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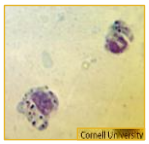
Mammalian Chlamydiosis

Slide 2

Overview

- Organism
- History
- Epidemiology
- Transmission
- Disease in Humans
- Disease in Animals
- Prevention and Control



In today's presentation we will cover information regarding the organism that causes chlamydiosis and its epidemiology. We will also talk about how it is transmitted, species that it affects (including humans), and clinical and necropsy signs observed. Finally, we will address prevention and control measures, as well as actions to take if chlamydiosis suspected.

[Photo: This impression smear, made from the exudate of infected tissues, shows intracytoplasmic inclusions associated with *Chlamydophila psittaci* infection. Source: Used with permission for educational purposes from Cornell University College of Veterinary Medicine, Partners in Animal Health, and the United States Department of Agriculture at http://partnersah.vet.cornell.edu/avian-atlas/]

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THE ORGANISM

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The Organism

- Chlamydiaceae
  - Obligate intracellular bacteria
  - Gram negative
- Two forms
  - Infective elementary body
  - Metabolically active reticulate body
- Species
  - *Chlamydia* spp., *Chlamydophila* spp.

The zoonotic chlamydiae with reservoirs in mammals are members of the family Chlamydiaceae, an unusual group of obligate intracellular bacteria. The members of this family are considered to be Gram negative, due to their relationships with other Gram negative bacteria, but are difficult to stain with the Gram stain. They have metabolic and structural differences from most bacteria, including a dependence on adenosine triphosphate (ATP) and guanosine triphosphate (GTP) from the host. They cycle through two forms: a metabolically inert, infective elementary body and a metabolically active reticulate body found only inside cells. Until recently, the Chlamydiaceae contained only a few species. However, this family has been reorganized, based on analyses of ribosomal RNA. A new genus, *Chlamydophila*, was established, some species were renamed, and some strains were assigned to new species. Both *Chlamydia* spp. and *Chlamydophila* spp. cause the disease chlamydiosis.

[Photo: This impression smear, made from the exudate of infected tissues, shows intracytoplasmic inclusions associated with *Chlamydophila psittaci* infection. Source: Used with permission for educational purposes

from Cornell University College of Veterinary Medicine, Partners in Animal Health, and the United States Department of Agriculture at http://partnersah.vet.cornell.edu/avian-atlas/]

[Photo: *Chlamydia pneumoniae* in human epithelial cell. Acute bronchitis. 1 - infected epitheliocyte, 2 - uninfected epitheliocytes, 3 - chlamydial inclusion bodies in cell, 4 - cell nuclei. Micrograph. Source: Public domain via wikimedia-commons at http://upload.wikimedia.org/wikipedia/commons/c/c5/Chlamydia_pneumoniae.jpg]

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Species

- Zoonotic
  - *Chlamydophila abortus*
  - *Chlamydophila felis*
  - *Chlamydophila pneumoniae*

Some of the organisms that cause chlamydiosis are zoonotic. Chlamydophila *psittaci* (formerly *Chlamydia psittaci*, avian strains) is found in birds and causes psittacosis (avian chlamydiosis). It is responsible for most cases of zoonotic chlamydiosis in humans. This organism is described in a separate presentation.
The zoonotic mammalian species, described in this presentation, are:

- *Chlamydophila abortus* (formerly *Chlamydia psittaci*, mammalian abortion strains or serotype 1),
- *Chlamydophila felis* (formerly *Chlamydia psittaci*, feline strains),
- *Chlamydophila pneumoniae* (formerly *Chlamydia pneumoniae*).

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Species

- Non-zoonotic
  - *Chlamydia trachomatis*
  - *Chlamydophila caviae*
  - *Chlamydophila pecorum*
  - *Chlamydia suis*
  - *Chlamydia muridarum*

Some of the organisms that cause chlamydiosis are not zoonotic. Briefly, they are:

- *Chlamydia trachomatis* is a human pathogen that causes genitourinary tract infections, trachoma, neonatal conjunctivitis and pneumonia, and some forms of arthritis. It does not affect animals.
- *Chlamydophila caviae* (formerly *Chlamydia psittaci*, guinea pig strains) mainly causes conjunctivitis in guinea pigs. *C. caviae* is very host specific; with the exception of a single infection in a gerbil, experimental infections of mice, hamsters, rabbits and gerbils have failed.
- *Chlamydophila pecorum* (formerly *Chlamydia pecorum*) causes encephalitis, pneumonia, enteritis, polyarthritis, conjunctivitis and abortions in sheep, goats, cattle and pigs. It can cause genitourinary disease in koalas. Asymptomatic infections are also seen.
- *Chlamydia suis* (formerly porcine *Chlamydia trachomatis*) is found in the intestinal tract of many pigs. It has been associated with conjunctivitis, enteritis and pneumonia in this species.
- *Chlamydia muridarum* (formerly *Chlamydia trachomatis* of mice) is found in mice and guinea pigs.

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EPIDEMIOLOGY

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Geographic Distribution

- Worldwide
  - *C. felis*
  - *C. pneumoniae*
- Most sheep-raising regions
  - *C. abortus*

C. felis and *C. pneumoniae* occur worldwide. *C. abortus* has been reported from most sheep-raising countries but is not found in Australia or New Zealand.

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Morbidity and Mortality: Humans

- *C. abortus, C. felis*
  - Abortion rarely reported
- *C. pneumoniae*
  - Not clearly zoonotic
  - Non-zoonotic form common in humans
    - Causes 10-15% of all cases of community-acquired pneumonia, bronchitis and sinusitis

Zoonotic chlamydiosis caused by *C. abortus* or *C. felis* seems to be rare. Approximately 20 confirmed human abortions caused by *C. abortus* were documented between 1987 and 2000. Most of these cases were severe and, if untreated, progressed to septicemia. *C. pneumoniae* from animals may be zoonotic but this has not been established. Zoonotic transmission of this species may be unimportant, as it is a very common pathogen in humans. Non-zoonotic *C. pneumoniae* is responsible for 10-15% of all cases of community-acquired pneumonia, bronchitis and sinusitis in humans. It can occur more than once in a lifetime. Seroprevalence increases from 22% of children aged 1 to 4, to 63-79% of adults over 20 years old, and 97% of adults over 60 years old.

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Morbidity and Mortality: Animals

- *C. abortus*
  - Important cause of enzootic abortion
    - Sheep: up to 30% affected
    - Goats: 60-90% affected
  - Cyclic pattern in endemic herds
- *C. felis*
  - Infections common in cats
    - Conjunctivitis in kittens

In many countries, *C. abortus* is an important cause of abortion in sheep and goats. Outbreaks of enzootic abortion are seen regularly in these two species, and an epizootic has been reported in llamas, but only sporadic cases occur in cattle. In naïve flocks, enzootic abortion can affect up to 30% of pregnant sheep and as many as 60-90% of pregnant goats. Most animals abort only once. Immunity persists for several years or longer; it seems to last approximately 3 years in goats. In endemically infected flocks, the overall morbidity rate usually drops to 5-10%. A cyclic pattern may be observed in endemically infected goat herds, with abortion rates of approximately 10% for several years followed by a new outbreak with all yearlings aborting. Death of the dam is rare in all species. *C. felis* infections are common in cats; approximately 2-12% of cats have antibodies to this organism. Conjunctivitis is most often seen in 5 to 12 week old kittens. Immunity is usually transient but reinfections tend to be milder. The morbidity and mortality rates for *C. pneumoniae* have not been well established in animals. Koalas often seem to carry *C. pneumoniae* asymptomatically, but respiratory disease has also been reported. Sporadic deaths have been reported in amphibians and reptiles. A mortality rate greater than 90% was seen in one colony of frogs. Photo: (Top) Goat and kids.; (Bottom) Kittens. Source: Wikimedia Creative Commons]

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TRANSMISSION

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Life Cycle

- Elementary body (EB)
  - Small, metabolically inert
  - Stable in the environment
- Taken up by host cells
- Transforms in to reticulate body (RB)
  - Metabolically active
  - Divide and differentiate into EB
- EB released from cell

Chlamydiae have a unique life cycle involving two forms, an elementary body and a reticulate body. The elementary body is smaller, metabolically inert and relatively stable in the environment. *C. abortus* elementary bodies can remain infective in the environment for several days in typical spring weather, and for months if the temperature is freezing or near freezing. Elementary bodies are taken up by host cells via endocytosis, but remain inside a membrane-bound inclusion body in the cytoplasm. After several hours, the elementary body transforms into a reticulate body. The reticulate body is metabolically active and divides several times within the inclusion body. Its progeny eventually differentiate into elementary bodies, which are released when the cell disintegrates or the inclusion body fuses with the cell membrane. The reticulate bodies are not infectious.

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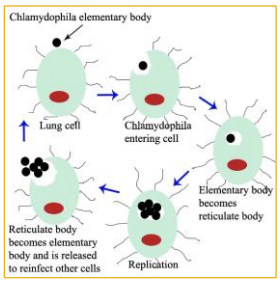

[Photo: *Chlamydophila* life cycle. Source: InvictaHOG/Public Domain via Wikipedia http://en.wikipedia.org/wiki/File:Chlamydophila_pneumoniae.jpg]

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Transmission in Humans

- Ingestion
- Aerosol
- Direct inoculation (eye)
- Venereal (possibly)

The zoonotic chlamydiae can be transmitted by ingestion, aerosols, direct inoculation into the eye and possibly venereal transmission. Animals can carry these organisms asymptomatically.

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Transmission in Animals

- *C. abortus*
  - Shed in placenta, uterine discharges, other abortion products
  - Ingestion, aerosol, venereal
- *C. felis*
  - Shed in ocular and nasal secretions
- *C. pneumoniae*
  - Unknown

Pregnant ruminants shed large numbers of *C. abortus* in the placenta and uterine discharges when they abort or give birth. Many infections occur by ingestion, but aerosol transmission is also possible and recent research suggests that venereal transmission may be important. In addition, *C. abortus* can be found in the feces and urine of some ruminants, as well as in goats' milk. Both sheep and goats can be chronic carriers. *C. felis* is shed in ocular and nasal secretions. It has also been recovered from various internal organs. Persistent infection of the oviduct has been reported, suggesting that venereal transmission may be possible.
The method of transmission for *C. pneumoniae* in animals is unknown. In koalas, *C. pneumoniae* has been isolated from the respiratory tract, the eye and the urogenital tract. In horses, this species has been found only in the respiratory tract.

[Photo: Sheep and lambs. Source: Stephen Ausmus/USDA ARS]

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DISEASE IN HUMANS

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C. abortus in Humans

- Initial signs nonspecific
  - Influenza-like illness
- Abortion
  - 14th-36th week of pregnancy
- Other clinical manifestations
  - Septicemia, hepatitis, kidney dysfunction, pneumonia, DIC

Zoonotic infections mammalian chlamydiae are rare and the incubation period does not seem to be published. In most of the cases reported in the literature, the initial symptoms of *C. abortus* infection have been nonspecific and influenza-like with fever, headache, dizziness and vomiting. Abortions usually occurred soon after the onset of the clinical signs, and were reported between the 14th and 36th weeks of pregnancy. Untreated infections progressed to septicemia with hepatitis, kidney dysfunction, pneumonia and disseminated intravascular coagulation.

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C. pneumoniae in Humans

- Zoonotic exposure not linked to any cases of human disease
- Symptoms likely
  - Fever
  - Non-productive cough
  - Sinusitis, pneumonia, bronchitis
  - Arthritis
  - Ocular disease
  - Genital and skin infection

C. pneumoniae in animals may be zoonotic but has not been linked to any cases of human disease. The symptoms would probably be similar to those caused by the human isolates of *C. pneumoniae*: respiratory disease with a fever and a non-productive cough. Most *C. pneumoniae* infections in humans are asymptomatic or mild, but some develop into sinusitis, pneumonia, or acute or chronic bronchitis. *C. pneumoniae* can also cause arthritis, ocular, genital and skin infections in humans. In addition, links to atherosclerosis, asthma, sarcoidosis, reactive airway disease, multiple sclerosis, erythema nodosum, Alzheimer's disease and other diseases have been suggested.

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Diagnosis

- Difficult to diagnose
  - No gold standard tests
- Serology
  - Immunofluorescence
  - PCR
    - Usually designed to detect *C. trachomatis*
- Culture

With the exception of *C. trachomatis*, chlamydial infections are difficult to diagnose in humans. Good standardized tests for most chlamydial species are not widely available. Serologic tests including immuno-fluorescence and microimmunofluorescence may be available; however, antibody production is variable and often delayed, the tests may not be standardized, and chlamydial species can cross-react in these tests. PCR assays are mainly designed to detect *C. trachomatis*, but "in-house" PCR to detect other species may be available in some laboratories. Most PCR tests for the former *Chlamydia psittaci* do not distinguish between *Chlamydophila psittaci*, *C. abortus*, *C. felis* and *C. caviae*. Chlamydiae can also be isolated in embryonated chicken eggs or cell cultures including McCoy, BGM or BHK cells. Culture requires special facilities and is not available at all laboratories. *C. pneumoniae* is difficult to culture. [Photo: Diagnostic testing. Source: Danelle Bickett-Weddle, Iowa State University/CFSPH]

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Treatment

- Antibiotics
  - Tetracycline
  - Erythromycin
  - Quinoloes

Chlamydiosis can be treated with tetracycline, erythromycin or other macrolides, and quinolones. In at least one *C. abortus* infection, the infant survived when the mother was treated early with erythromycin and the fetus was delivered by caesarian section before 34 weeks of gestation.

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DISEASE IN ANIMALS

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Species Affected

- *C. abortus*
  - Sheep, goats, deer, cattle, llamas
- *C. felis*
  - Cats, iguanas
- *C. pneumoniae*
  - Horses, dogs, koalas, rats, iguanas, frogs

Chlamydophila abortus often affects sheep and goats, and occasionally deer, cattle or llamas. This species has also been reported from a rabbit, a horse, guinea pigs, mice, green sea turtles and snakes. *Chlamydophila felis* is normally found in cats. It has also been reported from iguanas. *Chlamydophila pneumoniae* was, until recently, thought to affect only humans. Since the 1990s, this species has been found in a horse, dogs, koalas, rats, iguanas and frogs. [Photo: Flock of sheep. Source: USDA ARS]

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C. abortus in Animals

- Causes enzootic abortion
  - Late term abortion, stillbirth, weak or low birth weight lambs
- Dams usually remain healthy
- Experimentally infected males
  - Orchitis, epididymitis
  - Decreased fertility
- May be carried asymptomatically

C. abortus causes outbreaks of abortions (enzootic abortion) in sheep and goats. Sheep and goats infected early in gestation abort late in the same gestation, but animals infected late in gestation usually abort late in the following pregnancy. Congenitally infected lambs and kids may abort their first pregnancy. An epizootic was also reported in llamas, but only sporadic abortions occur in cattle. Enzootic abortion is characterized by late term abortions, stillbirths and the birth of weak, low birth weight or premature offspring. A reddish-brown vaginal discharge may be seen for several days after the abortion or parturition but the dam usually remains otherwise healthy. In most ewes, there are no symptoms before the abortion, and post-abortive sickness, retained placentas and metritis are unusual. Metritis and retained placentas are also uncommon in goats, although they may be more common than in sheep. Occasionally, some affected goats develop a persistent cough, polyarthritis or keratonconjunctivitis. In experimentally infected males, *C. abortus* can cause orchitis, epididymitis and seminal vesiculitis, with decreased fertility or infertility in the flock. Ruminants can also carry *C. abortus* asymptomatically. *C. abortus* has also been isolated from abortions in a horse, a rabbit, guinea pigs and mice.

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C. felis in Animals

- Conjunctivitis in cats
  - Often begins in one eye but becomes bilateral
  - Blepharospasm, chemosis, congestion, ocular discharge
- Mild to moderate rhinitis
- Pneumonitis

In cats, conjunctivitis due to *C. felis* appears in approximately 3 to 10 days. The symptoms often begin in one eye but eventually become bilateral. They typically include blepharospasm, chemosis, congestion and an ocular discharge that may become purulent. Fever usually begins several days after the onset of the ocular signs. The symptoms are generally most severe during the second week of disease and subside over the next 2 to 3 weeks; however, they can persist for longer in some cats. Complications may include vascular keratitis, corneal ulcers, pannus and corneal scarring. Some cats also develop mild to moderate rhinitis, with serous nasal discharge and sneezing. Pneumonitis is occasionally seen and, in a single case, a *Chlamydia* spp. was recovered from a cat with peritonitis. Chronic salpingitis and persistent infection of the oviduct have been reported, suggesting that infertility could be a sequela.

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C. pneumoniae in Animals

- Koalas
  - Asymptomatic
  - Respiratory disease
- Horses
  - Asymptomatic

C. pneumoniae has been isolated from asymptomatic koalas as well as from koalas with respiratory disease. The only known equine strain, found in the respiratory tract of a horse, caused no symptoms in experimentally infected horses.

[Photo: Koala, eye. Reddened conjunctiva with a focal erosion and serous exudate. Source: Armed Forces Institute of Pathology/CFSPH]

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Chlamydiae in Reptiles and Amphibians

- *C. abortus, C. felis, C. pneumoniae*
  - Lethargy
  - Anorexia
  - Suppurative pneumonia
  - Chronic nephritis
  - Hepatitis
  - Increased mortality rates

Lethargy, anorexia, suppurative pneumonia, chronic nephritis, hepatitis and increased mortality rates have been reported in amphibians and reptiles affected by *C. abortus*, *C. pneumoniae* or *C. felis*. The full spectrum of clinical disease in amphibians and reptiles is unknown. In a colony of African clawed frogs (*Xenopus tropicalis*), an epizootic of chlamydiosis was characterized by lethargy, sloughing of the skin, edema and a very high mortality rate. On necropsy, there was evidence of hepatitis. It is possible that co-infecting pathogens, including a chytrid fungus, may have played a role in this disease.

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Post Mortem Lesions

- *C. abortus*
  - Placentitis
    - Necrotic cotyledons
  - Relatively normal fetus
  - Petechiae
- *C. felis*
  - Conjunctivitis
  - Rhinitis

Enzootic abortion (*Chlamydophila abortus)* is characterized by placentitis with a relatively normal fetus. The cotyledons and surrounding intercotyledonary areas may be necrotic, edematous, thickened, inflamed and covered in exudate. The fetus is usually fresh, may be autolyzed, but is not usually necrotic. It generally has only nonspecific lesions. Often, the fetus is covered in reddish-brown exudate from the placenta. Occasionally, there may be clear or blood-stained edema, blood-stained fluid in the abdominal and pleural cavities, or pinpoint white foci of necrosis in the liver. In goats, petechiae are often found on the tongue, in the buccal cavity and on the hooves. Microscopically, there may be interstitial pneumonia or evidence of necrosis in the spleen and liver. The lesions caused by *C. felis* are usually limited to conjunctivitis and rhinitis. Occasionally, there may be mild, focal interstitial pneumonia or hyperplasia of the lymphoid follicles in the spleen and peribronchial lymph nodes. [Photo: (Top) Goat, placenta. The intercotyledonary placenta is thickened, opaque, and multifocally covered by tan clumps of exudate. Margins of several cotyledons are tan (necrosis), and centers are mottled red-brown (congestion and exudation). Source: Dr. J. Arzt/Plum Island Animal Disease Center, USDA/CFSPH; (Bottom) Bovine, kidney. Diffuse petechial hemorrhages are present in the kidney. Source: Armed Forces Institute of Pathology/CFSPH]

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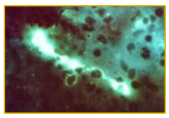
Diagnosis

- Antigen detection
  - Immunofluorescence
  - Immunoperoxidase
  - ELISA
  - PCR
- Culture
- Serology
  - Paired sera preferable



Chlamydiosis can be diagnosed by identifying the organisms or their antigens in tissue scrapings/smears, tissue sections and secretions. Chlamydiae can be stained with Machiavello, Giemsa, *Brucella* differential and modified Ziehl–Neelsen stains. Immunofluorescent or immunoperoxidase staining, and enzyme-linked immunosorbent assays (ELISAs) can detect chlamydial antigens. Most of these tests can identify the organism only as a member of the Chlamydiaceae; they generally cannot identify the species. Human *C. trachomatis* ELISAs are sometimes used to diagnose *C. abortus* in ruminants. In aborting animals, smears can be made from affected chorionic villi or adjacent areas of the placenta. They can also be taken from vaginal swabs of animals that have aborted within the last 24 hours, or the moist fleece of a freshly aborted or stillborn lamb. *C. felis* infections in cats can be diagnosed by demonstrating the organism in conjunctival scrapings. The organisms can also be found in lung sections. Polymerase chain reaction (PCR) assays have been mainly used in research but are beginning to be introduced into diagnostic laboratories. Chlamydiae can also be isolated in embryonated chicken eggs or cell cultures including McCoy, BGM and baby hamster kidney (BHK) cells. *C. abortus* can be cultured from the placenta, placental membranes, fetal lung or liver, and vaginal swabs. *C. felis* can be isolated from cases of conjunctivitis, but this is rarely done. Chlamydiosis can also be diagnosed by serology, preferably using paired sera. Serologic tests include complement fixation, ELISAs and micro-immunofluorescence. In many cases, serologic tests for the chlamydiae are not species-specific. Complement fixation is used most often in aborting ruminants, particularly as a herd test. Cross-reactivity with *C. pecorum* can be a problem, as many animals carry the latter organism asymptomatically in the intestines. [Photo: This direct FA stained mouse brain impression smear reveals the presence of the bacterium *Chlamydia psittaci*. 400X. Source: CDC Public Health Image Library]

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Treatment

- Antibiotics
  - Tetracyclines
  - Erythromycin
  - Tylosin
  - Quinolones
  - Chloramphenicol

Chlamydiosis is usually treated with tetracyclines. Other antibiotics including erythromycin and other macrolides, tylosin, quinolones and chloramphenicol may also be used.

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PREVENTION AND CONTROL

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Prevention in Humans

- Pregnant women
  - Avoid contact with pregnant or aborting ruminants
  - Consider avoiding contact with all sheep and goats
- Good hygiene

Pregnant women should avoid contact with pregnant or aborting ruminants and, if possible, sheep or goats in general. Women seem to be susceptible to *C. abortus* infections at any stage of their pregnancy. Good hygiene such as hand washing can reduce the risk of transmission of *C. felis* from symptomatic cats; however, human infections seem to be very rare.

[Photo: Hand washing. Source: CDC Public Health Image Library]

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Prevention in Animals

- Use disease-free replacement stock
- Isolate sick animals
- Practice good hygiene
  - Wash hands
  - Footwear
- Clean and disinfect infected premises
- Vaccinate

Ruminants can carry *C. abortus* asymptomatically, and enzootic abortion is often introduced into a flock in new animals. Replacement stock should be bought from sources known to be free of this disease. Sick cats, aborting ruminants and other animals with chlamydiosis should be isolated. Personal hygiene, including hand washing and cleansing/ disinfection of footwear, is important to prevent spreading the infection between animals. Affected ruminants should be kept isolated for approximately three weeks. The premises should be cleaned and disinfected after an abortion, and any aborted fetuses, dead lambs, contaminated bedding or placentas should be removed. The main flock should, if possible, be moved to uncontaminated pens. If possible, a flock of affected ruminants should be maintained separately from the "clean" flock once the outbreak subsides. Vaccines can reduce the incidence and severity of abortions in ruminants or chlamydial conjunctivitis in cats, but are not completely protective. A live vaccine has been reported to decrease the shedding of *C. abortus* in sheep and may be useful for eradication programs. It is not available in all countries. Treatment with tetracyclines can prevent abortions in ruminants, but organisms may still be shed at birth. [Photo: Cow in isolated area. Source: Bryan Buss, Iowa State University/CFSPH]

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Disinfection

- Quaternary ammonium compounds
  - 1:1,000 dilution
- 1% sodium hypochlorite
- 70% ethanol
- Glutaraldehyde
- Formaldehyde
- Moist heat (121°C for 15 minutes)
- Dry heat (160-170°C for 1 hour)

Chlamydia and *Chlamydophila* spp. are susceptible to most disinfectants and detergents, including a 1:1,000 dilution of quaternary ammonium compounds, 1% sodium hypochlorite, 70% ethanol, glutaraldehyde and formaldehyde. They are resistant to acids and alkali. Chlamydiae can be destroyed by moist heat (121°C for a minimum of 15 minutes) or dry heat (160-170°C for 1 hour or more).

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Acknowledgments

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