Zoonotic Chlamydiae Maintained in Mammals

Chlamydiosis

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Importance

Members of the genus *Chlamydia* cause reproductive losses, conjunctivitis, respiratory disease and other illnesses in animals and people. While each chlamydial species tends to be associated with one or a few animals, it appears that their host range may be much broader than previously thought. In some cases, this can include humans. *Chlamydia abortus*, which causes enzootic abortion in small ruminants, can result in abortions, premature births and life-threatening illnesses in pregnant women. Other animal-associated mammalian chlamydiae have rarely been found in people; however, some studies suggest that such infections could be underdiagnosed.

Etiology

Members of the genus *Chlamydia* are coccoid, obligate intracellular bacteria in the family Chlamydiaceae and order Chlamydiales. They are considered to be Gram negative, due to their relationships with other Gram negative bacteria, but they are difficult to stain with Gram stain. Chlamydiae have a unique life cycle, alternating between two different forms called the elementary body and the reticulate body (see “Transmission and Life Cycle” for details).

Pathogenic species of *Chlamydia* maintained in mammals include *Chlamydia abortus* (formerly mammalian abortion strains, ovine strains or serotype 1 of *C. psittaci*), *C. pecorum* (formerly serotype 2 of *C. psittaci*), *C. felis* (formerly feline strains of *C. psittaci*), *C. pneumoniae* (formerly the TWAR agent of *C. psittaci*), *C. caviae* (formerly guinea pig strains of *C. psittaci*), *C. trachomatis*, *C. suis* (formerly porcine *C. trachomatis*) and C. *muridarum* (formerly *C. trachomatis* of mice). There may be undiscovered species of *Chlamydia*, particularly in less frequently studied species such as wildlife. Apparently novel chylamydial species were recently identified in asymptomatic wild roe deer (*Capreolus capreolus*) and sick farmed Siamese crocodiles (*Crocodylus siamensis*), and a new species, *C. sanzinia*, was proposed in snakes.

The nomenclature of the genus *Chlamydia* has undergone a number of changes over the years. At one time, all of the chlamydial organisms in birds, humans and other mammals were called either *Chlamydia psittaci* or *Chlamydia trachomatis*. At this time, *C. psittaci* included some organisms that are now known to be maintained primarily in mammals, and others that are mainly associated with birds. Many of the mammalian chlamydiae were distinguished only by names such as "the feline strains of *C. psittaci*." In 1999, the chlamydiae were reorganized, and only bird-associated strains (with minor exceptions) were retained in *C. psittaci*. Many of the chlamydiae maintained in mammals received their species names at this time. The genus *Chlamydia* was also split in two, and some organisms were transferred to the new genus *Chlamydophila*. However, this classification was not accepted by many microbiologists, and the two genera were recently recombined into the single genus *Chlamydia*.

Several new families of *Chlamydia*-like organisms (e.g., the Parachlamydiaceae, Simkaniaceae and Waddliaceae) were recently added to the Chlamydiales. Some of these organisms, such as *Parachlamydia acanthamoebae* and *Waddlia chondrophila*, are suspected to be pathogenic for humans or other animals. These organisms are still incompletely understood, and they are not discussed in this factsheet.

Species Affected

Mammalian chlamydiae tend to be associated with one or a few maintenance hosts, but they are also found occasionally in other species.

C. abortus causes enzootic abortion in sheep and goats, which are the primary reservoir hosts for this organism. It has also been reported in many other species of mammals, both domesticated and wild, and in some reptiles (snakes, green sea turtles [*Chelonian mydas*]) and amphibians (frogs). It is known or suspected to cause illnesses in cattle, yaks (*Bos grunniens*), water buffalo (*Bubalus bubalis*), llamas, pigs, horses and deer. Rare reports of *C. abortus* in cats and rabbits were not linked to clinical signs. This organism has been detected occasionally in various birds,

including poultry, psittacines and pigeons. It is not entirely clear whether all reports of *C. abortus* in birds are real: recombination between this organism and the bird-associated species *C. psittaci* can result in high homology in a gene (ompA) that has been used for many PCR assays. Improved PCR tests to distinguish *C. psittaci* and *C. abortus* have been published.

C. pecorum has been associated with disease in sheep, goats, cattle, water buffalo, horses, pigs, Alpine chamois (*Rupicapra rupicapra*), koalas (*Phascolarctos cinereus*) and western barred bandicoots (*Perameles bouganville*). It is also carried in healthy ruminants and other species, typically in the intestinal tract. Reports of asymptomatically infected hosts have included Australian marsupials, deer, Alpine ibex (*Capra ibex*), and some birds, such as wild pigeons, pet birds and chickens.

C. pneumoniae is a common pathogen of humans, but it has also been reported from horses, cattle, cats, dogs, various wild ruminants and cervids, and Australian marsupials (e.g., koalas, bandicoots, potoroo). Among animals, clinical cases have mainly been seen in koalas, but *C. pneumoniae* was found in the eyes of some cats with conjunctivitis. It has also been found in sick or healthy reptiles and amphibians, including a number of snakes, several species of turtles, iguanas (*Iguana iguana*), flap-necked chameleons (*Chameleo dilepis*) and frogs. A recent article from Argentina reported that *C. pneumoniae* was common in captive birds, including household pets, although it was not detected in wild birds.

C. suis mainly occurs in domesticated pigs and other members of the pig family, such as European wild boar. It has also been reported in cattle, healthy and sick sheep, a few horses, a cat suspected of chlamydiosis, poultry (chickens, ducks and geese in isolated flocks in China) and both healthy and sick frogs.

C. felis is normally found in cats. It has been reported from dogs and iguanas, and it was suspected to be involved in some clinical cases in dogs.

C. caviae affects guinea pigs. Early attempts to inoculate mice, hamsters and rabbits failed. However, this organism has now been detected, at least by PCR, in rabbits, horses, a cat and a dog. Some infected horses, a rabbit and the dog had clinical signs. *C. muridarum* occurs in mice and other rodents, and it has been detected in a few flocks of chickens, ducks and geese in China. Organisms related to *C. muridarum* were found in roe deer, but they are suspected to be a new species of *Chlamydia*. Unspecified chlamydial agents were suspected in illnesses in some animal species (e.g., snowshoe hares, muskrats, opossums).

C. trachomatis occurs almost exclusively in humans. It has been detected by PCR in a few urban pigeons and wild Eurasian coots (*Fulica atra*). It was also found in the reproductive organs of a few culled repeat breeder pigs.

Zoonotic potential

Illnesses caused by *C. abortus* are reported occasionally in people. All cases, to date, have been linked to contact with small ruminants. *C. felis*, *C. suis* and *C. pecorum* were demonstrated or suspected to be involved in a few human illnesses. *C. suis* was also found (by PCR and/or culture) in ocular, nasal and pharyngeal swabs and stool samples from pig farmers, and in the conjunctiva of two asymptomatic employees at a pig abattoir. One report found *C. caviae*, using PCR, in the eyes of a person who had a number of infected guinea pigs.

C. pneumoniae is maintained in both human and animal (e.g., koala) populations. There are no reports of zoonotic cases. However, genetic analyses suggest that human isolates of *C. pneumoniae* are likely to have evolved from animal strains, implying that isolates in animals might be zoonotic, and also that humans might be able to infect animals. Because this organism is common in people, zoonotic transmission would be difficult to detect. No evidence for zoonotic transmission of *C. muridarum* has been published, as of 2017.

Geographic Distribution

C. felis, *C. pneumoniae*, *C. pecorum* and *C. suis* are cosmopolitan, and seem to occur in most or all locations with suitable hosts. *C. abortus* has been reported from most sheep-raising countries, but it has not been detected in Australia or New Zealand. There is no information about the distribution of *C. caviae* or *C. muridarum*, but they are presumably widespread.

Transmission and Life Cycle

Life cycle

Chlamydiae have a unique life cycle involving two forms, the infectious elementary body, which is smaller and relatively inert, and the non-infectious reticulate body. The reticulate body is found only inside cells. An elementary body taken up by a host cell remains inside a membrane-bound inclusion body in the cell's cytoplasm, where it transforms into the reticulate body. Reticulate bodies divide for a time, then transform back into elementary bodies, which are released when the cell disintegrates or the inclusion body fuses with the cell membrane. The latter process leaves the cell intact.

Chlamydiae can sometimes persist for long periods in unknown locations in the body. Organisms in this state might be refractory to antibiotics. Whether persistence occurs similarly in humans and other animals, and whether its characteristics are identical between chlamydial species, is not known.

Transmission

Chlamydiae can be acquired by inhalation, ingestion, direct inoculation into the eye and venereal transmission. Sources of these organisms may include birth products, vaginal discharges, feces, urine, semen, and ocular and

nasal secretions. Agents that have been found in semen include *C. abortus* and *C. pecorum* in ruminants, and *C. suis* in boars. *C. abortus* was detected in the milk of some ruminants.

The predominant routes of transmission can differ between chlamydial species, disease syndromes and hosts. *C. abortus* is often transmitted to other animals in birth products, although it also occurs in other secretions and excretions, such as feces. Pregnant ruminants can shed large amounts of *C. abortus* in the placenta and vaginal fluids when they abort or give birth. Shedding in vaginal fluids can sometimes begin more than 2 weeks before an abortion, especially in goats, and it may continue (often intermittently) for a few weeks afterward. Sheep and goats can become carriers of *C. abortus*, with persistent infections reported for at least 2-3 years in some sheep. These animals may shed the organism around the time of estrus and during subsequent pregnancies, although recent studies suggest that the quantities are small.

Cats shed *C. felis* in ocular and nasal secretions. In cats with conjunctivitis, this organism tends to disappear from ocular secretions after 2 months, although persistent colonization has been reported. Vaginal and fecal shedding have been reported in some cats with conjunctivitis. *C. felis* has also been recovered from various internal organs in experimentally infected cats, although the significance of this finding is uncertain.

In koalas, *C. pneumoniae* and *C. pecorum* may be common in the respiratory tract, the eye and the urogenital tract. Young koalas are thought to be infected from their dams in many cases, and venereal transmission is also thought to be significant. *C. pecorum* is common in the intestinal tract of other animals, and *C. pneumoniae* is primarily a respiratory pathogen in humans.

Humans are likely to be infected with zoonotic chlamydiae by the contamination of mucous membranes (including the conjunctiva) and inhalation, but other routes may also be possible.

Environmental survival

Varying environmental survival times have been reported for different species of *Chlamydia*. *C. psittaci*, which circulates in birds, is reported to persist for 15 days on dry environmental surfaces such as glass, and sometimes for longer when it is protected in organic materials (e.g., in straw for 20 days, in bird feed for up to 2 months). *C. abortus* elementary bodies are estimated to remain infective in the environment for several days during typical spring weather, and for months if the temperature is freezing or near freezing. Chlamydiae maintained in humans seem to be relatively fragile except when they are suspended in culture media expected to optimize their survival, where they have sometimes been reported to survive as long as 2-4 weeks under laboratory conditions, at temperatures up to 30°C (86°F). When dried on various solid surfaces, the maximum survival time for *C. trachomatis* and *C. pneumoniae* was 4-30 hours in two studies, with the organisms remaining infectious for only 10-30 minutes on human skin. One study found few or no viable *C. trachomatis* in a balanced salt solution after approximately 2 days at room temperature or 5 days at 4°C, while another reported that this organism became undetectable by one week (at room temp, in the dark) in tap water or dried in the presence of blood. Infectious *C. pneumoniae* could not be recovered after 3 days in autoclaved soil. DNA from this organism was, however, found much longer by PCR, and the authors speculated that the organism might enter a viable but non-cultivable state. It might also be possible for pathogenic chlamydiae to survive for prolonged periods in environmental amoebae; however, this is still speculative.

Disinfection

Chlamydiae are expected to be susceptive to a number of disinfectants, based on their similarities to other bacteria. One study found that *C. trachomatis* was inactivated by 0.25-2.5% bleach (sodium hypochlorite), 70% ethanol, 2% glutaraldehyde, orthophthalaldehyde, 7.5% hydrogen peroxide and 0.2% peracetic acid. Quaternary ammonium compounds are also expected to be effective. *C. psittaci* is reported to be resistant to acids and alkali.

Like most bacteria, chlamydiae should be susceptible to moist heat of 121°C (250°F) for a minimum of 15 minutes, and dry heat of 160-170°C (320-338°F) for one hour . One study found that *C. trachomatis* was inactivated by heating at 55°C (131°F) for 10 minutes.

Infections in Animals

Incubation Period

Feline conjunctivitis from *C. felis* appears approximately 3-10 days after exposure, often within 5 days. Sporadic bovine encephalomyelitis, which is caused by *C. pecorum*, has an incubation period of 6-30 days in experimentally infected calves. The incubation period for *C. abortus* is highly variable. Some pregnant sheep and goats abort soon after becoming infected. Nonpregnant animals may carry this organism subclinically and abort during their next pregnancy, or mount an effective immune response and never abort.

Clinical Signs

Chlamydiae tend to cause conjunctivitis, reproductive losses, arthritis, respiratory disease and urinary tract infections in mammals and marsupials. They are sometimes involved in other conditions (e.g., sporadic bovine encephalomyelitis) in certain hosts. It is not unusual to find the same organism in both sick and healthy animals.

Some syndromes caused by chlamydiae, such as enzootic abortion, chlamydial polyarthritis and *C. felis* conjunctivitis, are well known. In other cases, the evidence that chlamydiae caused an illness (and were not simply

present in an animal infected with another pathogen) is sometimes still circumstantial.

Enzootic abortions, chlamydial polyarthritis and other diseases in small ruminants: C. abortus, C. pecorum and C. suis

C. abortus causes enzootic abortion in sheep and goats. This disease is characterized by late term abortions, stillbirths, and the birth of weak or premature offspring. Animals seem to be especially susceptible to reproductive losses when they are infected around the third month of the pregnancy. Animals infected soon after conception may lose the fetus inapparently and appear infertile. Vaginal bleeding is sometimes observed during the 2 weeks before an abortion, particularly in goats; however, most animals do not appear ill. Typically, the first sign of an outbreak is the appearance of stillborn lambs or kids, 2-3 weeks before parturition is expected. Both healthy and dead or weak lambs can occur in the same animal. Stillborn lambs look relatively normal, although the abdomen is sometimes distended by fluid. Post-abortive sickness, retained placentas and metritis are unusual in the dam, although they are reported to be more common in goats than sheep. A reddish-brown vaginal discharge may be seen for several days after abortion or parturition. Occasionally, flocks/ herds experiencing enzootic abortion may also have animals with chlamydial polyarthritis, keratoconjunctivitis or respiratory disease (primarily evident as a persistent cough). Animals that abort usually deliver normal offspring in subsequent pregnancies. In experimentally infected males, *C. abortus* can cause orchitis, epididymitis and seminal vesiculitis.

Modified live vaccine strains of *C. abortus* are now known to be responsible for a few cases of enzootic abortion. Most reports have not described any unusual features in these cases, but one suggested that the vaccine was responsible for an unusually severe outbreak with autolyzed fetuses, evidence of systemic disease in the dam, and high maternal mortality with toxemia.

C. pecorum is often carried asymptomatically in the intestinal tract, but it can cause keratoconjunctivitis and chlamydial polyarthritis, and it has been implicated occasionally in cases of abortion, respiratory disease, orchitis or mastitis. Polyarthritis tends to be seen in young animals up to 10 months of age, especially weaned lambs. Joint stiffness may or may not be accompanied by swelling of the joints. Some lambs appear to "warm out" of the stiffness upon exercise. Concurrent lethargy, fever and/or conjunctivitis may occur in some animals with polyarthritis.

C. suis was detected in the eyes of some sheep, using PCR. Most but not all animals had signs of keratoconjunctivitis.

Sporadic bovine encephalomyelitis, reproductive losses and other diseases in cattle and water buffalo: C. pecorum, C. abortus and C. suis

Sporadic bovine encephalomyelitis, caused by *C. pecorum*, has been reported in cattle and water buffalo. This disease may appear sporadically in individual animals, or as an outbreak. It tends to occur mainly in calves < 6 months of age. Despite its name, this disease is systemic. Common clinical signs include fever, depression, inappetence, weight loss, mild diarrhea, excessive salivation, nasal discharge and respiratory signs. Most animals also develop neurological signs. Stiffness and knuckling at the fetlocks tend to be seen initially, but progress to frank neurological signs (e.g., incoordination, staggering, circling, falling, recumbency). Clinical cases are often fatal if not treated in the early stages. Survivors usually recover slowly.

C. pecorum is reported to cause enteritis, characterized by mucoid, watery or bloody diarrhea, in very young (< 10-day-old) calves. This syndrome can be reproduced in colostrum-deprived calves. *C. pecorum* has also been linked to, or suspected in, cases of abortion, keratoconjunctivitis, pneumonia, polyarthritis and nephritis in cattle, and abortions in water buffalo.

C. abortus has been linked to occasional abortions in cattle, water buffalo and yaks. In cattle, these abortions tend to occur near the end of the last trimester. Some cows may retain the placenta. *C. abortus* was suggested to be responsible for premature calving and increased perinatal losses in some herds. It is also reported or suspected to cause decreased conception rates, subclinical and clinical mastitis, epididymitis, seminal vesiculitis, upper and/or lower respiratory signs, arthritis and keratoconjunctivitis in cattle. Some authors suggest that *C. abortus* may have subclinical detrimental effects on the pulmonary function and general health of calves.

One study reported finding *C. suis* in the placentas of some cattle that had aborted, but could not rule out contamination from the environment.

Reproductive losses caused by C. abortus in other hosts

Chlamydia spp. can cause abortions and the birth of weak crias in llamas. *C. abortus* was the causative agent in some cases. This organism has also been linked to, or suspected in, reproductive losses in other species (e.g., pigs, a horse and a rabbit), and it can cause abortions in experimentally infected guinea pigs. Based on serology and the response to tetracycline treatment, *C. abortus* was suspected to cause ovarian hydrobursitis in some dromedary camels. Ovarian hydrobursitis is characterized by fluid accumulation and encapsulation of the ovary, accompanied by early embryonic deaths, abortions and other reproductive lesions. It is poorly understood, and may have more than one cause.

C. suis, C. pecorum and C. abortus in pigs

The effects of chlamydial infections in pigs, and the contributions of coinfections, are still incompletely understood. In various reports, *C. suis* was implicated in

reproductive losses (abortions, stillbirths, early embryonic losses and increased neonatal mortality) in sows; pericarditis, polyarthritis and polyserositis in piglets; orchitis, epididymitis and urethritis in boars; and conjunctivitis and respiratory disease (rhinitis, cough, dyspnea, pneumonia). Experimentally infected, young gnotobiotic piglets developed diarrhea, but weaned pigs were unaffected. A definitive link with diarrhea has been difficult to prove in naturally infected herds.

C. pecorum has been linked to various conditions in pigs, including mastitis, encephalomyelitis, polyarthritis and abortions. *C. abortus* was associated with abortions, stillbirths and early embryonic losses in at least one herd. Both *C. suis* and *C. pecorum* can occur in the intestines of asymptomatic pigs, and *C. sui*s has been found in the eyes of pigs without ocular disease.

Conjunctivitis and other syndromes in cats: C. felis and C. pneumoniae

C. felis causes conjunctivitis in cats. It generally affects animals less than a year of age, and is especially prevalent in 5-12 week old kittens. Kittens born to infected mothers may be severely affected around the time their eyes would normally open, but most are protected by maternal antibodies at this time. The signs of *C. felis* conjunctivitis often begin in one eye, but usually become bilateral. They are sometimes accompanied by upper respiratory signs such as mild to moderate rhinitis, serous nasal discharge and sneezing. Most cats with conjunctivitis do not otherwise appear ill, although transient fever and inappetence may be seen occasionally, and there have been reports of pneumonitis. Chlamydial conjunctivitis often improves even without treatment; however, milder signs may persist for months, and can wax and wane. Complications involving the cornea (e.g., vascular keratitis, corneal ulcers, pannus and corneal scarring) seem to be uncommon, and are mainly thought to occur in animals concurrently infected with secondary bacterial invaders or FHV-1. Nevertheless, there are reports of keratitis in cases where only *C. felis* was detected.

Descriptions of *C. felis* suggest that this organism does not normally cause upper respiratory signs in cats without conjunctivitis. However, a recent study found no pathogens other than *C. felis* in 6 cats with rhinitis. A possible association between *C. felis* conjunctivitis and transient lameness has been suggested but this phenomenon, if real, does not seem to be well documented or characterized. This organism can also be shed in vaginal secretions, and might be a cause of reproductive losses in cats. There are rare reports of other conditions seemingly linked to *C. felis*, including some cases of gastritis.

One study detected *C. pneumoniae* in the eyes of some cats with conjunctivitis, with or without upper respiratory signs. This syndrome was indistinguishable from cases caused by *C. felis*, except that the cats were 2 to 14 years of age, older than typical for *C. felis* conjunctivitis.

C. caviae in guinea pigs and other species

C. caviae can cause mild to severe keratoconjunctivitis in guinea pigs, especially young animals. Alveolitis was seen in a few infected animals, but it could not be definitively linked to *C. caviae*. This organism may also be involved in salpingitis, cystitis and abortions in females, and urethritis in males.

C. caviae has been found rarely in the eyes of other species, including horses (see chlamydial disease in horses), an asymptomatic cat and a rabbit with mild conjunctivitis. The cat and the rabbit belonged to a person who had large numbers of infected guinea pigs. *C. caviae* nucleic acids were also detected in tissues and/or fecal samples from rabbits and in one dog suspected of chlamydiosis.

Chlamydial disease in dogs

There have been very few reports of chlamydial illnesses in dogs. *C. abortus*, *C. felis*, unspecified chlamydial species and "*C. psittaci*" (at a time when this species included both avian and mammalian chlamydiae) were identified in a few cases of conjunctivitis or keratoconjunctivitis. A chlamydial organism was suspected in an outbreak characterized by fever, inappetence, bronchopneumonia, peritonitis, vomiting, diarrhea and skin lesions, and a similar syndrome was reproduced experimentally by "the agent of ovine polyarthritis" (possibly *C. pecorum*). Recently, *C. caviae* was found, by PCR, in tissue and fecal samples from a dog suspected of chlamydiosis.

Chlamydial disease in horses

Chlamydial diseases have rarely been reported in horses, although cases might be underdiagnosed. *C. caviae* nucleic acids were found in nasal samples, together with *Streptococcus equi* subsp. *zooepidemicus*, during one outbreak of conjunctivitis and rhinitis in 2-3-week-old foals. Some foals also had diarrhea, and one developed fatal pneumonia. Older horses on this farm had recurrent conjunctivitis. *C. caviae* was also detected in respiratory samples from horses on another farm, but no details are available.

C. abortus has been linked to an abortion in at least one horse. In older studies, unspecified *Chlamydia* spp. were implicated in some cases of ocular disease and an outbreak of bronchopneumonia in foals. Horses infected experimentally with the "agent of goat pneumonitis" developed pneumonia. *C. pneumoniae* that had been isolated from a horse's respiratory tract caused no clinical signs in experimentally infected horses.

Chlamydial illnesses in koalas and other Australian marsupials: C. pecorum and C. pneumoniae

C. pecorum and, less frequently, *C. pneumoniae* can cause keratoconjunctivitis, reproductive disease (failure to conceive, metritis, infections of the male reproductive tract), urinary tract infections including cystitis, respiratory illnesses (e.g., pneumonia, rhinitis) and other syndromes in

koalas. Untreated infections may lead to severe complications including blindness, incontinence and infertility. Systemic spread affecting various internal organs was described in some animals infected with *C. pecorum*.

Chlamydia spp. have been associated with ocular disease in other Australian marsupials, but seem to be carried asymptomatically in most cases.

C. abortus, C. felis, C. suis and C. pneumoniae in reptiles and amphibians

Various localized or systemic syndromes characterized by nonspecific signs (e.g., lethargy, anorexia, unexpected deaths), conjunctivitis, chronic respiratory disease, chronic nephritis and hepatitis have been reported in reptiles infected with *C. abortus*, *C. pneumoniae*, *C. felis* or unspecified chlamydiae. Conjunctivitis was documented in several species of turtles and tortoises, as well as crocodiles. A captive snake that died during hibernation, apparently from a *C. pneumoniae* infection, had granulomatous lesions in its internal organs, *C. pneumoniae* and other species of *Chlamydia* have also been found in asymptomatic reptiles.

C. pneumoniae was detected in the lungs of a giant barred frog (*Mixophyes iteratus*) with pneumonia. Captive African clawed frogs (*Xenopus tropicalis*) infected with this organism developed an illness characterized by lethargy, sloughing of the skin, edema and a very high mortality rate. On necropsy, there was evidence of hepatitis. Co-infections, including a chytrid fungus, may have played a role in this outbreak. In another report, *C. pneumoniae* was found in submissions from a few captive frogs that died unexpectedly. *C. suis* or a similar organism was detected in some free-living frogs (*Rana temporaria*) during a mass mortality event in 1991–1992, but this may have been coincidental. *C. suis*, *C. pneumoniae* and *C. abortus* have been found in healthy free-living or captive frogs.

Post Mortem Lesions

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Enzootic abortion in small ruminants

Abortions caused by *C. abortus* are characterized by varying degrees of necrotic damage in the placenta. Typically, there are dark reddish-brown cotyledons and thickened, red to brown intercotyledonary areas covered in creamy exudate. The fetus is usually fresh, may be autolyzed, but is not usually necrotic. It generally has only nonspecific gross lesions (e.g., edema, blood-stained fluid in the abdominal and pleural cavities, congestion or pinpoint white foci of necrosis in the liver), is often covered in reddish-brown exudate from the placenta, and may have a distended abdomen. In goat fetuses, petechiae have been reported on the tongue and hooves and in the buccal cavity.

Similar placental lesions have been described in abortions caused by *C. pecorum*. Intestinal lesions (fibrinosuppurative and necrotizing enteritis), as well as histological lesions of hepatitis, were described in some aborted goat fetuses infected with *C. pecorum*.

Sporadic bovine encephalomyelitis

Sporadic bovine encephalomyelitis is a systemic disease that affects the internal organs; common lesions include serofibrinous peritonitis, pleuritis and pericarditis. Hyperemia and edema may be present throughout the brain.

Diagnostic Tests

Chlamydiosis can be diagnosed by identifying the organisms, their nucleic acids or antigens in affected tissues, secretions and excretions. In cases of enzootic abortion, chlamydiae are usually most abundant in the affected chorionic villi or adjacent areas of the placenta, but samples can also be taken from vaginal swabs of animals that have aborted within the last 24 hours, or from the abomasal contents, lung or liver of a freshly aborted or stillborn fetus.

PCR assays are increasingly used to diagnose chlamydial infections in animals. Assays to identify the *B. abortus* 1B vaccine strain have been developed, and may be available at some specialized laboratories. DNA microarray hybridization tests can distinguish different species of *Chlamydia*. Chlamydial antigens can be detected by immunostaining methods (immunohistochemistry, immunofluorescence) and antigen capture ELISAs. Antigen-detection tests cannot usually identify the species of *Chlamydia*.

Histology can suggest a tentative diagnosis or be used to support other diagnostic methods. In aborting ruminants, smears from clinical samples (including moist, uncleaned fleeces from aborted fetuses) may also examined. Chlamydiae can be stained with Machiavello, Giemsa, *Brucella* differential and modified Ziehl-Neelsen stains. Caution must be used in interpreting the results, as elementary bodies can resemble some other agents such as *Coxiella burnetii.*

Culture of chlamydiae requires specialized expertise, and is available in a limited number of laboratories. Special transport media and cold conditions are required to maintain the viability of these organisms during transport. Mammalian chlamydiae are usually isolated in various cultivated cell lines, although embryonated eggs may also be used. Organisms from pigs are reported to be difficult to isolate in the standard cell culture systems used for other species.

Serology is also used for diagnosis. Various tests such as ELISAs, microimmunofluorescence and complement fixation may be used. Test availability depends on the host species. Most serological tests are specific for the genus *Chlamydia*, and cannot distinguish antibodies to different chlamydial species. A four–fold rise in titer should be seen in paired samples. Ruminants that abort do not always have a rise in titers, and serology is often employed as a herd test in this situation. Some localized chlamydial diseases, such as conjunctivitis, are not readily diagnosed by serology.

Treatment

Only a limited number of antibiotics, such as tetracyclines, macrolides (e.g., erythromycin, azithromycin) and fluoroquinolones have good efficacy against chlamydiae. Sulfonamides are only useful for *C. trachomatis* and its close relatives, such as *C. suis*. Tetracyclines are used most often to treat animals; however, chloramphenicol is commonly employed in koalas, which can have serious side effects from some other drugs. Tetracycline-resistant strains of *C. suis* are common in some areas.

Continuing antibiotic treatment for several weeks after clinical resolution helps ensure that chlamydiae have been eliminated, and the condition will not recur. Two additional weeks has been advised in cats with conjunctivitis. Prolonged treatment is generally impractical in large animals. In some cases, chlamydiae have been shed even from some animals that were treated long-term.

Control

Disease reporting

Veterinarians who encounter or suspect chlamydial diseases should follow their national and/or local guidelines for disease reporting. In particular, enzootic abortion is notifiable in some countries and U.S. states.

Prevention

C. abortus often enters small ruminant herds in new animals, and maintaining a closed flock/ herd can be helpful. If replacement stock are added, they should be bought from sources known to be free of this disease. Diagnostic tests cannot reliably identify infected sheep or goats until they abort. Flock accreditation programs are available in some countries. Vaccines can reduce the incidence and severity of reproductive losses in ruminants, but are not completely protective. Although live attenuated vaccines have been linked to a small number of abortions, they are still considered to be the most effective means of control in infected herds. Tetracyclines used prophylactically near the beginning of an abortion outbreak can help protect other pregnant animals, although animals will still abort if the placenta is already damaged. Antibiotics should only be used when necessary, to avoid the development of antibiotic resistance.

Vaccines are also available for feline conjunctivitis caused by *C. felis*, and are in development for koalas. The *C. felis* vaccines cats reduce the severity and incidence of clinical signs, but are not completely protective.

Cleaning and disinfection, including personal hygiene, (e.g., hand washing, cleansing/ disinfection of footwear) are important in preventing transmission on fomites. Aborting ruminants, their offspring and other animals with chlamydiosis should be isolated while they are at risk of infecting others. Abortion or birth products from infected animals should be removed, and the area cleaned and (where feasible) disinfected. This can be facilitated by establishing a dedicated area for ruminants to give birth.

Morbidity and Mortality

Pathogenic chlamydiae are often carried asymptomatically in animals. Surveys sometimes find evidence of infection with some organisms, such as *C. pecorum* and *C. abortus*, in 50% or more of healthy individuals. However, *C. felis* seems to be uncommon in the eyes of healthy cats.

Many clinical syndromes caused by chlamydiae have a low mortality rate except in the fetus. The morbidity rate for chlamydial polyarthritis can sometimes reach 80% in lambs, but the estimated mortality rate is less than 1%, and affected animals may recover without treatment. Sporadic bovine encephalomyelitis is, however, often fatal if it is not treated in the early stages. One source estimates the case fatality rate for this condition to be 60%.

Enzootic abortion, caused by *C. abortus*, is an important cause of reproductive losses in small ruminants. In naïve flocks, as many as 30-60% or more of the pregnant animals may lose a fetus when they are first exposed. A common pattern is to see only small numbers of abortions during the first year, followed by an abortion storm the second year. After a few years, the abortion rate usually decreases to < 10%. However, some herds can have a cyclic pattern, with low abortion rates for several years, followed by a new outbreak when large numbers of susceptible animals are again present. Death of the dam is rare, and most animals abort only once. The number of abortions induced by live inactivated *C. abortus* vaccines, and the circumstances under which this occurs, are still uncertain. A 3-year study of submissions from reproductive losses in vaccinated sheep found that vaccine strains appeared to be responsible in approximately 30% of the cases, with field strains accounting for the remainder. Reproductive effects of chlamydiae on other species are less well understood. One study from Switzerland, where cattle may contact small ruminants in summer pastures, suggested that *C. abortus* may be responsible for a significant number of abortions in this region. Other reports suggest that abortions in cattle are rare, but chlamydiae might have subtle effects on fertility, milk production (e.g., due to mastitis) and growth rates in calves.

The effects of chlamydiae on wild animals are still uncertain, but *C. pecorum*, and to a lesser extent *C. pneumoniae*, are a significant concern in koalas. In most wild koala populations, the prevalence of these organisms ranges from 10% to 70-100%. Debilitation from untreated illnesses and their complications is thought to contribute to the declining numbers of wild koalas in Australia. Stressors and coinfections may also play a role in promoting overt disease.

Infections in Humans

Incubation Period

Few zoonotic chlamydial infections have been reported, and the incubation period is mostly unknown. One researcher infected by C. *abortus* developed pneumonia after 10 days. For reference, the incubation period for avian chlamydiosis (*C. psittaci*) in humans is usually 5-14 days.

Clinical Signs

Chlamydia abortus

Approximately 20 published clinical cases document abortions, stillbirths and pre-term labor caused by *C. abortus*. In most of these cases, women initially became ill with nonspecific, flu-like symptoms such as fever, malaise, headache, abdominal pain, dizziness, vomiting, and in at least one case, a dry cough. Abortions usually occurred soon after the onset of the clinical signs. Many or most women became seriously ill, with complications such as septicemia, hepatitis, kidney dysfunction, pneumonia/ respiratory distress and disseminated intravascular coagulation. Most recovered, with supportive care and antibiotics, after the termination of the pregnancy. It is possible that milder illnesses, with or without reproductive losses, are underdiagnosed. In one instance, two nonpregnant relatives who had helped with lambing developed much milder flu-like illnesses.

C. abortus was isolated from one woman with severe pelvic inflammatory disease characterized by chronic abdominal pain, increased vaginal discharge, unusually heavy menses, fatigue, general malaise and an occasionally elevated temperature. The symptoms resolved after antibiotic treatment. Two recent studies also suggest that *C. abortus* might be involved in reproductive and urinary tract diseases. A study from Egypt found *C. abortus* DNA, using PCR, in a significant number of women who presented with various gynecological complaints including mucopurulent vaginal discharge, lower abdominal pain, recurrent abortion and/or infertility. A study from Greece found *C. abortus* DNA in some urinary samples from men with chlamydiosis whose condition was originally thought to be caused by *C. trachomatis*.

C. abortus has been reported from at least two cases of respiratory disease. It caused respiratory signs in a researcher exposed to this organism in the laboratory. His illness was characterized by fever, malaise, chills, dry cough, chest pain and shortness of breath. *C. abortus* was also detected in a case of community-acquired pneumonia in Germany.

A few clinical cases had only circumstantial evidence for the involvement of *C. abortus*. For instance, a chlamydial organism was isolated from cerebrospinal fluid in a febrile child who had been exposed to cases of enzootic abortion in sheep.

Chlamydia felis

Only a few cases of *C. felis* conjunctivitis have been documented in people. One case, which was chronic, occurred in an HIV-infected person. Genetic analysis of the organism suggested that he had acquired it from an infected cat. The other cases were suspected, but not definitively proven, to be caused by *C. felis*.

Three systemic chlamydial illnesses were attributed to *C. felis*. All were diagnosed serologically, based on antibody titers that reacted more strongly to *C. felis* than to other chlamydial species. In one case, a renal transplant recipient developed malaise, a cough and abnormal liver function. Another person had infective endocarditis and glomerulonephritis. The third case occurred in a healthy man who developed a febrile illness with malaise, pneumonia and mental impairment. *C. felis* nucleic acids have also been detected in respiratory samples collected from a few people, including nasal swabs from a healthy person.

Chlamydia pneumoniae. S. suis, C. caviae and C. pecorum

C. suis was found in one case of community-acquired pneumonia in Germany. Nucleic acids of *C. suis* and *C. pecorum* were detected, by PCR, in the eyes of some people with trachomatous ocular inflammation in Nepal. (This condition is usually caused by *C. trachomatis*, which was also found in some cases.)

Zoonotic chlamydiae have also been reported in people who appeared to be unaffected by these organisms. *C. suis* has been found in upper respiratory, ocular and/or stool samples from a number of people, most healthy, who were regularly exposed to pigs. *C. caviae* nucleic acids were detected in the eyes of one person who had a number of infected guinea pigs. His only symptom was mild serous ocular discharge, which could have been caused by many things other than the presence of *C. caviae*.

There are no reports of zoonotic clinical cases caused by *C. pneumoniae*. Human isolates of *C. pneumoniae* usually cause a respiratory disease with a fever and a non-productive cough. Laryngitis is also common. The illness tends to be prolonged and relatively mild in most cases, but more serious cases with pneumonia and other complications are possible. *C. pneumoniae* has also been implicated in arthritis, ocular disease and genital conditions. Possible links to a wide variety of respiratory and non-respiratory diseases, such as asthma, chronic obstructive pulmonary disease (COPD), atherosclerosis and other conditions have been suggested, although there is no definitive evidence for its involvement.

Diagnostic Tests

Tests to diagnose chlamydial infections in humans are similar to those used in animals, and may include serology, PCR, antigen detection assays and culture. Most of the tests in diagnostic laboratories are intended to diagnose the

human pathogens *C. trachomatis* and *C. pneumoniae*. Some tests, particularly serological assays and antigen-detection tests, can determine that an illness is caused by chlamydiae, but do not distinguish different chlamydial species. Serological assays that can recognize antibodies to different species of *Chlamydia* (e.g., microimmunofluorescence) have been developed. Culture is not done routinely, and its availability in diagnostic laboratories is limited.

Treatment

Clinical cases are treated with drugs effective against chlamydiae, combined, if necessary, with supportive care. In addition to the antibiotics used in animals, ketolides (e.g., telithromycin) have been employed in people.

The best treatment to clear persistent infections is still uncertain, although prolonged (e.g., 6-month) course with a combination of antibiotics appeared promising in some cases.

Prevention

To prevent infections with *C. abortus*, pregnant women should avoid small ruminants, especially animals that are pregnant, have aborted or recently given birth, or were recently given live attenuated vaccines. Most clinical cases occurred after direct contact with ruminants, but a few women had only indirect contact. These exposures included living on farms, visiting barns and/or washing contaminated clothing. Pregnant women should also be aware that other livestock can occasionally carry *C. abortus*, although there are currently no reports of clinical cases associated with these species.

General precautions around animals infected with chlamydiae include good hygiene, such as hand washing after contact, and avoidance of exposure to aerosolized organisms. Contaminated clothing is considered safe to handle after it has been washed in a hot water cycle.

Morbidity and Mortality

Approximately 20 confirmed human abortions and stillbirths caused by *C. abortus* have been described in the literature since 1987, and 1-2 cases are estimated to occur each year in the U.K. Most affected fetuses died, although a few older fetuses survived after premature delivery or a C-section. Concurrent treatment with erythromycin might have been helpful in some of these cases, but it seemed unable to cure the infection on its own. Most women recovered with treatment, although at least one death has been reported.

There are a few reports of infections with other animal chlamydiae in people, but very few clinical cases have been documented. However, some illnesses might be underdiagnosed or attributed to the human pathogens *C. pneumoniae* and *C. trachomatis*, which cause similar diseases. A serological study in Japan found that the prevalence of antibodies to *C. felis* was higher (9%) in veterinarians who work with small animals than the general population (2%). In contrast, a study in Italy reported that the antibody prevalence to chlamydiae was approximately 8% in cat owners and veterinarians, as well as in people who have no contact with cats. In this study, the collected sera also reacted to *C. pneumoniae*.

Internet Resources

Centers for Disease Control and Prevention, U.S.
https://www.cdc.gov/

European Centre for Disease Control and Prevention. *Chlamydia*
http://ecdc.europa.eu/en/healthtopics/chlamydia/Pages/index.aspx

International Veterinary Information Service (IVIS)
http://www.ivis.org

Public Health Agency of Canada. Pathogen Safety Data Sheets
http://www.phac-aspc.gc.ca/lab-bio/res/psds-ftss/index-eng.php

Public Health England. Guidance: *Chlamydophila abortus*
https://www.gov.uk/guidance/chlamydophila-abortus

The Merck Manual
http://www.merckmanuals.com/professional

The Merck Veterinary Manual
http://www.merckvetmanual.com/mvm/index.html

World Health Organization
http://www.who.int/about/en/

World Organization for Animal Health (OIE)
http://www.oie.int/

World Organization for Animal Health (OIE). Manual of Diagnostic Tests and Vaccines for Terrestrial Animals
http://www.oie.int/international-standard-setting/terrestrial-manual/access-online/

OIE Terrestrial Animal Health Code
http://www.oie.int/international-standard-setting/terrestrial-code/access-online/

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