


## Chlamydia abortus: from ovines to humans

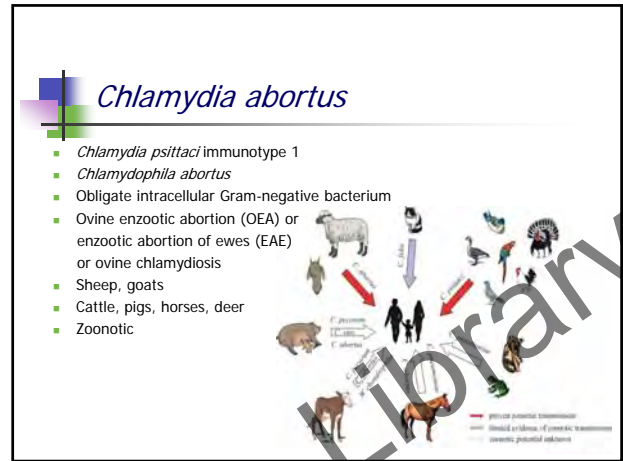


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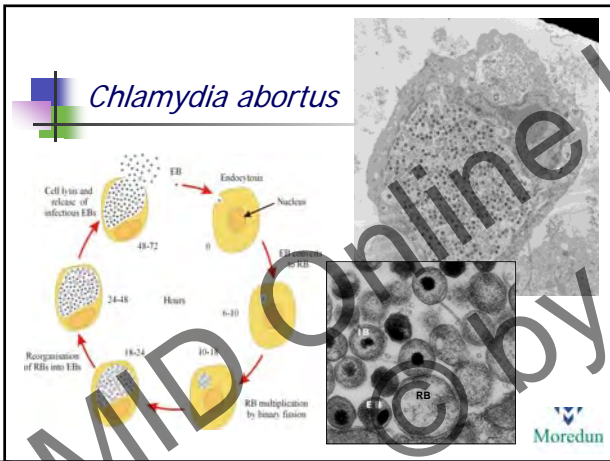
Thursday, 29 August 2013 - Clinical presentation, diagnostic approaches and treatment (Part 3)

## Chlamydia abortus

- *Chlamydia psittaci* immunotype 1
- *Chlamydophila abortus*
- Obligate intracellular Gram-negative bacterium
- Ovine enzootic abortion (OEA) or enzootic abortion of ewes (EAE) or ovine chlamydiosis
- Sheep, goats
- Cattle, pigs, horses, deer
- Zoonotic



## Chlamydia abortus



## Key clinical features of EAE

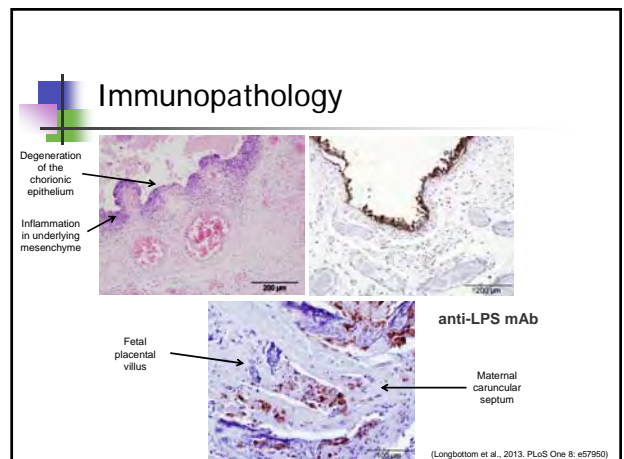
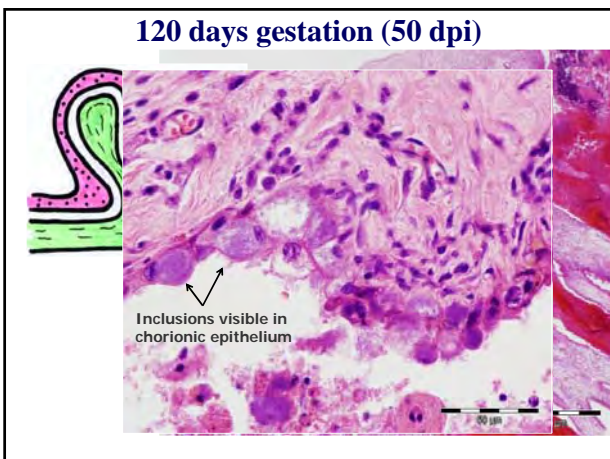
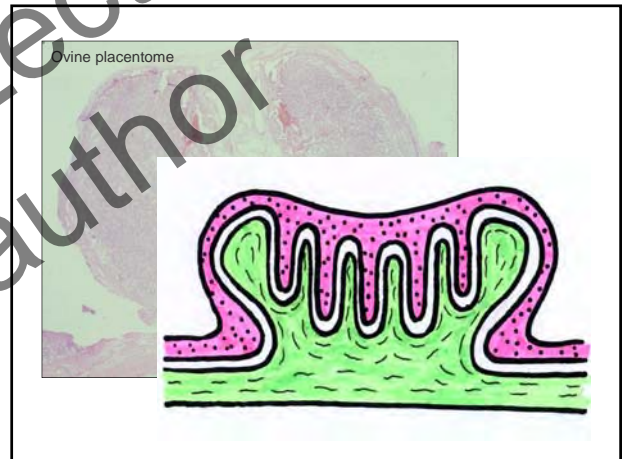
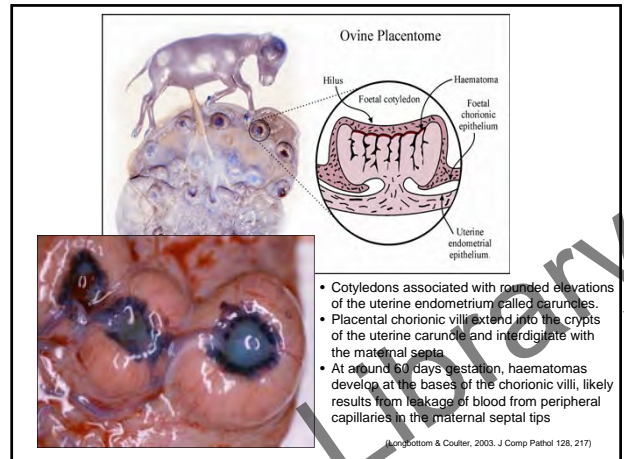
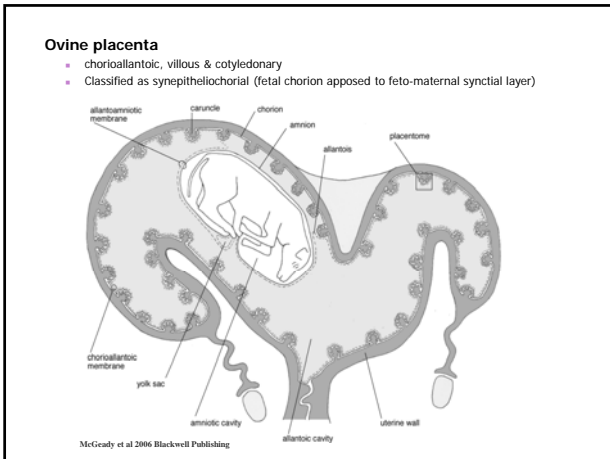
- Following infection in the non-pregnant ewe the organism becomes undetectable
  - Latency or persistence (Longbottom et al., 2013. PLoS One 8: e57950)
- Infection in female only becomes apparent during pregnancy
  - Organism detectable post 90-95 days of gestation (dg) (Mailey et al., 2009. Vet Microbiol 135, 122)
- Infection establishes in foetal chorionic epithelium (trophoblast cells)
  - Necrosis develops in placenta (pathological changes after 90 dg)
  - Abortion occurs at 125-140 dg
- Rarely any premonitory signs of impending abortion
- After abortion maternal antibody levels rise (basis of diagnosis) which coincides with the ewe developing protective immunity
- Protective immunity involves both humoral and cell-mediated responses (Longbottom & Coulter 2003. J Comp Pathol 128, 217; Entrican et al., 2001. J R Soc Med 94, 273)

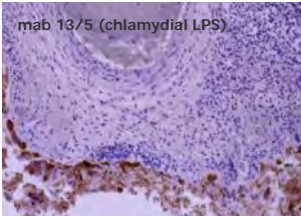
## Ovine Enzootic Abortion



## Progression of infection

- Primary infection likely established in the tonsil
- Dissemination by blood or lymph to other organs
- Establishment of latency in non-pregnant animal
  - Involves suppression of the organism by interferon  $\gamma$  (Entrican et al., 2012. Comp Immunol Microbiol Infect Dis 35, 271)
  - Through induction of enzyme indolamine 2,3-dioxygenase that degrades Trp
- Recrudescence of infection occurs during pregnancy
- When? How?
- Placentation

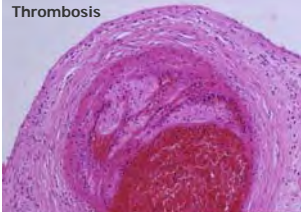




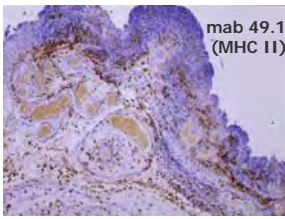
mab 13/5 (chlamydial LPS)

- Anti-LPS mAb: chlamydial antigen & inclusions
- Vasculitis with luminal platelet adhesion
- Partial or complete thrombosis
- Pathological processes may be triggered by locally produced LPS and by interaction of chlamydial effectors and surface antigens
- LPS shown to cause thrombus formation and inducing TNF- $\alpha$  production in mice

Thrombosis

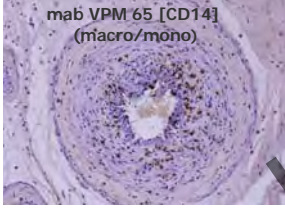


(Gutierrez et al., 2011. Vet Microbiol 147, 119; Maley et al., 2009. Vet Microbiol 135, 122; Sammin et al., 2006. J Comp Pathol 135, 83; Buxton et al., 2002. J Comp Pathol 127, 133)



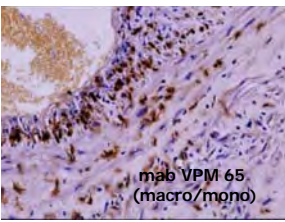
mab 49.1 (MHC II)

- Few CD4+ and CD8+ T cells in inflammatory infiltrate
- Few B cells
- Numerous cells expressing MHCII – mononuclear
- Most cells consisted of monocytes/macrophages
- Macrophages (CD14) in deeper zones of inflammation in mesenchyme, plus some also in arterioles and arteries



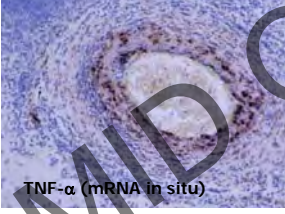
mab VPM 65 [CD14] (macro/mono)

(Gutierrez et al., 2011. Vet Microbiol 147, 119; Maley et al., 2009. Vet Microbiol 135, 122; Sammin et al., 2006. J Comp Pathol 135, 83; Buxton et al., 2002. J Comp Pathol 127, 133)



mab VPM 65 (macro/mono)

- Few cells expressing IFN-gamma mRNA
- Numerous mononuclear cell types expressing mRNA encoding for TNF- $\alpha$  within infected arterioles and arteries as well as inflammatory exudate
- Results in inflammation and destruction of placental tissue
- Changes in endocrine control of pregnancy and parturition
  - LPS induces production of prostaglandin E<sub>2</sub> (PGE<sub>2</sub>) through action of TNF- $\alpha$
  - Changes in levels of progesterone (due to destruction of trophoblast cells) and locally synthesised PGE<sub>2</sub> and 17 $\beta$ -oestradiol (Leaver et al., 1987, 1989)




TNF- $\alpha$  (mRNA in situ)

### OEA: Mechanism of disease

- C. abortus* infects chorionic epithelial cells (trophoblast cells)
- Destruction of chorionic epithelium
  - Release of chlamydial LPS
  - Reduction in progesterone levels
- Chlamydial antigen triggers foetal cell mediated immune response
  - Monocyte/Macrophages & TNF- $\alpha$
  - Increase in PGE<sub>2</sub> levels
- Arteritis & Platelet adhesion/thrombosis
- Inflammation/oedema in placental membrane
- Endocrine control affected: progesterone ( $\downarrow$ ), 17 $\beta$  oestradiol ( $\uparrow$ ), PGE<sub>2</sub> ( $\uparrow$ )
  - $\rightarrow$  precipitates premature expulsion of fetus

### Human foetopathy and *Chlamydia abortus*

- Rare
- Most cases are associated with human pregnancy
  - Exposure to infected sheep or goats
- Sporadic cases of respiratory illness reported in laboratory staff and workers in vaccine plants and abattoirs
- Few reports of flu-like illness and conjunctivitis in children and adults following exposure to sheep



(Groud et al., 1966; Roberts et al., 1967; Tersikih et al., 1977; Beer et al., 1982; Johnson et al., 1985; McKinlay et al., 1986; Kampinga et al., 2000; Reviewed in Sillis & Longbottom (2011). Chlamydiosis. In: Zoonoses. Oxford University Press, pp. 146-57)

### Human foetopathy and *Chlamydia abortus*

#### Clinical symptoms and signs in pregnancy

- First trimester: spontaneous abortion
- Later infection: stillbirths or preterm labour
- May observe several days of acute influenza-like illness, headache, nausea & malaise
- Spontaneous contractions 3-8 days after onset
- Disseminated intravascular coagulation
- Profound thrombocytopenia
- Renal failure
- Hepatic dysfunction
- Significant mortality

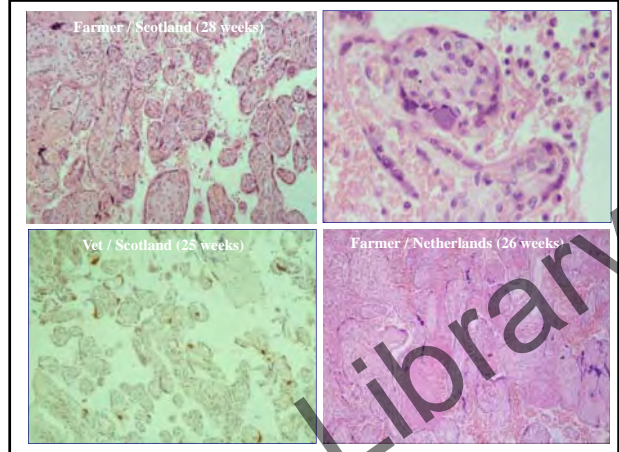
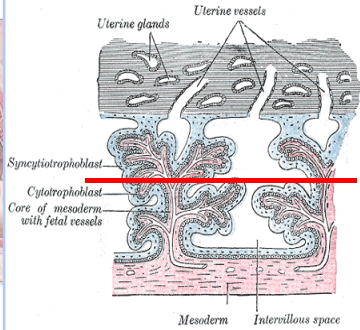


## Human foetopathy and *Chlamydia abortus*

Placenta



Haemochorial placentation



## Pathogenesis: *Chlamydia abortus*

### Ovine infection

Subacute/chronic

necrosis + inflammation  
(macrophages and TNF- $\alpha$ )  
grave risk to fetus  
minimal risk to ewe

### Human infection

Peracute/acute

destruction of trophoblast cells  
DIC, renal failure & hepatic dysfunction  
grave risk for fetus and mother

Thank you for  
your attention

