow by unconjugated bilirubin.
- **In some peracute cases**, there is minimal hemoglobinuria or jaundice,
- But the brain still shows the characteristic capillary congestion

from which imprint preparations are usually diagnostic, with many intraerythrocytic organisms present.

Bovine Babesiosis- Babesia bovis

Histologically, there is thickening and congestion of pulmonary capillaries with hemosiderin in intravascular macrophages.

- Kidneys and liver have the histological lesions to be expected of an acute hemolytic disease.
- There is variably severe hemoglobinuric nephrosis with severe congestion, focal hemorrhage and hemosiderin in tubular epithelium, and diffuse vacuolar degeneration with interstitial mixed mononuclear cell reaction.
- There is hepatic periacinar congestion uninfected red cells, and vacuolar degeneration in midzone and periacinar hepatocytes, accompanied by canalicular cholestasis.

Bovine Babesiosis- Babesia bovis

- There is hemosiderin accumulation in both hepatocytes and Kupffer cells, and the latter contain both infected and noninfected red cells.
- Lymphocytes and plasma cells accumulate in portal areas and around central veins.
- ***Parasitized erythrocytes may be seen in vessels in all tissues***, but
- they are particularly common in interstitial capillaries in the kidney, in the gray matter of the brain, in the heart, and especially in skeletal muscle; in these locations, nearly every red cell packed into the distended capillaries appears to contain 1-2 parasites.

Bovine Babesiosis

- Animals that die with peracute disease have necrosis of lymphocytes in germinal centers of node and spleen, while there may be some degree of recovery in animals surviving a week and general depletion of lymphocytes in those dying after protracted illness.
- Characteristic changes in the medullary region of nodes include sinus histiocytosis with extensive erythrophagocytosis.
- The histology of the spleen is often unhelpful, the organ being so suffused with intra- and extracorpuscular hemoglobin that evidence of erythrophagocytosis is obscured.

Bovine Babesiosis- Babesia bovis

- There is little extramedullary hematopoiesis in liver or spleen.
- **The bone marrow** has an erythroid shift and, in animals that survive the acute stage, there is a strong reticulocytosis and slow recovery in red cell numbers.
- There is mild hemosiderin increase, suggesting that marrow is also a site of erythrolysis.
- **Babesiosis results in metabolic disease more complex than a simple syndrome of intravascular hemolysis.**

Bovine Babesiosis- Babesia bovis

- **Metabolic alkalosis occurs in *B. bovis* infections, whereas acidosis is the rule in severe *B. canis* infections.**
- *The result of these profound metabolic upsets is a syndrome of circulatory failure, likely due to extensive plugging of microvasculature by sequestered red cells.*

Bovine Babesiosis- Babesia bigemina

- **Babesia bigemina** infection may be transmitted by the same tick as **B. Boris**.
- Babesia bigemina, however, usually causes a much less severe syndrome, notwithstanding the fact that parasitized erythrocytes circulate early, sometimes before clinical signs are apparent, and in much greater numbers than they do in B. boris infection.
- B. bigemina causes erythrocyte destruction.
- There are few of the vasoactive and red cell adherence effects.
- Thus the anemia in severe cases may be severe before the animal becomes ill and, as in any case of severe anemia, death may occur suddenly.

Bovine Babesiosis- Babesia bigemina

- **The pathology of B. bigemina and B. boris infections is similar, except that in B. bigemina infection there is little capillary congestion of the viscera and none of the cerebral gray matter, the presence or absence of the cerebral flush being the most reliable gross feature for differentiating the two infections.**
- **Pulmonary edema** may be more often seen in fatal cases of B. bigemina infections, probably because the greater severity of anemia causes **terminal left ventricular failure.**
- Neural findings are not seen.

Differential diagnosis of bovine babesial infections

- Babesia bovis and B. bigemina may be distinguished from one another in well-prepared blood smears but erythrocytes parasitized **by B. bovis are rare in jugular blood, or even in blood from deep skin punctures.**
- Babesia bigemina-containing erythrocytes, on the other hand, are quite numerous in circulating blood while clinical signs are severe.
- The preference of B. bovis for capillaries of organs such as kidney, heart, brain will in most cases serve to distinguish the infections.
- Although *B. divergens* is small and resembles *B. bovis* in size, and B.*major* is as large as *B. bigemina,* the pathology and pathogenesis of the disease produced by these organisms is apparently very similar to that produced by *B. bigemina*.

Canine babesiosis

- Babesia canis is transmitted by different ticks in different countries.
- **Clinically;** Mildly affected animals develop *anemia and fever,* and are lethargic and have a poor appetite.
- Icterus and red urine are not seen.
- They recover after a clinical course of a few days.
- More severe cases show a wide variety of signs, including severe depression, drooling, vomiting, jaundice and hemoglobinuria, mucosal petechiae and congestion, ulcerative stomatitis, and angioneurotic edema of the head, legs and body.
- Anorexia and weight loss may be persistent.
- A few dogs may show nervous signs that are associated with erythrocyte sludging in cerebral capillaries and cellular infiltration of the meninges.
- **Acidosis is particularly important in this disease.**

Canine babesiosis

Grossly, there is staining of tissues both with bilirubin and hemoglobin.

- The kidneys are dark brown and there is copious thick bile in the gallbladder and splenomegaly.
- There is evidence of vascular injury in the form of hemorrhages and edema, which may be severe in the lung.
- Parasitized erythrocytes may be found plugging capillaries in smears and sections of cerebral cortex.
- *Disseminated intravascular coagulation* is a consistent occurrence in severe *B. canis* infection, and is presumably related to, and is likely to aggravate, the hemolysis and the vascular damage.
- Microthrombi can be demonstrated in many tissues.
- **Babesia canis and B. bovis infections clearly resemble** one another in the severity of the syndromes and the involvement of pathogenetic mechanisms other than simple hemolysis.

Anaplasmosis

- There are three species of the genus Anaplasma, order Rickettsiales:
- **A. marginale and A. centrale** are infectious **for cattle;**
- **A. ovis** infects **sheep and goats.**
- These parasites are now classified with the Rickettsiales notwithstanding that the disease produced, and its mode of transmission, have much in common **with babesiosis.**
- Division occurs by binary fission.The organisms are spherical or oval, from 0.3 to 1.0 cm in diameter, and situated in the erythrocytes, usually near the margin (A. marginale and A. ovis).
- Anaplasmosis in **cattle** is probably transmitted under field conditions by *Dermacentor* and other ticks, as well as by *Boophitus microplus,* and may be transmitted mechanically by blood-sucking flies.

Anaplasmosis

- Mechanical transmission has resulted from the careless use of hypodermic needles during immunization procedures and bleeding, and by instruments used for dehorning, castration and ear tagging.
- The disease can be transmitted by blood from an infected animal, although in the chronic carrier state the level of parasitism is very low and organisms are difficult to find in the peripheral blood.
- **Unlike Babesia, the intraerythrocytic antigens are relatively easily separated from red cells and form the basis of an efficient diagnostic test based on complement fixation**.
- Much of what has already been said of babesiosis is applicable to anaplasmosis.

Anaplasmosis

- Young animals are susceptible to infection but relatively resistant to the disease.
- The natural incubation period of anaplasmosis is 1-3 months or longer, and the disease which follows closely resembles babesiosis.
- **One important distinction is that hemoglobinuria does not occur in anaplasmosis as the destruction of erythrocytes occurs intracellularly rather than intravascularly.**
- ***Clinically;*** *Animals with acute anaplasmosis have mucosal pallor, icterus, depression, and occasionally incoordination.*
- The animals resist movement and have a rapid heart rate and increased respiratory rate.

Anaplasmosis

- Urine may be brown but not red.
- The clinical syndrome in cattle is usually subacute illness, with variable fever, anemia, weakness and ill-thrift.
- The severity of the disease is related to the proportion of the erythrocyte mass destroyed, which may equal 70%.
- At a variable period prior to the onset of clinical signs, usually 5-10 days, the *Anaplasma* organisms appear in red cells in the peripheral blood.
- Since the organisms continue to appear and increase in number, **it is apparent that in the acute phase the parasitic multiplication proceeds more rapidly than removal of parasitized red cells in the monocyte-macrophage system.**

Anaplasmosis

- The erythrocyte count in acute disease drops to as low as 1×10^{12}/L and the hemoglobin to 30-40 g/L.
- The hematocrit tends to stabilize at 0.10-0.15 L/L, at which time there is rapid ongoing destruction with a competent marrow response resulting in **a macrocytic, mildly hypochromic, anemia.**
- At this time, as many as 50-60% of the red cells may be parasitized.
- *The strong erythroid response to anaplasmosis, which does not occur in babesiosis, is possibly due to the intracellular rather than intravascular destruction of erythrocytes,* thereby avoiding hemoglobinuria and allowing recycling of iron and proteins.
- **Characteristically, anemia is accompanied by neutrophilic leukocytosis.**

Anaplasmosis

- Chronicity results in apparent recovery or **chronic disease** with debility and **nonresponsive normochromic normocytic anemia** in which the *Anaplasma* bodies are rarely observed in the peripheral blood.
- **There are no pathognomonic gross lesions of anaplasmosis**.
- There is pallor of all tissues and mild icterus, with relatively good body condition in those animals dying acutely and cachexia in chronic cases.
- The lungs are pale and discolored and may have bullous emphysema if there has been severe terminal dyspnea.
- There are frequently ecchymotic hemorrhages on the epicardium, and the heart is flabby and dilated.

Anaplasmosis

- The liver is anemic and icteric and the gallbladder is usually distended.
- The spleen is enlarged, turgid and congested in acute cases and firm, dark red and fleshy in chronic ones.
- The enteric tract is unremarkable and the bladder may contain deeply bilirubin-stained urine.
- The marrow cavity is variably expanded, depending on the stage of the disease, and may have serous atrophy with chronicity.
- The tissue changes in anaplasmosis are similar to those in babesiosis, although hemosiderosis is much more marked in anaplasmosis.

Anaplasmosis

- Anaplasma centrale produces a natural infection of cattle, but is also employed, being a mild pathogen, as an immunizing agent against A. marginale in some areas of endemic infection.
- It usually produces a mild disease, although sometimes it can be severe, with fever and anemia but no icterus.

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Mycoplasma (Eperythrozoon) suis

- **Eperythrozoon wenyonii** cattle
- " **ovis** sheep and goat
- " **suis** swine
- " **parvum** swine

- The disease is enzootic.
- It is transmitted in the pig by lice ; in sheep and goat by blood-sucking insect; in cattle by tick.
- CATTLE➔ It is severe in helminth invasions. It is mild in appearance or asymptomatic. Splenomegaly occurs.
- SHEEP GOAT➔ Mild fever, icteric hemolytic anemia, hemoglobinuri, Anisocytosis in the blood, basophilic bodies, leukocytosis
- SWINE➔ high fever, mild or severe icterus.

Mycoplasma (Eperythrozoon) suis

- **Pathological Findings**
- Anemia, icterus
- Spleen: swelling and Splenomegaly
- Liver: Fatty degeneration,
- Gallbladder: bile in gelatinous appearance
- Hydropericardium
- Ascites
- Bladder: Mucosal petechia
- Bone marrow: Red bone marrow increases

- **Microscopic**

- Fatty degeneration; sentral necrosis and the hemosiderin in the liver
- Hyperplasia in bone marrow

Hemotrophic Mycoplasma infection (Haemobartonellosis)

- Hemotrophic mycoplasma are found in **cattle, goats, cats and dogs**, and in each species they are capable of causing hemolytic anemia.
- ***Haemobartonella bovis* of cattle**
- **H muris of rat and mouse**
- **H. Canis of dog**
- **H. Felis of cat**

Hemotrophic Mycoplasma infection (Haemobartonellosis)

- M. haemofelis is responsible for the natural disease "**feline infectious anemia."**
- The organism is ubiquitous, but the uncomplicated disease is unusual.
- Hemotrophic Mycoplasma is an opportunistic infection.
- One of the most common causes of reduced resistance in the cat is an occult lymphoma.
- Infection is presumably spread by fleas and other biting insects and is an important infection in cats.
- Males are at twice the risk of females of developing the clinical disease, and the risk of infection increases with age and in the spring.
- Direct contact is thought to be important in transmission.

Feline infectious anemia

- The most common signs in cats are lethargy and anorexia for a short period of time.
- Often there is some other history of stress including transport or trauma resulting in sepsis.
- The anemia is severe and appears suddenly; the erythrocyte count may drop as low as 2 × 109/L with hemoglobin levels of 20-60 g/L and hematocrit of 0.06-0.23 L/L.
- The anemia is responsive and macrocytic and mildly hypochromic.
- Diagnosis is dependent on identification of the rod- and ring-shaped organisms that are characteristically arranged in chains around the periphery of the erythrocyte membrane.

- There may be leukopenia due to marrow failure, or neutrophilic leukocytosis due to intercurrent sepsis, or leukocytosis of leukemia.
- Icterus is inconstant and generally mild.
- Since hemolysis is largely intracellular and not intravascular, the urine may be dark if the animal is icteric but hemoglobinuria is not a feature of the disease
- **The gross examination** is dominated by pallor with or without mild icterus, and usually splenomegaly and mild generalized lymphoid hypertrophy.
- There is usually reddening of the femoral marrow.
- Histologically there is splenic sinus hyperplasia and moderate generalized follicular hyperplasia.
- In uncomplicated cases, the marrow is hypercellular with an erythroid shift.

Ehrlichiosis

- Ehrlichieae of **the family Rickettsiaeceae** includes three species, **Ehrlichia canis, E. bovis and E. ovina**, which produce disease in dogs, cattle and sheep respectively.
- A similar agent has been described **(E. equi)** which causes disease in the horse.
- The agent infecting the horse causes cytoplasmic morulae in granulocytes, whereas that infecting the dog causes inclusions in lymphocytes and monocytes.
- A tick-borne anemia of dogs caused by Rickettsia canis has been known for many years.
- Subsequently a disease which occurred among introduced breeds in Southeast Asia became known as **canine tropical pancytopenia.**

Ehrlichiosis

- Unlike the disease in horses, which is selflimiting, the disease in dogs is characterized by fatal or protracted course in dogs of all ages.
- Although included here with the infectious hemolytic diseases, canine ehrlichiosis when fully expressed is a symptomatic aplastic pancytopenia with identification of the leukocyte inclusions giving specificity to the disease syndrome.
- Ehrlichiosis in German Shepherd Dogs often produces a severe hemorrhagic syndrome.
- The disease is characterized by an incubation period of 10-20 days followed by a febrile phase with variable pyrexia, anorexia, weight loss, depression and weakness.
- Some animals die at this acute stage, but most enter a subclinical stage that is of variable duration but generally ends in about 90 days with either epistaxis and generalized hemorrhage or pancytopenia with progressive renal failure.

Ehrlichiosis

- The anemia is characterized by moderate anisocytosis and polychromasia, with increasing poikilocytosis and loss of polychromasia as marrow failure progresses.
- There is marked variation of platelet size following the first attack of thrombocytopenia, but signs of production decrease terminally.
- **Diagnosis** *is based on hematological changes and the presence of the rickettsial inclusion bodies in the cytoplasm of lymphocytes and monocytes.*
- **Grossly,** there is *emaciation with subcutaneous and interstitial edema.*
- A consistent finding is epistaxis with petechial hemorrhages on gingiva and conjunctiva.

- Large subcutaneous hemorrhages are present and there are hemorrhages on the serosa and mucosa of the intestinal tract and on the bladder mucosa.
- There is mesenteric lymphadenopathy with irregular enlargement of other nodes and medullary discoloration due to hemorrhage.
- The liver is of normal size and consistency with pallor, focal areas of hemorrhage and an anemic periacinar pattern.
- The spleen is of normal size, or slightly enlarged and firm with congestion and obscured splenic corpuscles.
- Typically hemorrhages are found on the surface of the heart and in the myocardium, and the lungs are edematous and mottled, often with focal areas of hemorrhage associated with sepsis.

- The postmortem diagnosis is best made by demonstration of morutae in the cytoplasm of pulmonary macrophages obtained from direct imprints of the cut surface of fresh lung.
- There are focal subcapsular hemorrhages on the kidney with mild yellowing of the medulla.
- **Histologically,** there is lymphoplasmacytic cuffing of veins in the central nervous system and around many vessels in other organs.
- The liver has panlobular atrophy of cords with sinusoidal dilation, focal plasmacytic cuffing in portal areas, and ischemic periacinar degeneration.
- There is mild alveolar septal thickening with hypercellularity mononuclear cuffing around pulmonary vessels.

- In lymph nodes, the germinal centers are depleted, the paracortical areas are atrophic and there is marked medullary cord plasmacytosis and sinus histiocytosis, often with prominent erythrophagocytosis.
- Glomeruli are often ringed with aggregates of lymphocytes and plasma cells, and there are focal interstitial infiltrates of mononuclear cells.
- The bone marrow is hyperplastic early in the disease, with few fat cells and dense cellular packing, and aplastic terminally with dilated sinusoids and loci of hemorrhagic infarction.
- **The disease in the dog has been called radiomimetic because of the prominent destruction of proliferating cell populations.**

Ehrlichiosis in horses

- The incubation period varies from 1-9 days with the onset characterized by pyrexia, depression and complete anorexia.
- Edema of the ventral midline, limbs and prepuce persists for 1-2 weeks.
- There is leukopenia, thrombocytopenia, elevated plasma bilirubin and granular inclusion bodies.
- Gross lesions include petechial hemorrhage, ecchymoses and edema, particularly in subcutaneous tissues and on the ventral abdominal wall.
- There is often increased fluid in serous cavities as well as icterus, emaciation, and secondary bacterial infections, including bronchopneumonia, arthritis, lymphadenitis and cellulitis.
- Histologically there is vasculitis in the areas of edema and hemorrhage.

Anemias of vascular parasitism: Trypanosomiasis

- Trypanosomes are unicellular organisms, uniform in type.
- Not all species of Trypanosoma of mammals are pathogenic.
- The pathogenic trypanosomes differ widely in virulence and are apparently nonpathogenic in mammalian reservoir hosts.
- The important trypanosomes to human and animal health are transmitted by arthropods that carry the metacyclic stages in either the oral or anal tracts.
- Trypanosoma cruzi, the cause of Chagas' disease in humans and animals in South America, is known as a stercorarian parasite because it is spread by passage in the feces of the reduviid insects (Triatominae spp.); after the insects bite (often around the mouth or eye), they defecate and the trypanosomes gain entry to the host through the bite wound, often assisted by the host scratching.

Anemias of vascular parasitism: Trypanosomiasis

- The important African trypanosomiases of animals (T. congolense, T. vivax, T. brucei brucei) and of humans (T. brucei rhodesiense and T. bmcei gambiense) are called salivarian parasites because of their transmission through the salivary glands of the tsetse fly.
- Other biting and sucking insects, such as tabanids, stable flies or fleas, and vampire bats may transmit trypanosomes mechanically.
- Trypanosoma equiperdum, the cause of dourine, does not require a vector host but is transmissible by direct contact with mucous membranes.

Anemias of vascular parasitism: Trypanosomiasis

- T. Gambiense- human (sleeping sickness)
- T. evansi - dogs Surra
- T. Congelense- cattle Nagana
- T. brucei - dogs, rabbits, rats and mice Nagana
- T. Equinum- horse mal de caderas
- T. cruzi - dogs chagas
- T. Equiperdum – horse Durin
- T. *vivax* and T. *congolense* has been directed at defining the disease in British breeds of cattle.

Anemias of vascular parasitism: Trypanosomiasis

- The components of pathogenicity of trypanosomes are largely unknown.
- Their effects vary with their tissue tropism.
- The edema and interstitial reactions caused by T. brucei are due to the fact that this parasite resides in perivascular tissues, in contrast to the more serious pathogens of humans and animals which are obligate intravascular parasites.

Bovine Trypanosomiasis

- *Trypanosoma vivax is more virulent than T. congolense.*
- In cattle, parasitemia regularly occurs a week after inoculation with 10^5 or more organisms that have been passed in rats and columnseparated.
- By the second week of infection, there is a sharp drop in the red cell count and hemoglobin levels, accompanied by an erythroid shift and macrocytosis, anemia being the predominant aspect of the disease.
- There is concurrent thrombocytopenia of moderate degree and hypocomplementemia, with irregular appearance of immunoglobulin and complement on red cell membranes.
- Fibrinogen is reduced to about half of normal levels.
- Kinetically the red cell lifespan is reduced to a half or less of normal, and iron utilization is initially rapidly increased, but slows down with cachexia and inhibition of the erythroid response due to inflammatory changes.

Bovine Trypanosomiasis

- The platelet lifespan is not shortened in infections with Trypanosoma congolense, although it may be with T. vivax.
- Red cells are destroyed in an "innocent bystander" fashion by adsorbing toxic and metabolic products of the trypanosomes, as well as suffering direct injury from a parasite-derived phospholipase.
- There is competition between the stem cells for erythroid and myeloid proliferation.
- Calves infected during the first week of life have less severe hematologic disease than calves infected at 6 months or older.
- Some of these animals become cachectic and die.

Bovine Trypanosomiasis

- When viewed from behind, infected animals have poorly covered bony prominences, poor "spring of rib," and a deep and pendulous abdomen.
- The skin is scurfy and rough, particularly about the head, ears and hind quarters.
- There is chronic low-grade pyrexia with intermittent temperature increases, and periodic watery diarrhea with passage of poorly digested ingesta of normal color.
- There is irregular oculonasal discharge, but no loss of appetite and the animals continue to eat.
- There is mild mucosal pallor without petechial hemorrhages, and the urine may be dark but never blood-tinged.
- The heart and respiratory rates are not remarkably altered

Bovine Trypanosomiasis

- *Anemia is of moderate degree,* generally between 50 and 80g/L, which is initially macrocytic and normochromic, and later becomes normochromic, normocytic and poorly responsive.
- *There are no pathognomonic* **gross lesions** of *trypanosomiasis.*
- Chronically affected animals are cachectic and have a rough haircoat, and there is increased clear fluid in body cavities.
- There is generalized lymph node enlargement to 2-4 times normal, and the hemal nodes become prominent in subcutaneous areas and in association with the para-aortic and pelvic nodes where they may reach 1 cm in diameter or larger.
- The lungs are heavy and have increased density on palpation, and may show intercurrent cranioventral bronchopneumonia.

Bovine Trypanosomiasis

- The heart is generally flabby, with serous atrophy of pericardial fat, and there may be white foci 1-2 mm in diameter on the epicardium and on the cut surface.
- The liver and kidneys are symmetrically enlarged and constitute a greater than normal percentage of body weight.
- The liver is unusually firm and not easily penetrated by digital pressure, and there is a fine lobular pattern visible through the capsule and on cut surface.
- Renal medullary fat has serous atrophy. There are fine focal, raised, reddened areas 1-2 turn in diameter throughout both layers of the omentum.
- The enteric tract is unremarkable, except that the small intestine is atonic and contains an excessive amount of normal-appearing fluid content.

Bovine Trypanosomiasis

- **The most remarkable changes** occur **in lymph nodes, which have generalized medullary pigmentation, and in bone marrow** where there is a regular increase in hematopoietic areas,.
- The spleen is uniformly enlarged and bulges, but does not ooze blood, on cut surface.
- The Malpighian corpuscles are generally visible grossly.
- **Microscopically**, there is a generalized increase in septal width in the lungs and accumulation of intravascular hemosiderin-bearing macrophages.
- There are multifocal areas of fiber atrophy with sclerosis and lymphoplasmacytic proliferation in the myocardium , most prominently in those animals which have succumbed to the disease.

Bovine Trypanosomiasis

- The bone marrow goes through a cycle of changes similar to those in equine infectious anemia.
- There is early conversion of fatty to hematopoietic marrow with high cell density, erythroid shift and plasmacytosis, followed by a reduction in cellular packing and dilation of sinusoids, and ultimately by reduction in hematopoiesis and serous atrophy of the remaining tissue.
- Trypanosomes may be found free and phagocytosed in small vessels throughout the body, but are most commonly observed in the liver and cerebral cortex.
- Hepatic changes are constant, and consist of atrophy of hepatocellular cords with sinusoidal dilation and periportal lymphoplasmacytic proliferation.

Bovine Trypanosomiasis

- There is increased interstitial stroma, without change in lobular organization, and generalized Kupffer cell hyperplasia.
- Changes in the lymphoid tissue are remarkable and constant in all areas of the body. There is first follicular hyperplasia, with a competent response and the formation of large and densely cellular germinal centers.
- The changes are those of continuing stimulation with an initial competent response followed by hyperplasia, then atrophy and sclerosis.
- Concurrent with the changes in lymph nodes, there is *remarkable atrophy of the thymus,* with the reduction most prominently affecting cortical regions.
- In kidney, overall changes in glomeruli are compatible with membranoproliferative glomerulonephritis

SPECIFIC INFECTIONS OF THE LYMPHOID TISSUES

- **Caseous lymphadenitis**
- **Anthrax**
- Streptococcal adenitis in swine
- *Streptococcal adenitis* in dogs
- **Tularemia**
- **Pseudotuberculosis**
- **Histoplasmosis**
- **Leishmaniasis**
- **Theileriosis**
- Jembrana disease
- *Tick borne fever*
- Salmon poisoning in dogs
- Bovine petechial fever

Leishmaniasis

- The genus *Leishmania* is of protozoan parasites which are classified in the family Trypanosomatidae.
- Species of the genus are parasites of *humans, dogs, and other mammals*.
- Species of sandflies *(Lutzomia)* are the intermediate hosts and are essential for the maintenance of virulence, whereas other blood-sucking insects, including members of the genera *Phlebotomus* and *Stomoxys* and the tick *Rhipicephalus,* may act as mechanical vectors.
- Direct transmission and vertical transmission may occur in kenneled dogs.
- Infection of mammals occurs when the sandfly sucks blood.

Leishmaniasis

- The protozoa proliferate by binary fission in the midgut of the emale sandfly and assume a *leptomonad form*, leaf-shaped with a single flagellum arising at the anterior pole.
- Infection of mammals occurs when the sandfly sucks blood, and in the mammalian host the protozoa assume the *leishmanial form* as rounded cells of ~2.0 nm in diameter with a vesicular nucleus and small kinetoplast but no flagellum.
- They multiply by binary fission and as leishmanial forms, **the Leishman-Donovan bodies**, are intracellular parasites of macrophages.

Leishmaniasis

- Leishmaniasis is important as a disease of humans, and wherever it occurs in humans it may also occur in dogs.
- Leishmaniasis actually includes **three diseases:**
- **cutaneous leishmaniasis** ("oriental sore") is caused by *L. Tropica* and occurs in countries about the Mediterranean Sea;
- **mucocutaneous leishmaniasis** ("espundia") is caused by L. *braziliensis* and occurs in Central America;
- **visceral leishmaniasis** ("kala-azar") is caused by *L. Donovani* and is endemic in parts of Europe, Africa, and Asia.

Leishmaniasis

- Both cutaneous and visceral forms of the disease have been described in **dogs**, as well as cases of visceral disease in which the organisms are diffusely present in the dermis.
- **Leishmaniasis is a disease of the monocyte-macrophage system**, and the **visceral disease mimics histoplasmosis**.
- The protozoa are not cytopathogenic in the usual sense, and destruction of host macrophages appears to be purely a mechanical consequence of proliferation of the protozoa in the cytoplasm.

Leishmaniasis

- **Cutaneous lesions** take the form of chronic ulcers that develop from inflammatory papules at the site of the insect bite.
- The organisms are inoculated by the biting insect and are soon ingested by histiocytes.
- Rapid proliferation of the protozoa disrupts the phagocytes, and the released organisms are ingested by further phagocytes to repeat the process.
- Lymphocytes and plasma cells surround the lesion and neutrophils are attracted to the debris.
- When the inflammation extends to the overlying epithelium, ulceration occurs.
- Numerous parasites are present within macrophages, and some are free in the tissue.

Leishmaniasis

- **The *clinical signs of visceral leishmaniasis*** in the dog are of chronic debility and often recurrent oculonasal discharge, with some crusting of the nose, and recurrent diarrhea.
- There may be mild enlargement of lymph nodes, and the spleen is always enlarged to some extent in the visceral form.
- **Grossly** there are often focal scurfy skin lesions, but generally, in visceral leishmaniasis, **the presentation is of a *mature do 2 in poor body condition with a rough hair coat.***
- *The* oral and cervical viscera are normal and the lungs generally have mild tan mottling but are otherwise normal, as is the heart.
- The liver contains numerous granulomas, and is symmetrically enlarged and dark brown.

Leishmaniasis

- The spleen is 2-3 times or more normal size with symmetrical enlargement and is dark brown to black on capsular surface.
- There is mild irregular enlargement of lymph nodes with no other significant changes in the abdominal cavity except that the kidneys are darker than normal, and while of normal contour, there may be significant immune-complex glomerulonephritis and chronic renal failure.
- The bone marrow is uniformly reddened in midfemoral shaft in well-developed cases, but the fat is generally of normal character.
- The lesions initially are of heroic-lymphatic hypertrophy with macrophage proliferation and focal granulomas.

Leishmaniasis

- Splenic follicles are hyperplastic, often with follicular hyalinosis. In advanced cases, there is atrophy of nodes and spleen, and the sinus areas may be diffusely occupied by large macrophages heavily laden with intracytoplasmic organisms and numerous plasma cells.
- The lesions in bone marrow may be focal, but consist of clusters of epithelioid macrophages with phagocytosed organisms.
- In the dog with a well-developed infection, the bone marrow will have remarkable plasma cell hyperplasia that may approach 50% of cells present and there is characteristically hypergammaglobulinemia.
- The protein is broadly polyclonal and the plasma cells lack atypia.

Leishmaniasis

- Renal changes are variable and may consist of interstitial scarring with some parasitic involvement; however, the effects of hyperproteinemia and inununе complexes appear to injure the kidney indirectly.
- Animals with leishmaniasis and amyloidosis have been described.

Theileriosis

- Theileria are protozoan parasites of the order Piroplasmida, family Theileriidae.
- **The species presently recognized as pathogenic for cattle include**:
- Theileria parva parva, the cause of East Coast fever of east and central Africa;
- Theileria parva lawrencei, the cause of Corridor disease (buffalo disease) of southern Africa;
- Theileria parva bovis, the cause of January disease (R.hodesian theileriosis) of east and central Africa;
- Theileria annulata, which causes Mediterranean or tropical theileriosis across north Africa and central Asia; and
- Theileria buffeli group (T. buffeli, T. orientalis; T. sergenti (invalid term)), which are widely distributed in East Asia and are relatively benign.

Theileriosis

- Theileria mutans causes benign theileriosis, a less important tickborne disease of cattle in Africa, North and South America, Asia, Australia, and Europe.
- Theileria hirci and Theileria ovis are parasites of sheep in North Africa, the Middle East, and southern parts of Eurasia.
- **Theileria spp. reproduce by schizogony in lymphocytes (leukocytic or tissue phase) and are subsequently found in red cells (erythrocytic *phase*).**
- *A* related genus is *Cytauxzoon,* which reproduces by schizogolly primarily in macrophages and by fission in red cells.
- The *Theileria* are spread **by *biological tick vectors,*** principally of the ***Rhipicephalus* and *Hyalomma* genera.**

Theileriosis

- Larval and nymphal ticks ingest parasites in the erythrocytes of infected hosts.
- After engorgement, they detach from the host animal and molt through to the next instar.
- During this period, the parasite migrates to the acinar cells of the salivary gland of the tick.
- At this stage, the parasite in the salivary gland of the unfed tick is not infective for cattle.
- Once the infected tick has started to feed, the parasites multiply in the salivary gland, and maximum infective stages for cattle are excreted in the saliva between 3-5 days after commencement of blood feeding.

Theileriosis

- The severity of the disease is directly proportional to the number of organisms inoculated into the animals by the ticks.
- From 4 to 20 days after infection by the transmission of **sporozoites** from an infected tick, **macroschizonts** are found in lymphoblasts of the lymph nodes draining the site of infection.
- These schizonts increase in number throughout the lymph nodes by an order of magnitude each 10 days, until virtually all of the lymphocytes are parasitized.
- Macroschizonts, 2-16 nm in diameter, may be identified in cytoplasm of infected lymphocytes using blood stains, and are known as **Koch's blue bodies**, which are considered diagnostic for the disease.

Theileriosis

- From the tenth day of lymph node infection, increasing numbers of macroschizonts enter **the microsehizont** stage in which the host cells are destroyed and **merozoites** are released to invade erythrocytes.
- **Piroplasms,** which are the intraerythrocytic stage of the parasite, are infective for ticks and first appear on the 12th day after infection.
- They increase rapidly in number until death, at which point a high proportion of the erythrocytes are parasitized.

Theileriosis

- **Clinically;**
- high fever, followed in a couple of days by red cell parasitemia.
- Drooling, lacrimation, depression, diarrhea, and particularly progressive and prominent enlargement of the superficial lymph nodes
- Severe pulmonary edema with dyspnea
- The course of the disease is ~1 month and the mortality is ~95%.
- During the acute phase of the disease, more than 60% oflymphocytes may contain Koch's bodies.
- The acute disease appears to be caused by massive lympholysis and progressive anemia.
- An outstanding feature of East Coast fever is leukopenia.

Theileriosis

- **Gross lesions:**
- **Pathomorphological findings of the disease are in the kidneys, abomasum and brain.**
- Of principal interest is the enlargement of lymphoid tissues, including Peyer's patches.
- On cut surface, the lymph nodes are diffusely discolored with a red-brown cortex containing focal hemorrhages, and a dark red-brown medullary area.
- Serous effusion and gelatinous or hemorrhagic edema of connective tissues are common.
- The spleen is enlarged in the acute disease, but in cases with a prolonged course it may be shrunken and strap-like.
- There is ulcerative abomasitis, likely nonspecific.

Theileriosis

- **Gross lesions:**
- The so-called "infarcts" of the liver and kidney are actually proliferative foci of perivascular lymphocytes.
- These foci, which project slightly, produce a mottling of small gray-white patches visible on the surface of the liver and kidney.
- The lungs are congested and edematous with increased texture on palpation, and increased weight.
- Small hemorrhages associated with foci of hyaline degeneration occur in the muscles, and petechiae are commonly present under the tongue and in the vulva.
- Erosive or catarrhal enteritis overlies lymphocytic hyperplasia and infiltration of the gut mucosa.

Theileriosis

- **Histologically**, in the early stages of infection, there is *diffuse lymphoid hyperplasia*, apparently at least partially due to constitutive production of IL-2 by infected lymphocytes.
- In animals that have died with East Coast fever, there is *widespread lympholysis* with hemorrhage and fibrinous exudate throughout the cortical areas of nodes.
- Lympholysis is prominent in germinal centers and there is a general loss of small lymphocytes.
- Ther is **hepatic** periacinar and, to a lesser extent, periportal lymphocytic infiltration and, in addition, there are focal infiltrations of the hepatic capsule.
- In some cases, there is periacinar hepatocellular necrosis and irregular canalicular cholestasis with loci of inspissated bile.

Theileriosis

- There is early **splenic** lymphoid hypertrophy that is later followed by lympholysis.
- Germinal centers remain prominent and are surrounded by areas of hemorrhage.
- The hypocellular follicular centers are usually occupied by fibrinous or hyaline exudate similar to that seen in **lymph nodes.**
- **The kidneys** are remarkably congested with focal hemorrhage, and there is interstitial infiltration with lymphocytes.
- The lymphocytic infiltration is prominent around vessels, and often around the parietal layer of Bowman's capsule.
- There is a variable level of parenchymal necrosis with the formation of hyaline casts and brown pigmentation of the remaining epithelium.
- **The pulmonary** changes are characteristic and consist of lymphocytic infiltration of the septa and interstitial tissues, resulting in widespread severe interstitial alveolitis.
- **The bone marrow** is hypocellular with early asynchrony of the granulocytic system and a less severely affected erythroid system accompanied by proliferation of large lymphocytes similar to those infiltrating other

Theileriosis -Turning sickness

- The disease is described as **"turning sickness"** although it is not clear whether the responsible organism is **T. parva, T. mutans,** or another.
- The condition occurs occasionally in partially resistant cattle re-exposed to heavy infestations of infective ticks.
- **Parasitized lymphocytes localize by embolism or sequestration in cerebrospinal vessels and produce hemorrhagic infarcts.**
- **Hemoglobinuria is not visible.**
- The infarcts are of usual character, but muddy discoloration of tissues and meninges with hemosiderin is suggestive of repetitive minor episodes of infarction. Infarcts of various ages may be found in other organs, especially kidney and spleen, but are small and easily overlooked.
- **Koch's bodies** may be rare or not demonstrable in peripheral blood or lymphoid organs.

Theileriosis -Corridor disease

- ***Theileria lawrencei*** is the cause of **Corridor disease** of calves, so named because it occurred in cattle moved into an area called "the Corridor" lying between two game reserves in South Africa.
- ***Rhipicephalus* ticks** collected in the area were able to infect cattle, but ticks feeding on infected cattle were not able to transmit the infection further to other cattle. Thus, cattle were not infective for ticks.
- While the disease in cattle closely resembled East Coast fever clinically and morphologically, there were differences in parasitic behavior.
- In cattle affected with Corridor disease, **less than 5% of red cells** in the blood and less than 5% of lymphocytes in smears of lymph nodes contained the parasite, whereas in East Coast fever the corresponding figures would be about 50 and 80%.

Theileriosis -Tzaneen disease

- *Theileria mutans* is the cause of **Tzaneen disease** of cattle, usually a mild and inapparent infection.
- Sheep can be infected artificially; the organisms in sheep do not appear in smears of blood.
- *Theileria mutans* is transmitted naturally by ticks of *Rhipicephalus, Amblyomma,* and *Haemaphysalis.*
- hemolytic anemia, icterus and hemoglobinuria.
- The lesions in lymphoid tissue are similar in type, but less severe than in East Coast fever.
- There is very heavy parasitism of erythrocytes, but schizonts are not observed.

Theileriosis -Tropical Theileriosis

- ***Theileria annulata*** *is the cause of* ***tropical theileriosis*** *in North Africa, the Middle East, and central Asia.*
- *The vectors are ticks of the genus Hyalomma.*
- *Infection with T. annulata is persistent and latent, relatively benign, and often with no parasitemia detectable in smears of blood.*
- *It is, however, readily transmitted by inoculations of blood.*
- *The parasite, both within erythrocytes and forming Koch's bodies, becomes very numerous in the blood during acute attacks of the disease.*
- *The majority of the parasites in red blood cells are ring- or oval-shaped and only a few are bacilliform.*

Theileriosis

- ***Theileria ovis*** *is the ovine equivalent of T. mutans; it is benign.*
- ***Theileria hirci*** *is somewhat more virulent and is also pathogenic for goats.*

Tick-borne fever

- Tick borne fever of **sheep and goats** and pasture fever of cattle is transmitted by the vector ***tick Ixodes ricinus*** *and occurs in Great Britain, Ireland,The Netherlands, Norway, and Finland.*
- **The causative agent is Anaplasma phagocytophilum** (formerly Cytoecetes phagocytophila, Rickettsia phagocytophila, Cytoecetes bovis, Ehrlichia equi)
- The infection is transmitted stage to stage in ticks, but not hereditarily, and other blood-sucking arthropods may also transmit the agent.
- *Tick-borne fever is a transient and mild illness that causes some loss of condition.*
- ***Clinically,*** *adult ruminants are more susceptible to tick-borne fever than are the young. Ewes* in late pregnancy may abort. In terms of laboratory diagnosis, *with the onset of fever, the organism is detectable in circulating granulocytes and large lymphocytes.*

Histoplasmosis

- Histoplasmosis is caused by **Histoplasma capsulatum**, a facultative **intracellular parasite of macrophages**, and is characterized by diffuse involvement of the mononuclear phagocyte system.
- Histoplasma capsulatum is a dimorphic ascomycete fungus. The parasitic phase is yeastlike, whereas the nonparasitic phase produces an abundant mycelium.
- Histoplasmosis has a worldwide distribution.
- It is a largely noncontagious disease **of humans, dogs, cats, swine, cattle, horses, and wild animals.**
- The disease in animals is seen most frequently in dogs and less often in cats. Transmission from dog to dog has been established.

Histoplasmosis

- It is generally agreed that *infection is obtained from soil,* either by ingestion or by inhalation of dust, and a distinct association has been repeatedly demonstrated between *Histoplasma capsulatum* and places where *pigeons* congregate, with abandoned *chicken* runs and houses, and with *bat* caves.
- Chickens themselves are not infected **because their high body temperature is not conducive to growth of the organism.**
- *Transmission is by inhalation of airborne conidia,* followed by phagocytosis in the lung and then transport in phages to other areas of the body.
- This route accounts for the high incidence of infection in the bronchial and cervical lymph nodes. Since intestinal lesions are usually present, it is felt that ingestion might provide a direct route of infection.

Histoplasmosis

- Animals with advanced disease due to Histoplasma capsulatum show emaciation, persistent diarrhea, pyrexia and enlargement of liver, spleen and lymph nodes.
- The clinical signs are most commonly related to either the respiratory or the gastrointestinal tract.
- Animals with histoplasmosis most consistently have **mild nonresponsive, normochromic anemia.**

Histoplasmosis

- **Grossly,** the pulmonary lesions of histoplasmosis may be in the form of gray, rounded nodules of 1-2 cm in diameter and with a distinct tendency to become confluent, or there may be a diffuse increase in the consistency of the lungs.
- When the intestine is involved, as it frequently is, the lesions are located chiefly in the lower part of the small intestine.
- The mucosa is the site of nodular thickenings or of corrugations similar to those seen in Johne's disease of cattle.
- The thickenings are due to infiltration of lymphocytes, plasma cells and macrophages in the lamina propria and submucosa, and they may extend also through the wall to the subserosa giving the gut a thickened pipestem appearance.

Histoplasmosis

- The lymph nodes are greatly enlarged, but are discrete and without adhesions.
- There may be no indication of normal architecture on the cut surface, with the uniformity resembling lymphoma, except that the nodes are firm and dry.
- **Histologically,** there are coalescing granulomas with histiocytosis, and cortical replacement by the reaction.
- The spleen is enlarged, sometimes to several times its normal size, gray and firm.
- There is marked sinus expansion and filling by fixed cells of stromal origin and by colonization with macrophages, many of which contain the ingested organisms.

Histoplasmosis

- There is lymphoid atrophy, varying in degree with the stage of debility of the animal.
- The liver is uniformly enlarged, firm and gray.
- The discoloration is diffuse and related to capsular thickening without focal lesions.
- The infiltrating cells collect in miliary foci in the portal triads and sinusoids, causing extensive displacement and atrophy of the parenchyma.
- The adrenal glands are often involved.
- **The *enlargement of organs is due to extensive proliferation and infiltration with monocytes and epithelioid macrophages in whose cytoplasm many of the typical yeasts in small or large numbers are found.***

Pseudotuberculosis

- **Yersinia pseudotuberculosis (corynebacterium pseudotuberculosis)** occurs worldwide in wild rodents and birds and is widespread in nature, recoveries having been made from soil, milk and feed.
- The organism regularly produces disease, often in epidemic proportions, only in rodents and birds.
- Cats, because of their contact with rodents and birds, are the domestic species most apt to be secondarily involved by outbreaks of the disease in its natural hosts.
- Losses of serious proportion, however, occur **in sheep** which are exposed to large numbers of organisms during outbreaks of the disease in rodents during cold weather.
- **The ovine disease** is known as "**pyemic hepatitis.«**

Pseudotuberculosis

- Yersinia pseudotuberculosis is a facultative intraceltular parasite.
- The route of transmission is by ingestion and, in susceptible animals, organisms enter the body through the intestine.
- Small necrotic foci develop in the Peyer's patches of the ileum and colon, and extend as lymphangitis to the regional nodes.
- The organism becomes septicemic and may kill susceptible rodents at this stage; more typically, and in all domestic species, caseonecrotic foci form in the mesenteric nodes, spleen and liver, often in association with fibrinohemorrhagic inflammation in the small intestine.
- The hepatic foci, which are the most obvious, are 1-10 mm in diameter, white and have no or scant tendency to encapsulation or softening. They are interspersed with irregular areas of parenchymal collapse that probably result from vasculitis and thrombosis.

Pseudotuberculosis

- **Microscopically,** there is necrosis, with bacterial colonies and fragmented leukocytes surrounded by macrophages.
- Giant cells are absent, even from later contracting granulomas.
- The mesenteric nodes and spleen contain similar foci, and are enlarged by lymphoid and histiocytic hyperplasia.
- The mesenteric nodes in the cat may be 2-4 cm in diameter and can be grossly confused with intestinal toxoplasmosis or lymphomatosis.
- In addition to the *mesenteric lymphadenitis and hepatitis, enteritis* is consistently present and characteristic in its histologic expression.
- Numerous bacterial colonies are present in the lamina propria, associated with multiple suppurative foci or a diffuse suppurative enteritis.

Tularemia

- Tularemia (deer fly fever) is caused by Francisella tularensis.
- The organism is a tiny, gram-negative, very pleomorphic coccobacillus that is a strict aerobe and shares many cultural and epidemiological features with *Yersinia pestis,* **the cause of bubonic plague.**
- *Francisella tularensis* infects a wide range of species, including most *domestic animals, humans, and wild rodents,* and it is in these last two that the disease is most often fatal.
- *The organism is abundant in nature as an infection of many species of rodents,* and it is from these, either directly or by the mediation of insect vectors, that humans and domestic animals acquire the infection.
- The organism is able to penetrate intact skin and mucous membranes, but it is also infective by ingestion, inhalation, and inoculation by biting insects and ticks.

Tularemia

- Tularemia in humans is a severe systemic disease, with various manifestations depending on dissemination or localization.
- The disease in rabbits and rodents is recognized by the presence of miliary white foci 2 mm or more in diameter in the liver, spleen and lymph nodes.
- They are indistinguishable grossly from the lesions caused by Yersinia pseudotuberculosis.
- Histologically, the lesions are characterized by very focal but complete necrosis.
- Neutrophils and pus may be present early and macrophages accumulate, but in slightly older and larger lesions there is total coagulative necrosis with a granularity that resembles caseation.
- The lesions in lymph nodes are often larger than those in the liver and may be readily visible grossly as wedge-shaped areas of cortical necrosis demarcated by a narrow zone of intense reactive hyperemia.
- The affected nodes are palpably enlarged in the living animal and may discharge a thin red pus on to the skin.The lymphadenitis may be generalized or restricted to the nodes draining the site of infection which, if visible, is an ulcerated papule.

Anthrax

- Anthrax is caused by **Bacillus anthracis**, a large, gram-positive, spore-forming organism that is highly pathogenic for most herbivorous animals and humans, whereas carnivorous birds and reptiles are resistant.
- Domestic animals are susceptible to B. anthracis in the decreasing order of goats, sheep, cattle, horses, pigs and dogs.
- Farmed mink are highly susceptible. In ruminants, the disease is usually brief and septicemic; in horses, pigs, and dogs, it is frequently localized to the throat or intestine and may be fatal before invasion of the blood occurs.
- When the disease is septicemic, as it usually is in herbivores, the blood and tissues of the animal swarm with vegetative organisms which, when exposed to air or oxygen, form spores of most remarkable durability.

Anthrax

- It is the combination of these two factors, the number of organisms and the resistance of spores, which is of paramount importance in the epidemiology of the disease.
- Bacillus anthracis probably has limited capacity for growth in the external environment, due in part to antagonistic soil bacteria.
- Growth may occur in alkaline soils with much decaying vegetable matter, and alternate periods of rain and drought and temperatures in excess of 15.5°C may also facilitate growth.
- The spores are known to remain viable in soil for at least 15 years, and probably much longer, since they have been noted to retain their vitality and virulence for 50 years in the laboratory.

Anthrax

- As a general rule, *the spores are very resistant to methods of disinfection,* with the exception of chemical disinfectants which are oxidizing agents. Spores on skin have even survived tanning processes to become a hazard for humans.
- Vegetative bacilli are unlikely to cause the disease since they are rapidly destroyed in the acid medium of the stomach.
- Cattle and sheep are presumed to obtain the infection by ingestion of contaminated food and water, entry through mucous membranes possibly being aided by local trauma.
- Cutaneous infection is rare in cattle. Infection through the skin is occasionally seen in sheep, and may be assisted by grass seed infestation. Ingestion is an important mode of infection in horses and dogs, as indicated by the common occurrence of lesions in the throat.
- It is also thought that infection can be transmitted to horses by blood-sucking insects.
- Intestinal anthrax in pigs probably reflects infection by ingestion.

Anthrax

- **The pathogenesis of *anthrax*** *is an initial lymphangitis and lymphadenitis, which develops into septicemia.*
- Spores that are inhaled are ingested by cells lining alveoli and transported in them to the tracheobronchial nodes, in which vegetation and true initiation of the infection occur.
- Spread to the blood is via lymphatics as well as by lymphovenous connections within lymph nodes, and numerous bacilli spread in the lymph from node to node as the filtering mechanism of each is successively swamped.
- Bacilli that enter the blood are taken up in other parts of the mononuclear phagocyte system, especially the spleen, to establish secondary centers of infection and proliferation.

Anthrax

- Physiological disturbances, clinical signs and death depend on the development of a massive septicemia.
- Vegetative cells produce a small array of toxins.
- **The toxin consists of three complementary components designated factors I, II, and III, or edema factor, protective antigen, and lethal factor, respectively**.
- **Edema factor** is an adenylate cyclase that increases cyclic AMP after activation by calmodulin.
- **Protective antigen** is likely a receptor-binding protein that appears to be essential for the biological effects of edema and lethal factors.
- **Lethal factor** is a CNS depressant, but its major effects may be elsewhere.

Bovine Anthrax

- is usually septicemic, and *sudden death* is usually the first indication of its presence in a herd.
- they may be dead within 1 hour of showing signs of illness, although some will show general signs of illness for about 24 hours before death.The signs of illness vary with the route of entry and when, as usually happens, entry is by inhalation or ingestion with no area of localization, the animals are depressed and listless.
- On examination there is high fever, increased heart and respiratory rates, and congested and terminally cyanotic mucosae that show evidence of bleeding.
- Animals that survive for a day may have dysentery, abortion, edematous swellings of the perineum, throat and abdominal wall, and blood-stained milk.

Bovine Anthrax

- *The carcass of an animal dead of this disease putrefies quickly,* becomes very rapidly distended with putrefactive gases, and blood exudes from the natural orifices
- Anthrax in the fulminating disease is very largely an intravascular infection with most of the organisms in the blood and the rest in the spleen.
- Septicemia in anthrax is a terminal event, and smears of blood may not be helpful when prepared more than a few hours before death.
- The morbid picture of the disease in cattle is characterized by splenomegaly, multiple hemorrhages, and edematous effusions in connective tissues.
- A very large soft spleen is the most significant lesion, and very rarely is it absent.

Bovine Anthrax

- Splenomegaly occurs in other diseases of cattle, but rarely is it as large in association with sudden death.
- In anthrax the spleen is soft, sometimes it ruptures spontaneously, and when it is incised incised the pulp exudes very thick black-red blood which brightens in color on exposure to air.
- Smears and sections of the spleen reveal very large numbers of bacilli if the carcass is fresh but, when decomposition is advanced, they are destroyed by putrefactive changes.
- In some cases, splenomegaly is the only lesion.
- **The histology of the spleen** is not revealing.The sinus areas are distended with sludged red cells and the lymphoid follicles are widely separated and hypocellular, but numerous leukocytes and bacilli in chains are present.

Bovine Anthrax

- *It is typical of septicemic anthrax that the organisms are always intravascular.*
- The blood is thick and dark, frequently described as tarry, and either it is not clotted or the clots are very soft and friable, compatible with the effects of the combined toxins in inhibiting the clotting system.
- There are likely nonspecific effects present, such as the disseminated coagulopathy and fibrinogenolysis that accompany hyperthermia.
- Small hemorrhages are common in the mucous and serous membranes and in the subcutaneous connective tissues.
- Loose connective tissues in any location may be infiltrated with gelatinous fluid, and accumulations of such fluid in serous cavities are stained with blood.
- There is congestion, swelling, and degeneration of parenchymatous organs.
- The myocardium is dull and flabby.

Bovine Anthrax

- Cattle are moderately resistant to *B. anthracis* so that local lesions may occur at the site of entry.
- Local lesions are usually in the small intestine and take the form of *ulcerative hemorrhagic enteritis,* but acute inflammation in the abomasum and large intestine may also occur.
- The most severe lesions may be over the lymphoid tissues of the intestine, or extend for a considerable distance from these.
- The mucous membrane is intensely red, and at a greater distance is sprinkled with small hemorrhages.
- The contents of the intestine are then deeply stained with blood.
- Superficial necrosis and ulceration occur in some areas of most intense hyperemia.

Bovine Anthrax

- The corresponding mesentery, up to the regional nodes, is infiltrated with gelatinous fluid as a result of acute lymphangitis, and the fluid may be stained with blood.
- The regional nodes have the appearance of the spleen. They are enlarged, red-black, and on cut surface are moist and shiny.
- The vessels are intensely congested, and hemorrhage extends into the peripheral sinuses and cortex. Bacilli are numerous and leukocytes are present, but there is no necrosis.
- the organisms gain entry through the oropharynx, there is hemorrhagic lymphadenitis of the nodes of the throat and edema of the connective tissues in these regions.
- The occasional case of ***pulmonary anthrax*** in cattle is characterized by acute congestion and consolidation of a portion of the lung with larger areas of interstitial edema, edema of the mediastinum, and regional hemorrhagic lymphadenitis. The pulmonary lesion is exudative, but lacks the full gamut

Ovine Anthrax

- Sheep are more susceptible to *B. anthracis* than are cattle, and local lesions do not occur except in the unusual instances ofpercutaneous infection, in which the lesion may take the form of spreading edema from the outset or initially appear as hard circumscribed nodules.
- The disease in sheep takes the same course as that in cattle except that it is even more rapid.
- Splenomegaly is not as prominent in sheep as in cattle, likely because of the greater level of collagen in the splenic capsule of sheep.
- The parenchyma is, however, dark and soft.
- Edematous effusions do not occur in sheep.

Equine Anthrax

- Clinical signs of anthrax in horses may last for several days and are characterized by colic or by large edematous swellings.
- The swellings, which can be very extensive, occur on the ventral part of the abdomen and thorax, the legs, in the perineal region and about the external genitalia.
- Dysentery may accompany the acute colic. When ingestion is the route of infection in horses, the primary lesion may be in the throat or the intestine, and death may occur from the local reaction and without septicemia. Intestinal lesions are similar to those described above for cattle, and pharyngeal lesions are similar to those described below for swine.
- When septicemia occurs, the morbid changes are the same as in cattle, same as in cattle, including very prominent enlargement and congestion of the spleen.

Swine Anthrax

- Pigs are relatively resistant to anthrax.
- They acquire the infection from eating infected flesh and the infection remains localized to the throat or intestine.
- Since septicemia is exceptional, splenomegaly is not a prominent part of the gross picture.
- **The characteristic sign** is swelling of the pharyngeal region and neck. Some pigs have diarrhea and dysentery, but it is unusual to have intestinal localization without pharyngeal localization.Anthrax without illness has been observed in swine; in such cases the disease is limited to isolated mesenteric or pharyngeal nodes.
- The local lesion of anthrax is swine is a typical carbuncle at the point of entry, with acute regional lymphadenitis and lymphangitis.

Swine Anthrax

- Some bacilli no doubt reach the blood, but they do not establish septicemia.
- Bacteria may localize in liver, spleen or kidney to produce a metastatic **carbuncle** but, usually, only individual nodes near the site of entry are involved.
- The lymphadenitis may be diffuse or focal but in both cases it is, in the initial stages, hemorrhagic.
- An intense leukocytic infiltration occurs, all cells within the affected portions of the node die, and the focus becomes encapsulated. With necrosis, the affected tissue changes from a brick-red to a gray friable mass that can be easily shelled-out when the gland is incised.

Swine Anthrax

- **In primary intestinal anthrax in pigs, the initial lesion is focal or multifocal hemorrhagic enteritis, with a central zone of diphtheresis that eventually ulcerates**.
- The adjacent serosa and mesentery are thickened with edema fluid and yellow, with foci and streaks of hemorrhage; they are the site of focal hemorrhagic necrosis due to acute necrotizing vasculitis and lymphangitis.
- These mesenteric lesions extend only as far as the regional nodes, which show the type of lymphadenitis characteristic of anthrax in swine.

Caseous Lymphadenitis

- Caseous lymphadenitis (CLA) is a suppurative infection of the lymph nodes primarily of sheep and goats caused by Corynebacterium pseudotuberculosis (ovis).
- The disease occurs **in sheep** wherever they are raised, but horses, camels, deer, mules, and rarely cattle and humans may be affected.
- Cattle can develop a pathologic syndrome that resembles that in sheep, but they do so quite rarely, and the infection generally remains localized to 1-2 regional nodes draining an infected surface wound or a segment of intestine.
- *Coryne-bacterium pseudotuberculosis* is also the cause of *ulcerative lymphangitis* in cattle and horses, and of *pectoral abscesses* in horses.

Caseous Lymphadenitis

- There are two serotypes with *type I* in ovine, caprine and occasionally bovine isolates and *type H* in buffalo and most infections in cattle.
- An *exotoxin* that consists of a phospholipase D is an important aspect of virulence with effects including intravascular hemolysis, necrosis, pulmonary edema and shock.
- *C. pseudotuberculosis* survives briefly in the environment and is able to spread indirectly, which is an important means of spread in sheep and goats that are routinely corralled on the same bed ground to avoid predation.
- Infection also occurs in shearing wounds in sheep and and butting abrasions in males.

Caseous Lymphadenitis

- **In horses,** the disease occurs as ulcerative lymphagitis on the fetlocks, which is consistent with the concept that skin abrasions are important in spread of the organism.
- The disease in **goats** can be more severe than in sheep, the most frequent lesions being in the *lymph nodes of the head and neck*.
- The lesions in goats closely resemble those of pseudoglanders or melioidosis *(Burkholderia (Pseudomonas) pseudomallei,* and it is important to distinguish these diseases.
- Female goats and intact males have more extensive lesions than castrated males.
- ***Caseous lymphadenitis is widespread in goats and the disease differs from sheep in the distribution of the abscesses.***

Caseous Lymphadenitis

- Caseous lymphadenitis **in sheep** almost always **follows a wound infection, usually a shearing wound.**
- The organism can penetrate the intact skin of freshly shorn sheep however, and may be transmitted by dipping fluids.
- The initial lesion in lymphoid tissues is diffuse lymphadenitis that is probably the result of the soluble exotoxin.
- When the organism reaches the nodes, multiple microscopic abscesses form in the cortex.
- **Eosinophils are prominent in the reaction and cause the pus to be green.**
- These foci rapidly coalesce and the central areas caseate to form a structureless mass which contains fragments of nuclear material and discrete clumps of bacteria.

Caseous Lymphadenitis

- **The abscesses are rapidly encapsulated, and when this occurs the acute reaction in the surrounding tissues subsides, but the abscesses continue to enlarge.**
- With enlargement, **there is progressive necrosis and re-formation of the capsule, which gives the lesion a very characteristic structure of concentric lamellations; these are particularly prominent when calcareous granules are deposited in successive layers at the margin of the expanding lesion.**
- **In old lesions, the contents lose their green color, become inspissated and resemble putty.**
- The lamellation is specific to the organism, not the organ involved. The nodal lesions often attain a diameter of 4-5 cm and exceptionally they may reach 15 cm. The larger lesions in superficial nodes cause pressure atrophy and depilation of the overlying skin; they frequently rupture to discharge chronically through a narrow fistula.

Caseous Lymphadenitis

- ***Mature lesion of CLA is an encapsulated abscess with pus of a distinct green hue and of caseous or caseopurulent consistency.***
- *The* initial cutaneous lesion may not be evident, having resolved, but it is noted that occasional subcutaneous abscesses, principally of the face and belly, do occur without relation to known aggregations of lymphoid tissue.
- Mastitis, as occasionally observed in sheep and often observed in goats, probably represents an extension from a wound of the overlying skin; when the mastitis is early and acute it is diffuse and suppurative, and when chronic it is localized to encapsulated abscesses.

Caseous Lymphadenitis

- *Spread from the lymph nodes produces lesions in the lungs,* and these are rather common with advancing age.
- They also occur in young lambs, in which the progression is more rapid than in adults.
- The pulmonary lesions may consist of extensive bronchopneumonia, when abscesses rupture into bronchi in which there are soft caseopurulent foci, or there may be discrete nodules of various sizes and numbers.
- In cases of bronchopneumonia, and overlying those nodules which are immediately subserosal, there is pleuritis, often with adhesions.

Caseous Lymphadenitis

- When the adhesions are few and localized adjacent to the nodules, the remaining pleural cavity may be normal.
- When the adhesions are more diffuse,there is a large amount of serous fluid in the cavities and a thin layer of fibrin on the pleura. The nodular lesions in the lung are similar to those in lymph nodes, and have a narrow zone of bronchopneumonia outside the capsule.
- With time, the pulmonary nodulesecome sharply circumscribed, encapsulated, subpleural abscesses.
- The pulmonary lesions are associated with characteristic lesions in bronchial lymph nodes which may be much enlarged. Dissemination of the infection from the lungs to other viscera is uncommon.

Inflammatory Diseases of Lymph Nodes

- Lymphadenitis results when an infectious agent is present in the lymph node, as distinguished from benign lymphoid hyperplasia, in which the node is immunologically reactive but free of local invasion.
- Lymphadenitis may be **acute or chronic, suppurative, caseous, or granulomatous.**
- Cytologically, **acute lymphadenitis** is characterized by a mixture of small and large lymphocyte types accompanied by neutrophils and eosinophils that may constitute 25% or more of the cells present.
- Distribution of cell types present, including large macrophages, and the quality and character of the neutrophil nuclei are indicative of the cause of the process, which may be apparent if the phagocytic cells present have ingested bacteria

Inflammatory Diseases of Lymph Nodes

- **Acute lymphadenitis ;**
- Grossly in acute lymphadenitis, the lymph nodes are enlarged, soft, locally mobile and hyperemic to a variable degree. The capsule is taut and thinned due to the influx of cells, and on the cut surface the parenchyma bulges and exudes blood and lymph.
- Histologically, acute lymphadenitis is characterized by marked hyperemia with unusual prominence of small vessels in cortical areas.
- Neutrophils are often present, both through drainage from the subcapsular sinus and by migration from the postcapillary venules.
- When the inflammation is due to one of the pyogenic organisms, abscessation is likely. Necrosis in lymph nodes is an attribute of some acute infections, such as salmonellosis and toxoplasmosis.

Inflammatory Diseases of Lymph Nodes

- **In chronic lymphadenitis**, hyperemia and edema are irregularly present, and the infected nodes are large and firm, and may be fixed to local tissues if there has been cellulitis.
- The capsule is thickened as are the internal trabeculae, and with prolonged inflammation the node becomes dry and hard.
- Changes of this type are characteristically present in the supramammary lymph nodes of cows with brucellosis of long standing, and to a lesser extent in animals with chronic or recurrent bacterial mastitis. In the latter cases, the marked proliferation of the collagenous septa of the medulla.

Inflammatory Diseases of Lymph Nodes

- Lymphadenitis may be expressed by changes that are largely degenerative and affect the architecture of the tissue.
- Thus in some acute viral infections, there is rapid lysis of lymphocytes, as in canine parvoviral infection and in rinderpest.
- In salmon poisoning of dogs, the nodes may be much enlarged with follicular hyperplasia and accumulation of macrophages.
- In some chronic infections, particularly with the viruses causing immunodeficiency, the nodes are atrophic with wrinkled capsule and depletion of lymphocytes.