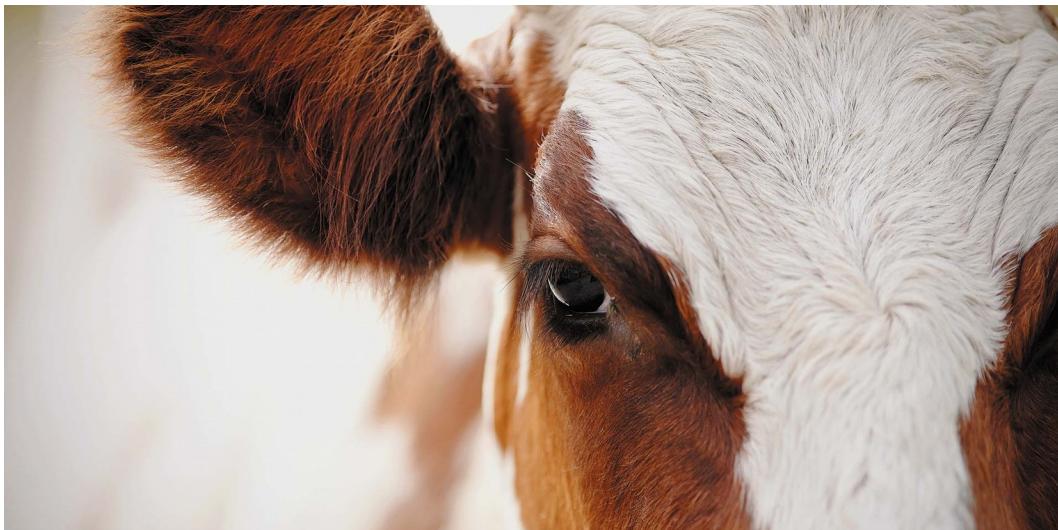


# PATHOLOGY of - Brucellosis and Pseudotuberculosis (Caseous Lymphadenitis)



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# Brucellosis

## **Introduction**

**Definition:** Brucellosis is an infectious bacterial disease of animals caused by *Brucella* sp. and characterized by **Abortions in Late Gestation (3<sup>rd</sup> Trimester)** and formation of **Granulomatous Lesions** in genital organs, joints and fetal liver. Infection is **ZOONOTIC**.

# Brucellosis

## Introduction

### History & Synonym:

***Brucella melitensis***, was the first member of the genus to be recognized, was isolated in 1887 from the spleen of patients who died from "Mediterranean Fever", "Gastric Fever", or "Bruce's Septicaemia", later called "Malta Fever" by **Sir David Bruce**.

Ten years later, in 1897, was isolation and identification of ***Brucella abortus*** from aborted bovine foetuses and foetal membranes by the Danish veterinarian **Frederick Bang**. The infection of cattle caused by *B. abortus* has since been known as "Bang's Disease" or "Bang's Abortion Disease". The characteristic undulating or recurrent fever usually seen in the human disease has given rise to the name "**Undulant Fever**"

# Brucellosis

## Introduction

### History & Synonym:

*Brucella suis*, was identified in 1914 by **Traum** in aborted pig foetuses.

*Brucella ovis*, as the cause of epididymitis in rams in 1950s; and

*Brucella canis*, as the cause of abortion in dogs in 1960s.

Bang's Disease,      Mediterranean Fever,      Gastric Fever,

Bruce Septicaemia,      Malta Fever

Undulant Fever In Humans

Rock Fever of Gibralter

Ram Epididymitis;      Contagious Abortion

# Brucellosis

## Etiology / Cause

Brucella is small, Gram-negative, bacillary (rod-like) or coccoid organisms:

- *Brucella melitensis*- Mainly Goat, but also in Sheep
- *B. abortus*- Cattle
- *B.suis*- Swine
- *B. ovis*- Sheep
- *B. canis*- Dogs

# Brucellosis

## Spread / Transmission

The infection in cattle is of worldwide distribution.

- The brucella organism usually spreads by contact or through ingestion of contaminated feed and water with aborted foetal contents or foetal membrane.
- It is also transmitted through inhalation and may pierce the intact or abraded skin or conjunctivae (most risky).
- The organism is also excreted in Milk.
- Congenital infection may also occur.

# Brucellosis

## Pathogenesis

- After entry, organisms first **localize in regional lymph nodes**; then proliferate within **reticulo-endothelial cells**.
- Mostly post-ingestion, organisms enter and travel through the intestinal **epithelial cells overlying Peyer's patches** by Endocytosis. Then they enter into the lymphatics.
- Development of bacteraemia allows localization of the bacteria in a variety of tissues. Bacteria have a particular **affinity for male and female reproductive organs, placenta, foetus, and mammary glands**.
- At all sites, Brucella organisms **proliferate intracellularly**.

# Brucellosis

## Pathogenesis

- Phagocytosed by macrophages, *B. abortus* survive and multiply inside macrophages & having resistant cell wall, **microbe blocks phagosome-lysosome fusion.**
- Thus, the bacteria are never exposed to lysosomal enzymes. Interestingly, lysosomes remain distributed in the cytoplasm and while **bacteria continues to grow within phagosome inside the macrophages.**
- The macrophages finally rupture due to expanding physical bulk of the growing bacteria. Wherever organisms are localized, a **granuloma develops.**

# Brucellosis

## Pathogenesis

- The affinity of brucella for placenta and foetus, particularly for **chorio-allantoic trophoblasts**, is due to the presence of sugar **Erythritol** in these tissues. It is the striking proliferation of brucella in trophoblasts which causes placentitis, infection of the foetus, and abortion, which characterize brucellosis in animals

# Brucellosis

## Signs & Symptoms

### Cattle

- Abortion in **last trimester** of gestation (between the 7th – 8th months of gestation)
- Retention of Placenta & Repeat Breeders
- **Arthralgia** symptoms in Joints (Joint Swelling; Arthertis; Synuvitis etc)
- **Orchitis** and accumulation of **fluid in scrotum** in male animals.

### Goat & Sheep

- Abortion and Retention of Placenta
- **Orchitis and Epididymitis** in Males
- **Arthralgia** symptoms in Joints (Joint Swelling; Arthertis; Synuvitis etc)

# Brucellosis

## Signs & Symptoms

### Pigs

- Infected sows abort between the second and third months of gestation.  
**Orchitis** occurs in infected boars

### Horses

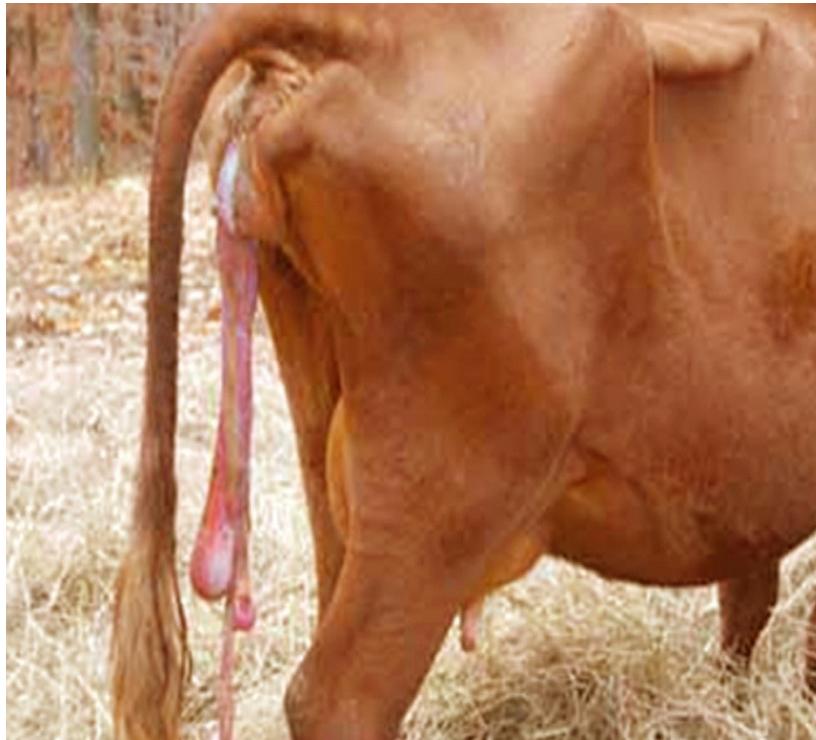
- *B. abortus* + *Actinomyces bovis* causes “**Poll evil**” and “**Fistulous withers**” which is suppurative inflammation of ligamentum nuchae at its attachment to occipital bone.

### Human

- Malta fever in man which is characterized by **Undulant Fever**, weakness, **articular rheumatism**, **night sweating** and muscular sweating.

# Brucellosis

## Signs & Lesions



# Brucellosis

## Signs & Lesions



# Brucellosis

## Signs & Lesions

A partially decomposed bovine foetus and placenta

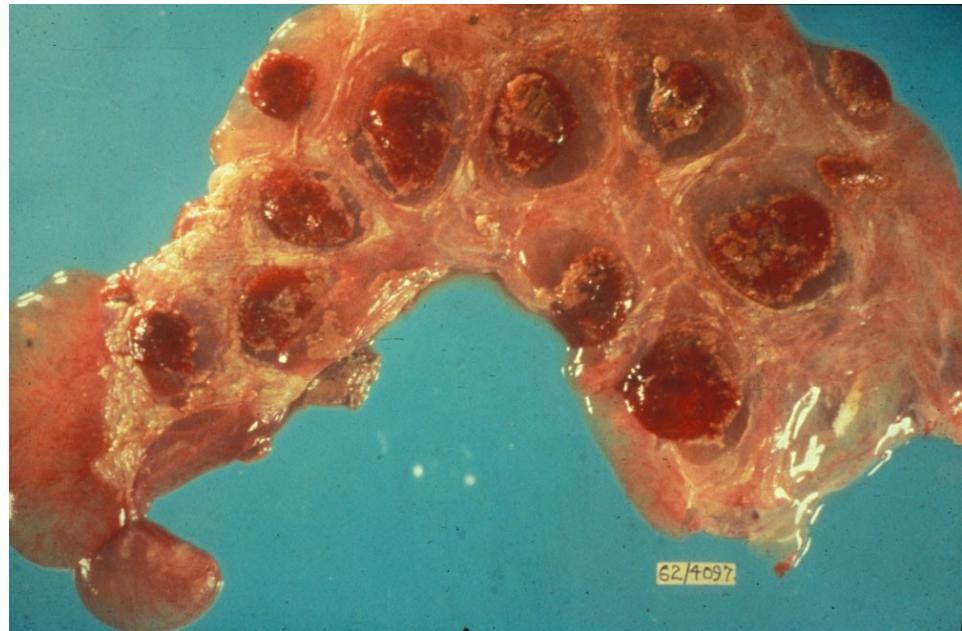


Severe placentitis revealing pale yellow foci in cotyledons and thickening of the intracotyledonary chorioallantois

# Brucellosis

## Signs & Lesions

Bovine, placenta: The placenta contains numerous hemorrhagic cotyledons.



Bovine, vertebrae: Purulent exudate within a vertebra extends into the adjacent spinal canal.

# Brucellosis

## Signs & Lesions



The carpal bursa is markedly swollen and fluctuant

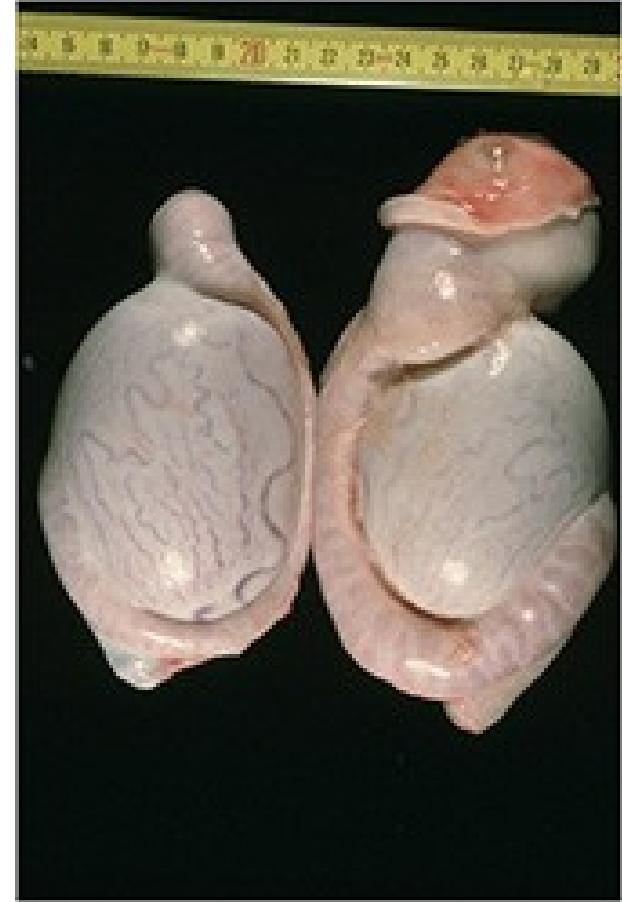
The carpal bursa contains purulent exudate



# Brucellosis

## Signs & Lesions

Enlargement of the entire epididymus in a ram with ovine brucellosis



Spermatic granuloma in the epididymal tail of a ram with ovine brucellosis

# Brucellosis

## Signs & Lesions



Johan Steyl



Pathology Section, Onderstepoort

# Brucellosis

## Lesions

### Gross Lesions

- Edematous Placenta, **Necrosis of Cotyledons.**
- Thickened and **Leathery Chorion.**
- Edema of foetus, serosanguinous fluid in body cavity.
- **Induration** of bovine mammary glands & Supramammary Lymph Nodes
- **Orchitis / Epididymitis** in Rams / Bulls

# Brucellosis

## Microscopic Lesions

- ✓ In the tissues, particularly the lymphoreticular system, the organisms attract macrophages and PROLIFERATE WITHIN THEM, PRODUCING SMALL GRANULOMAS.
- ✓ Granuloma formation is usually not always seen in lesion of placenta associated with abortion in Cattle/Goats, BUT **it is always present in *B. suis* infection** granulomas in all infected tissues.
- ✓ Abortion is the most serious outcome of brucellosis in most domestic animals.

# Brucellosis

## Microscopic Lesions

- ✓ In Bovine Placenta, *B. abortus* proliferate in **Chorionic epithelium and Trophoblasts**. This leads to **necrosis of Cotyledons**. Inter-cotyledonary chorion is oedematous & gets filled with odourless, sticky, brownish exudate.
- ✓ **Severe PLACENTITIS** revealing pale yellow foci in cotyledons and thickening of the intracotyledonary chorioallantois.
- ✓ In advances, yellowish granular necrotic areas, visible in placental Cotyledons. Rest of the chorion is opaque and thickened, with a **Leathery consistency**. Granulomas are not seen in placenta.

# Brucellosis

## Microscopic Lesions

- ✓ Aborted **Bovine Foetus** is Oedematous, with Serosanguineous fluid in body cavities. The most characteristic lesion is **Bronchopneumonia**, characterized by a **mononuclear infiltrate**, with less number of **neutrophils**. Foetal Lymph Nodes are hyperplastic, and Thymus smaller than normal.
- ✓ The bovine **Mammary Gland** and the **Supramammary Lymph Nodes** are common sites of localization of *B. abortus* and results in **Induration (Hardening)**. Microscopically, there is diffuse inflammation. The **Epididymitis**, and **Testicle** of the bull becomes enlarged and indurated. Contents of the sac (formed by the tunica) may result in suppuration, rupture, and discharge of the contents.

# Brucellosis

## Microscopic Lesions

- ✓ In rams, lesions of **Orchitis** & Epidiymitis are observed AND B. ovis infection typically involves **Tail of the Epididymis**. Primary changes do not occur in the testicle. However, stasis results in secondary testicular degeneration. Arthralgia lesions are observed, arthritis, bursitis, with carpal bursa containing purulent exudates is seen.
- ✓ In pigs, B. suis, Grossly, it is only in this type, that ALL affected organs show tiny white to yellowish Nodules (**Brucella granuloma**).
- ✓ B. canis infection in the bitch is accompanied by uterine and placental lesions similar to bovine brucellosis. Bronchopneumonia is seen in aborted pups.

# Brucellosis

## Diagnosis

- ✓ The disease is suspected based on CLINICAL SIGNS such as abortions, retention of placenta, orchitis etc and Characteristic LESIONS, but confirmation is made through Serological Tests at Herd level and then by prescribed Molecular Methods to identify the bacteria:
- ✓ For Serosurveillance (mass level), the Milk Ring Test (MRT) is applied on bulk milk tank samples.
- ✓ For Screening the ‘Suspected Herds’, Rose Bengal Plate Test (RBPT) is used and THEN Positive reactors are confirmed with Standard Tube Agglutination Test (STAT) and indirect ELISA.

# Brucellosis

## Diagnosis

- ✓ Polymerase Chain Reaction (PCR) is being used for identifying the specie-level of the Brucella involved
- ✓ Historically, (a) **CARD TEST** and (b) **STRAUSS TEST** in Male Guinea Pigs were also important in random testing.

Keywords: History-Synonyms-Hosts; MRT ; RBPT ; STAT ; Erythritol; Abortions-late trimester; Foetal Bronchopneumonia; affinity for chorio-allantoic trophoblasts

# Brucellosis

## Differential Diagnosis

Other cause of abortion and reproductive failures in Cattle, like:

- ✓ Trichomoniasis
- ✓ Vibriosis
- ✓ Leptospirosis
- ✓ Listeriosis
- ✓ Infectious bovine rhinotracheitis (IBR)
- ✓ Mycoses



On  
**BRUCELLOSIS ???**



# Let's Move On.

	Require	Desire	Meh. I'll	Yes.	Yay!
Disagree	Discussion	Discussion	Support It.	I'll Help.	I'll Lead!



# Corynebacterium Infections

Corynebacteria are **Gram-positive**, non acid-fast, and sometimes "beaded" in stained tissue sections. They share features with Mycobacteria and Nocardia, but can be easily differentiated. Other members of this group are referred to as "diphtheroid bacteria". The Lesions are variable AND Tissue reaction is either necrotizing, suppurative and/or Granulomatous.

S. No	Corynebacterium	Diseases
1.	<i>C. diphtheria</i>	Diphtheria in Humans
2.	<i>C. renale</i>	" <b>bacillary Pyelonephritis</b> ", <b>Chronic Purulent Cystitis and Urethritis</b> in Cattle; Mainly seen in Cows; it is rare in bulls
3.	<i>C. cystitidis</i>	Haemorrhagic Cystitis and Pyelonephritis in Cows
4.	<i>C. pilosum</i>	Severe Cystitis and Pyelonephritis in Cows

# Corynebacterium Infections

S. No	Corynebacterium	Diseases
5.	<b><i>C. pseudotuberculosis</i></b> ( <i>C. ovis</i> )	<b>Caseous Lymphadenitis</b> (pseudotuberculosis) in Sheep and Goats <b>Ulcerative Lymphangitis</b> and <b>Pectoral Abscesses</b> and <b>Folliculitis</b> ( <i>inflammation of hair follicle</i> ) in Horses
6.	<i>C. bovis</i>	Mastitis in Cattle
7.	<i>C. suis</i> (now as <i>Eubacterium suis</i> )	Pyelonephritis and Cystitis in Pigs
8.	<i>C. pyogenes</i> ( <i>Actinomyces pyogenes</i> )	Suppurative Infections in Cattle, Sheep, Goats & Pigs
9.	<i>C. equi</i> (now as <i>Rhodococcus equi</i> )	Pneumonia in Foals (Horses)

# Caseous Lymphadenitis

## Introduction

**Synonym:** Pseudotuberculosis (of Sheep and Goats)

**Definition:** Caseous lymphadenitis is a chronic, contagious, suppurative disease of sheep & goats, caused by *Corynebacterium pseudotuberculosis* [C. ovis], a Gram-positive '**diphtheroid bacillus**' that most frequently **infects the lymph nodes and lymphatic system** and is characterized by the formation of Abscesses in Lymph nodes.

It may also involve respiratory tract with abscess formation in the lungs and/or mediastinal or retropharyngeal lymph nodes.

# Caseous Lymphadenitis

## Etiology / Cause

- It is caused by soil-borne, *Corynebacterium pseudotuberculosis* [*C. ovis*], which is **Gram-positive**, non acid-fast, intracellular coccobacillus which appear "beaded" in stained tissue sections.
- There are 2 serotypes, with type I in sheep/goats and type II in buffalo/cattle.
- An exotoxin that consists of a **phospholipase D** is an important aspect of its virulence that enhances dissemination of the bacteria by damaging endothelial cells and increasing vascular permeability.

# Caseous Lymphadenitis

## Spread & Transmission

- ✓ The organism gains entry by way of **abrasions in the skin or oral mucous membranes**, and less commonly, through inhalation. It increases in prevalence with age and reaches a peak incidence in adults. Disease in **goats** can be more severe than in sheep.
- ✓ Caseous lymphadenitis (CLA) in **sheep** almost always follows a wound infection, usually a shearing wound or through contaminated hair clippers. Infection is rare in cattle.
- ✓ The disease is **considered Zoonotic** and is an occupational disease of shearers (persons who cut sheep's wool).

# Caseous Lymphadenitis

## Pathogenesis

- After penetrating into the host, which generally occurs through the oral, nasal and ocular mucosa, or through skin wounds, the agent disseminates freely or within macrophages, mainly through the afferent lymphatic system, to local lymph nodes and internal organs. *C. pseudotuberculosis* is an intracellular organism and lives inside cells.
- The lipid cell layer of the bacteria (containing Mycolic Acid) is pyogenic, but not immunogenic. This same layer makes phagocytosis of the bacteria difficult, increasing its virulence (cytotoxicity), and survival inside macrophages; abscesses form through the release of lysosomal enzymes.

# Caseous Lymphadenitis

## Pathogenesis

- *C. pseudotuberculosis* produces an Exotoxin **Phospholipase-D** (PLD) that increases **vascular permeability**, survival within **macrophages** and aids dissemination of bacteria from the location of primary infection (local lymph node) to other organs (lungs, regional lymph nodes, mesenteric lymph nodes, etc.), **where it forms Abcesses**, because *it lyses mammal cell membranes, causing microhemorrhages and vascular lesions.*
- These Abcesses can be found in either **Peripheral or Internal Lymph Nodes.**

# Caseous Lymphadenitis

## Pathogenesis

- The location of the affected lymph nodes **affects the clinical presentation.**
- With involvement of the thoracic lymph nodes, the affected animal may display clinical signs of respiratory disease such as **dyspnea, tachypnea, and chronic cough**, in addition to chronic weight loss.
- With **haematogenous spread**, organism may spread with abscess formation in many organs, including lungs, liver, kidney, brain, and spinal cord.

# Caseous Lymphadenitis

## Signs & Symptoms

- In its SUPERFICIAL / PERIPHERAL FORM is characterized by infection of external lymph nodes, such as the submandibular, parotid, pre-scapular lymph nodes,
- While the INTERNAL / VISCERAL FORM is characterized by abscessing of internal organs, such as lungs, liver, kidneys, uterus, spleen and internal lymph nodes, such as the mediastinal and bronchial lymph nodes. Internal abscesses are normally associated with weight loss and weakness, known in sheep as thin-ewe syndrome.
- The Visceral form is more common in Sheep, while the Superficial form is among Goats.

# Caseous Lymphadenitis

## Signs & Symptoms

- There is palpable enlargement of one or more of the superficial lymph nodes. Those most commonly affected are the **submandibular, parotid, pre-scapular, submaxillary, prefemoral, supramammary, and popliteal nodes.**
- The mature abscesses easily leak through fistulas and green pus is discharged into the environment or into the affected organ. Abscesses may **usually recur, months or years later**, in same animal, if it fails to eliminate.
- In cases of systemic involvement, **chronic pneumonia, pyelonephritis, ataxia (incoordination) & paraplegia** (paralysis of hind portion of the body & of both legs) may be present.

# Caseous Lymphadenitis

## Signs & Symptoms



# Caseous Lymphadenitis

## Signs & Symptoms



# Caseous Lymphadenitis

## Lesions

- Although both the External (Peripheral) and Internal forms of CL occur in sheep and goats, the External Form is more common in **GOATS**, and Internal Form is more common in **SHEEP**.
- In sheep these abscesses initially contain pale green material that eventually forms a **classical laminated “onion-ring” appearance** in cross section, with concentric fibrous layers separated by inspissated caseous exudate and matures into a calcified mass.
- Abscesses in GOATS are less organized, remain greenish-cream colored and the exudate may be **soft and paste-like texture**.

# Caseous Lymphadenitis

## Lesions

- Microscopically, the lesion starts as a **small nidus (focus) of epithelioid cells** but is soon transformed into caseous necrosis, which becomes the main feature.
- The central Caseous mass is soon surrounded by a thin Layer of **Epithelioid cells mixed with Lymphocytes**, to which an external layer of Fibrous Connective Tissue is added.
- As the lesion grows, the Epithelioid and Fibrous reactive layers undergo necrosis; the **epithelioid layer dies first**. While the fibrous Layer still remains visible, new reactive Layers form outside it, one after another become necrotic.

# Caseous Lymphadenitis

## Lesions

- Abscesses **rapidly encapsulated**; then acute reaction in 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 **onion-like concentric lamellations**. These lamellations are more prominent when calcified granules are deposited in successive layers at the margin of the expanding lesion.
- Although Calcification is seen, but giant cells are not seen. 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

## Lesions

- Lesions are usually restricted to lymph nodes, particularly **prescapular, prefemoral, and mediastinal nodes**, and less often, lungs, kidneys, and other viscera.
- The gross appearance of lymph nodes is characteristic. The entire node is greatly enlarged and almost **replaced by a single spherical lesion**. In cross section, it is concentrically laminated, mostly in sheep.
- Layers of fibrous capsule alternate with caseous, friable material which is greenish, and sometimes gritty: In the lungs, the lesions may resemble an abscess, with a central, semifluid mass of yellowish or greenish pus.

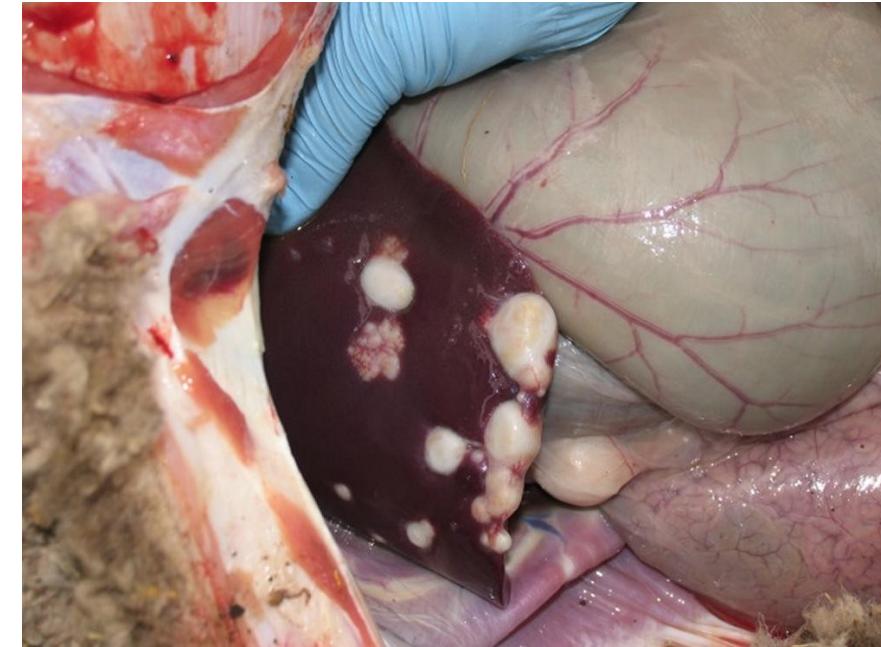
# Caseous Lymphadenitis

## Lesions



# Caseous Lymphadenitis

## Lesions



# Caseous Lymphadenitis

## Diagnosis

- ✓ By Demonstration of **typical gross and microscopic Lesions** . if typical, are practically diagnostic.
- ✓ **Culture & Identification** from active lesions is diagnostically definitive. Examination & Isolation of the causative organism from pus; demonstrating its **diphtheroid morphology** and cultural characteristics.
- ✓ The **Serological Tests** that detect antibodies to the exotoxin of *C. pseudotuberculosis* and include Indirect haemagglutination, haemolysis inhibition, and immunodiffusion.
- ✓ **ELISA** tests have also been developed to detect antibody to cell wall antigens as well as to exotoxin.

# Caseous Lymphadenitis

## Differential Diagnosis

- ✓ Pyogranulomatous lesions of Actinobacillosis
- ✓ Superficial Abcesses caused by *Staphylococcus aureus* and *Actinomyces bovis*
- ✓ Pneumonia associated with Tuberculosis.
- ✓ Submandibular Oedema due to parasites (*Fasciola hepatica*; *Haemonchus* spp.)
- ✓ Salivary Cysts, Lymphosarcoma etc.



**Remember to Fight  
Corona!!**

**With Personal Hygiene  
& Self Distancing**

# Questions?

## Thank you!



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