

Treatment and control of chlamydial and rickettsial infections in sheep and goats



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Chlamydial and rickettsial infections

- Small ruminants are susceptible to several infections caused by obligate intracellular Gram-negative bacteria
 - Ehrlichia ruminantium* (Heartwater)
 - Formerly *Cowdria ruminantium* (Cowdriosis)
 - Anaplasma ovis* (Anaplasmosis)
 - Anaplasma phagocytophilum* (Tick-Borne Fever)
 - Formerly *Ehrlichia phagocytophilum*
 - Coxiella burnetii* (Q. Fever)
 - Morphologically similar to *Rickettsia*
 - Chlamydia abortus* (Ovine chlamydiosis)
 - Chlamydia psittaci* immunotype 1; *Chlamydochlamydia abortus*



Chlamydial and rickettsial infections

- Proteobacteria (Phylum)
 - Alphaproteobacteria (Class)
 - Rickettsiales (Order)
 - Anaplasmataceae (Family)
 - Anaplasma* (Genus)
 - Anaplasma ovis*
 - Anaplasma phagocytophilum*
 - Ehrlichia* (Genus)
 - Ehrlichia ruminantium*
 - Gammaproteobacteria (Class)
 - Legionellales (Order)
 - Coxiellaceae (Family)
 - Coxiella* (Genus)
 - Coxiella burnetii*
- Chlamydiae (Phylum)
 - Chlamydia (Class)
 - Chlamydiales (Order)
 - Chlamydiaceae (Family)
 - Chlamydia* (Genus)
 - Chlamydia abortus*

Incidence, distribution, and control of disease

Heartwater (*Ehrlichia ruminantium*)

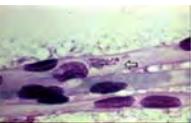
- Transmitted by *Amblyomma* ticks
- Endemic in domestic and some wild ruminants of sub-Saharan Africa, surrounding islands and the Caribbean
- High mortality in susceptible ruminants (up to 90%)
 - Goats and sheep more susceptible than cattle
- Strongly suspected in cases of rapidly fatal encephalitis in humans (Louw et al., 2005)
- Incubation period – 2-4 weeks
- Bacteria multiply in neutrophils, monocytes and vascular endothelial cells
- Develop sudden high fever (40-42°C)
- Symptoms related to leakage of fluid: brain & lungs





Heartwater (*Ehrlichia ruminantium*)

- Increased pressure on brain leads to sensitivity to external stimuli
 - Ears twitch, excessive blinking, high stepping gate when walking, continuous chewing
 - Recumbency and running movements
- Lung oedema
 - Rapid breathing, convulsions, may down from excessive fluid
- Diagnosis
 - PM: lungs heavy with fluid, white foam in trachea, cyanosis, clear fluid often found in heart sac and thoracic cavity
 - Definitive diagnosis: brain smear (Giemsa stained)



Heartwater (*Ehrlichia ruminantium*)

- Diagnosis
 - During febrile reaction bacterium can be isolated in culture from blood/plasma
 - Molecular detection (PCR): In blood of animals with clinical signs and in tick vectors
 - Serology: IFAT, Western blotting, ELISA - constrained by cross-reactions (*false positives*) and duration of antibody response
- Treatment
 - Antibiotic prophylaxis: early treatment with oxytetracyclines (2 x 5-10mg/kg BW or 1 x 20mg/kg) during febrile stage - Inefficient after onset of neurologic signs
- Control
 - Acaricides – to control vector??
 - Immune animals have to be bitten every 6-9 months in endemic areas to retain immunity
 - No safe, user-friendly, reliable commercial vaccine (best long term option)
 - Immunization by "infection and treatment" (Animals less than 3 weeks old have natural resistance) - deep frozen blood from infected animal



Further reading:
 Birles R (2011) Other bacterial diseases: Anaplasmosis, ehrlichiosis and neorickettsiosis. In: Oxford Textbook of Zoonoses: Biology, Clinical Practice and Public Health Control, 2nd edition, Oxford University Press, pp 180-187.
 Swan S & Longbottom D (2011) Treatment and control of chlamydial and rickettsial infections in sheep and goats. Vet Clinics N America Food Animal Practice 27, 213-233.

Tick-Borne Fever (*Anaplasma phagocytophilum*)

- Transmitted by *Ixodes* ticks
- Infects eosinophils, neutrophils, and monocytes
- Primarily affects sheep and cattle [deer, horses and dogs]
- Widespread in temperate regions of Europe (UK, Ireland, Norway, Finland, Netherlands, Austria & Spain)
- Incubation period: 5-14 days
- Main clinical sign: sudden fever (up to 42.0°C) for 4-10 days
- Disease multisystemic: most severe changes anaemia & leukopenia
 - Lethargy, ataxia, inappetence, painful limbs, lameness (Lyme disease)
 - Abortion can occur 2-8 days after onset of fever
- Seldom fatal unless complicated by other infections
- Zoonotic – human granulocytic anaplasmosis
 - Clinical expression ranges from self-limiting febrile illness to a life-threatening and fatal infection
 - Mostly causes nonspecific influenza like illness with fever, headache, myalgia and malaise
 - Leucopenia, thrombocytopenia and mild injury to the liver

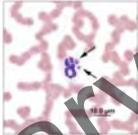



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Tick-Borne Fever (*Anaplasma phagocytophilum*)

- Diagnosis
 - Sudden onset of fever associated with haematological changes (anaemia & leucopenia) & cytoplasmic inclusions in phagocytes, especially neutrophils
 - Detect organisms within leukocytes – stained (May-Grunwald Giemsa) blood smears
 - Serological (Indirect Fluorescent Antibody Test)
 - PM: Enlarged spleen (up to 4-5 times normal size)
- Treatment
 - In endemic areas: regular dipping or pour-on treatment with pyrethroids
 - Oxytetracycline (10mg/kg BW, daily for at least 5 days)
 - Fluoroquinolone antibiotics, rifampicin, sulphamethazine, trimethoprim-sulphonamides
 - Humans: doxycycline therapy, 100 mg twice daily until fever subsides for at least three days
- Control
 - Control tick infestation (acaricides), through dipping, spraying or pour-on treatment
 - Concern: environmental safety & human health (antimicrobial resistance), cost of chemical control & resistance of ticks to pesticides
 - No specific vaccine currently available
 - Detection and culling of carrier animals

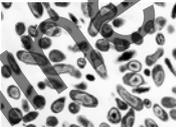



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 OIE Manual - Q Fever http://www.oie.int/eng/normes/mnroh/normes_01482.htm

Q Fever (*Coxiella burnetii*)

- Mostly affects cattle, sheep, goats & humans
- Worldwide distribution, with possible exception of New Zealand
- 2 antigenic phases: Phase I natural virulent form; phase II cultivated avirulent form
- 2 different morphologic forms: small cell variant and more metabolically and replicatively active large cell variant
- Highly resistant to environmental stresses and standard disinfectants
- In animals infections are generally asymptomatic, except for abortion (rate can vary from 5-35%), still-births & delivery of weak offspring
- Zoonoses – acute, chronic & subclinical infections
 - Acute form: undulant fever, malaise, myalgia, severe headache, hepatitis, atypical pneumonia & acute respiratory distress syndrome
 - Chronic form: valvular endocarditis
 - Prompt diagnosis and treatment essential for full recovery
 - Death is a risk, especially in elderly & immunocompromised
 - In pregnant women, can cause placentitis leading to premature birth, growth restriction & spontaneous abortion
 - Handling: extremely hazardous – Containment Group 3 pathogen (OIE)

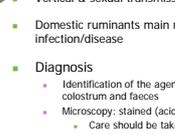



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Q Fever (*Coxiella burnetii*)

- Highly contagious: infectious dose of 1-10 bacteria
- Transmission: Principally inhalation of contaminated dust & contact with infected animals and their products of birth
 - Contaminated milk, meat, wool
 - Ticks
 - Rarely transmissible from person to person
- Domestic & sexual transmission can occur
- Domestic ruminants main reservoir but cats, dogs, rabbits, birds also implicated in human infection/disease
- Diagnosis
 - Identification of the agent: placenta, vaginal discharges, aborted fetus (liver, lung, stomach contents), milk, colostrum and faeces
 - Microscopy: stained (acid-fast) tissue smears – modified Ziehl-Neelsen (mZN), Giemsa, Gimenez
 - Care should be taken as microscopically can be confused with *Chlamydia abortus* and *Brucella* spp
 - Serology: IFAT, ELISA, CFT
 - Microscopy with positive serological result usually adequate for diagnosis
 - Immunohistochemical detection and PCR more specific and sensitive
 - PCR safer for laboratory personnel (heat inactivated samples)

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Q Fever (*Coxiella burnetii*)

- Treatment
 - Acute form: resolves quickly with antibiotic treatment
 - Doxycycline, ciprofloxacin, tetracycline, chloramphenicol, ofloxacin, hydroxychloroquine
 - Chronic form: prolonged antibiotic therapy (up to 4 years of treatment)
 - Doxycycline and quinolones or doxycycline with hydroxychloroquine
 - During pregnancy – five weeks of co-trimoxazole
 - Oxytetracycline (20mg/kg BW, twice during last month of gestation)
 - Does not stop all abortions or shedding at lambing
- Control
 - Stringent hygiene protocols
 - Destroy placentas, aborted fetuses; bedding and straw contaminated with birth fluids
 - Isolate aborted animals
 - Control spread: depends on population density, rearing system, management at parturition
 - Test and culling strategies not considered appropriate for infected flocks/herds as environment can remain infected for a long time and many species can be carriers
 - Netherlands outbreak (2007-2009): >50,000 pregnant goats culled; >3,000 humans cases recorded
 - Commercial vaccines using inactivated Phase I bacteria effective
 - Vaccination does not eradicate infection in animals infected prior to vaccination
 - Phase I vaccines dangerous to produce so aim to produce subunit vaccine

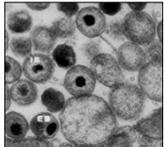



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 Aldren D & Longbottom D (2007) Chlamydial abortion. In: Diseases of Sheep, 4th Edition, Chapter 16, pp. 105-112, Blackwell Publishing.
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Ovine chlamydiosis (*Chlamydia abortus*)

- Ovine chlamydiosis or ovine enzootic abortion (OEA) or enzootic abortion of ewes (EAE)
- Hosts: Sheep, goats
 - Cattle, pigs, horses, deer
- 2 developmental forms: elementary body (0.3 µm) and reticulate body (0.5-1.6 µm)
- Worldwide distribution, with possible exceptions of Australia & New Zealand
- In animals infections are generally asymptomatic
- First indication of problem is delivery of dead, still-borne or weakly lambs/kids 2-3 weeks prior to expected parturition
- Zoonotic – human cases are rare, but in pregnant women can result in spontaneous abortion and miscarriage and can be fatal for woman




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 OIE Manual : EAE http://www.oie.int/eng/normes/m_nh/nh_id/nh_id_00461.htm

Ovine chlamydiosis (*Chlamydia abortus*)

- Transmission: Oronasal – ingestion/aerosol inhalation
 - Products of birth (placenta, fetus), vaginal discharge, infected bedding
- Vertical transmission can occur (little evidence for sexual transmission)
- Domestic ruminants main reservoir but birds and wildlife may play a role
- Diagnosis
 - Presumptive diagnosis: gross pathology (necrotic placentitis) and clinical history

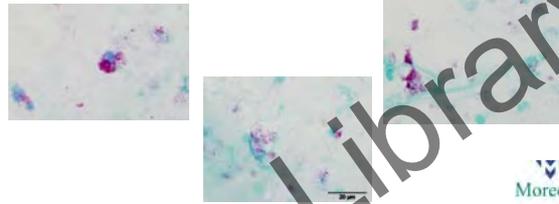


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Ovine chlamydiosis (*Chlamydia abortus*)

- Diagnosis
 - Confirmed by microscopic examination of smears prepared from placental material or vaginal swabs
 - mZN [modified Machiavello, Giemsa, *Brucella* differential]
 - Care should be taken to differentiate with *Coxiella burnetii*

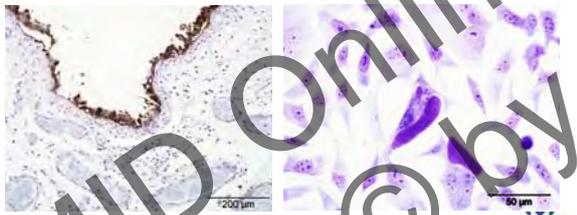


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Ovine chlamydiosis (*Chlamydia abortus*)

- Diagnosis
 - Antigen detection: ELISA (detect LPS), FAT, IHC (MQMP/LPS), histochemical (Giemsa)

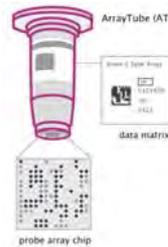


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Ovine chlamydiosis (*Chlamydia abortus*)

- Diagnosis
 - DNA: PCR, microarray (Alere ArrayTube platform)

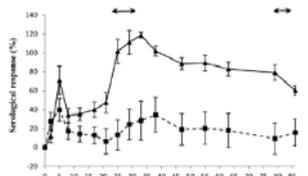


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Ovine chlamydiosis (*Chlamydia abortus*)

- Diagnosis
 - Isolation in cell culture or embryonated hens eggs (zoonotic: biosafety level 2)
- Serological tests:
 - CFT: paired blood samples (at time of abortion and at least 3 weeks later) should detect rising titre: Cross reactions (*C. pecorum/C. psittaci*): does not distinguish vaccinated vs infected animals
 - Microimmunofluorescence, competitive & indirect ELISAs
- Care must be taken as antibody persists in immune animals following abortion, thus not indicative of current infection



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Ovine chlamydiosis (*Chlamydia abortus*)

- Treatment
 - Antibiotics should be used only in exceptional circumstances to reduce losses
 - Oxytetracycline (20mg/kg BW soon after 95-100 days gestation, fortnightly)
 - Does not stop all abortions or shedding at lambing
 - Best to use flock management coupled with vaccination
 - In humans, early therapeutic intervention with tetracyclines, erythromycin or clarithromycin, is important
- Control
 - Stringent hygiene protocols
 - Carefully dispose of placentas, fetuses & contaminated bedding/straw
 - Isolate aborted animals
 - Control spread: depends on population density, rearing system, management at parturition
 - Accredited replacement animals: closed flock
 - Aborted ewes are immune to disease but may excrete infectious organisms
 - Inactivated and live attenuated vaccines available
 - Control but do not eradicate infection or shedding
 - Live vaccine has been shown to cause disease
 - Requirement for subunit vaccine

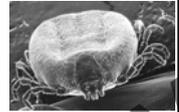


Thank you for
your attention

Further reading:
Shawn S & Longbottom D (2011) Treatment and control of thiamydial and rickettsial infections in sheep and goats. *Vet Clinics N America Food Animal Practice* 27, 219-233.

Anaplasmosis (*Anaplasma ovis*)

- Spread by variety of ticks (*Rhipicephalus* and *Dermacentor*)
- Distributed in tropical Africa, Europe (Mediterranean area), Asia, Russia and US
- Wide host range, including deer species
- Causes haemolytic anaemia in sheep and goats
- Normally subclinical in sheep; more pathogenic for goats
- Incubation period – 1-3 months
- Depression, fatigue, incoordination, pallor, icterus, without haemoglobinuria
- Mortality is low
- Can cause persistent infection



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Anaplasmosis (*Anaplasma ovis*)

- Diagnosis
 - Detect organisms within erythrocytes – stained blood smears
 - PCR & gene sequencing
 - Serological (ELISA; capillary tube agglutination)
 - Necropsy (watery blood; pallor; icteric tissues; increased fluid in body cavities; enlarged liver possible)
 - Urine dark yellow/brown due to bilirubin
 - Absence of haemoglobinuria
- Treatment
 - Most effective during bacteremic phase of infection
 - Oxytetracycline (10mg/kg BW, once daily for 2 days)
 - May not eliminate the carrier state
- Control
 - Control tick infestation, through dipping, spraying or pour-on treatment
 - No specific vaccine currently available
 - Detection and culling of carrier animals

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