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Zoonotic aspects of animal chlamydioses - a review

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ABSTRACT

The order Chlamydiales consists of a diverse group of organisms of considerable importance to both animal and human health and of major economic importance worldwide. Chlamydioses affect humans, most domestic mammals and birds. Infections caused by these bacteria are widespread all over the world. When looking for possible sources of infections among humans, the species *Chlamydophila psittaci*, *Chlamydophila felis* and *Chlamydophila abortus*, as well as other bacteria from the genus Chlamydiphila have been isolated from different species of domestic and wild animals. Zoonotic diseases caused by these micro organisms are the consequence of direct contact with domestic, wild and synantropic animals that are either affected or already dead. This helps us to understand new epidemiological facts and risks for humans of being infected by these bacteria from animals, in particular from pets. By reviewing papers on the incidence of chlamydial infections among animals and humans, we aim to reach a better understanding of new microbiological classifications of Chlamydia and gain a special view of relationships between Chlamydia and their hosts.

Key words: animal Chlamydiosis, zoonoses, pathogenicity, infection

Significance of the genus Chlamydophila bacteria in disease etiology of humans and animals

Taxonomic extensive research of the bacteria from the order Chlamydiales on the basis of morphological, physiological and genetic characteristics have revealed the existence of a large number of new species, some of which have not been completely studied and classified (EVERETT et al., 1999). As well as in birds, sheep and goats, some papers report successful isolations of chlamydia from a large number of domestic and wild animals.

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This is confirmed by abortion isolates in cattle (STORZ, 1971) and pigs (BLÖBEL and SCHLISSER, 1985; ZAHN et al., 1995), pneumonia in cats (MCKERCHER, 1952) and horses (MOORTHY and SPRADBROW, 1978), encephalitis in dogs and chlamydia abortions in rabbits, mice, guinea-pigs, and koalas (CANFIELD and LOVE, 1991). According to KRAUSS et al. (2003) the disease was identified in 32 species of mammals. Sporadic cases of chlamydial infections were reported in reptiles. Several strains of *Cp. pneumoniae* were isolated from reptiles; some of which are kept as pet animals (COST, 2002). The infections were identified in a giant tortoise (*Chelonia mydas*) with inflammatory changes on several organic systems (HOMER et al., 1994), snakes (*Bitis arietans*) with granulomatous inflammation of tissue (JACOBSEN et al., 1989; FRYE, 1991), chameleons (*Chamaeleo dilepis*) (JACOBSEN et al., 1989; FRYE, 1991) and crocodiles with inflammatory changes on conjunctiva (HUCHZERMEYER et al., 1994). There is a growing number of reports on research and recovery of chlamydia from naturally infected amphibians. These infections were also reported in the following species of frogs: *Xenopus laevis*, *Ceratobatrachus guentheri*, *Bufo maculatum* and *Mixophyes iterates* in the USA, Canada, Germany and Austria (NEWCOMER et al., 1982; WILCKE et al., 1983; HOWERTH, 1984; HONEYMAN et al., 1992; MUTSCHMANN and TIERARZTPRAXIS, 1998; BERGER et al., 1999). Several seroepidemiological studies revealed Chlamydial infections in wild ruminants as red deer (*Cervus elaphus*), mouflon (*Ovis musimon*) and fallow deer (*Dama dama*) in a Spanish national park (CUBERO-PABLO et al., 2000). Since the late 1990s, the identification of a number of obligate intracellular Chlamydia-related bacteria, such as endosymbionts of amoebae or arthropods (AMANN et al., 1997; KOSTANJSEK et al., 2004) has been carried out.

The knowledge that *Cp. psittaci*, *Cp. felis* and *Cp. abortus* can be transmitted from animals to humans is important for the understanding of the etiology and pathogenesis of Chlamydial infections in humans and animals (Figs. 1 and 2). The main characteristics of these diseases and the nature of the pathogens are shown in our papers are those by other authors (VANROMPAY et al., 1995; VLAHOVIĆ et al., 1998; GREGURIĆ, 1999; HATCH, 1999; VLAHOVIĆ, 2000; VLAHOVIĆ et al., 2001a; VLAHOVIĆ et al., 2001b; VLAHOVIĆ et al., 2001c; NAGLIĆ, 2002; LONGBOTTOM and COULTER, 2003; KALETA and TADAY, 2003; VLAHOVIĆ et al., 2003; VLAHOVIĆ, 2003; DOVČ et al., 2004; VLAHOVIĆ et al., 2004; VLAHOVIĆ, 2004; DOVČ et al., 2005; PAVLAK et al., 2005; PRUKNER-RADOVČIĆ et al., 2005).

The new genus Chlamydiophila (Cp.) was added to the family Chlamydiaceae which used to contain only the genus Chlamydia (C.). According to the currently valid classification the genus Chlamydia contains three species: *C. trachomatis*, *C. muridarum*, and *C. suis* while the new genus Chlamydiophila adopted the previous species *C. pecorum*,

C. pneumoniae and *C. psittaci* and the species names changed to *Cp. pecorum*, *Cp. pneumoniae* and *Cp. psittaci*. The three new species of Chlamydophila were established by dividing the species *Cp. psittaci* into *Cp. aborus*, *Cp. caviae* and *Cp. felis* (EVERETT et al., 1999; LONGBOTTOM and COULTER, 2003). The names "Chlamydiosis and Chlamydiae" are used as general terms when referring to members of both genera, Chlamydia and Chlamydophila. However, the new scientific names are used when listing specific species of Chlamydia (OIE, 2004). All the species belonging to the genus Chlamydophila are significant as pathogens in veterinary medicine. The most significant species of the genera, which also represent a possible source of infection for humans, are as follows: *Cp. psittaci*, causing chlamydial infections in birds, *Cp. felis*, causing chlamydial infections in domestic cats, and *Cp. abortus*, causing enzootic abortion in sheep (Fig. 1).

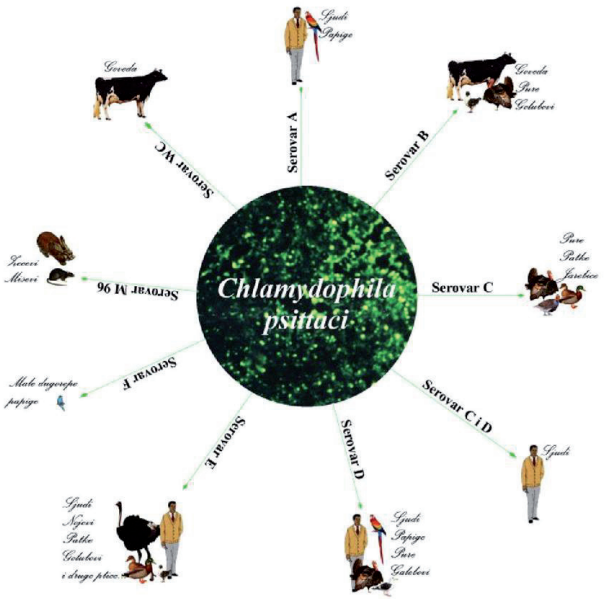

Fig. 1. Zoonotic potential of chlamydial pathogens
(COST, 2002; LONGBOTTOM and COULTER, 2003)

Animals that are often latently infected by clinically asymptomatic Chlamydioses pathogens over a longer period of time are particularly dangerous for human health. Latent chlamydial infections occur in natural conditions in birds, cattle, sheep and guinea-pigs. A

well-balanced relationship between the host and the microorganism does not lead to any damage of the host. However, occasionally the bacteria can be secreted and in unfavorable conditions transferred to a new host. The pathogen can also be latently present in a non-infectious form. It should be pointed out that out from an organism an elementary body, an infectious extra cellular form of this pathogen, stays contagious for anything from a few days to a few weeks. Furthermore, the pathogen in the form of an elementary body (diameter 0.2 to 0.3 μm) can be easily dispersed by aerosol as well as transmitted in other ways (SCHACHTER et al., 1973).

***Chlamydophila psittaci* infections in humans and birds**

The species *Cp. psittaci* is primarily a pathogen in birds. The avian strains all belong to the species *Cp. psittaci*. According to the present-day classification the previous strains of "mammals" belonging to the species *Cp. psittaci* are assigned as the new species *Cp. abortus*, *Cp. felis*, and *Cp. caviae* (EVERETT et al., 1999). All *Cp. psittaci* strains are similar in virulence, capacity of growth in cell culture and have less than 80% differences in 16S-rRNA genes. The *Cp. psittaci* strains can be divided into several serovars.

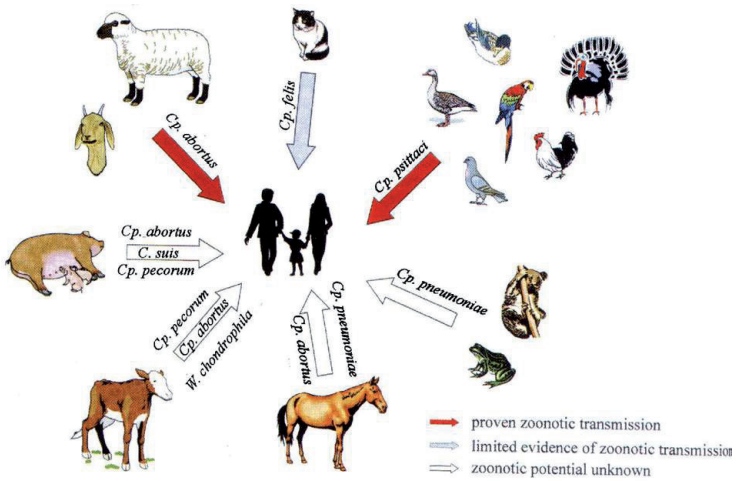

Fig. 2. The species *Cp. psittaci* with six known avian serovars (A,B,C, D,E and F) are transmissible to human and other animals and two mammalian serovars (M96 i WC) (VLAHOVIĆ et al., 2001b)

There are avian isolates (serovars A, B, C, D, E and F) (VANROMPAY et al., 1997) and two mammalian isolates (serovar M96, WC) (Fig. 2) (ANDERSEN, 1991; EVERETT et al.,

1999; ANDERSEN and VANROMPAY, 2000). The *Cp. psittaci* serovars were identified by using polymerase chain reaction (PCR) and restriction fragment length polymorphism chain reactions (RFLP) (SAYADA et al., 1995; EVERETT et al., 1999). The six serovars of the species *C. psittaci* (A to F) have endemic appearance in different species of birds around the world (Fig. 2). Serovar A is endemic among parrots but can also cause sporadic zoonotic disease in humans (Figs. 1 and 2), other mammals and tortoises. Seovar B is endemic among pigeons and has been isolated from turkeys. It also causes abortion in dairy herds (Fig. 2). Serovars C and D have been isolated from ducks and turkeys. Specific hosts for serovars C and D have not been identified, but they are known to represent a particular risk of zoonotic diseases among workers in poultry industry (Fig. 2). Serovar E, in particular isolates known as Cal-10, MP or MN have been identified in a large number of birds worldwide. However, their specific reservoirs are not known (ZHANG et al., 1989) (Fig. 2). Serovars M56 and WC were isolated from mammals (EVERETT et al., 1999). Generally, all species of birds can be a source of infection for humans. However, most human infections come from pets, in particular from latently infected parrots (CAR, 2000; NAGLIĆ, 2002: DOVČ et al., 2004). According to KALETA and TADAY (2003) the causative agent of this disease was identified in 469 different species of birds. As well as in birds and humans the species *Cp. psittaci* was isolated from mares after abortion (HENNING et al., 2000).

Chlamydophila felis infections of humans and cats

The species *Cp. felis* comprises all isolates from house cats which were earlier classified as *Chlamydia psittaci* (EVERETT et al., 1999). This species is believed to cause a disease with clinical symptoms of acute and chronic conjunctivitis in house cats, which has been reported around the world (SYKES, 2001). It was identified in humans who could have become infected from pets. Namely, the studies carried out show that the infected humans had contact with several cats over a longer period of time. Clinically the infection in humans resulted in follicular conjunctivitis (OSTER et al., 1969; OSTER and SCHACHTER, 1972), functional disorders of the liver (GRIFFITHS et al., 1978), endocarditis and glomerulonephritis (REGAN et al., 1979), as well as atypical pneumonia (COTTON and PARTRIDGE, 1998). A test infection of a conjunctival bag of four kittens with isolates obtained from infected hosts, caused hyperemia of conjunctiva. Sporadic cases of *Cp. felis* in spontaneously infected humans broaden our knowledge of pathogenic features of the bacteria and confirm the belief that chlamydial infections in humans are caused by the species *Cp. felis* (Fig. 1).

This species has almost completely identical isolates. However, they differ in extrachromosomal plasmids and pathogenic characteristics. The strains of *Cp. felis* FP

Pring and FP Cello have extrachromosomal plasmids which have not been identified in the FP Baker strain (MAY et al., 1996). The FP Cello strain causes a lethal disease in mice, which was not observed in a test infection of mice with the FP Baker strain. The attenuated FP Baker strain is used as vaccine for house cats.

Chlamydophila abortus infection in humans and sheep

Today the species *Cp. abortus* is known as a pathogen of "enzoonotic abortion in sheep". It comprises most isolates of abortion pathogens in ruminants which were previously classified as the species *Cp. psittaci*. Nowadays the species is used to determine new members of the family Chlamydiaceae (16S or 23S-rRNA should be >90% identical to the *Cp. abortus* genes). An extrachromosal plasmid was not identified in any *Cp. abortus* strain. It is primarily associated with cases of abortion in ruminants, but sporadic Chlamydial infections were identified in pregnant women (Fig. 1). A genetic analysis confirmed infections with the species *Cp. abortus* in women exposed to Chlamydia from dry birth liquid or in those who came into contact with infected lambs. Such causes reported were in the USA (JORGENSEN, 1997), the UK (CROSSE et al., 1991), France (BONNEAU et al., 1991), and Denmark (KAMPINGA et al., 2000). The consequence of *Cp. abortus* infection in women is a spontaneous abortion within the first three months of pregnancy, while later infections cause still or premature births (BUXTON, 1986; JORGENSEN, 1997).

The most frequent isolates obtained from cases of abortion in sheep, cattle and goats worldwide are B577, EBA, OSP, S26/3 and A22 (VON LOOCK et al., 2003). The disease occurs in all the countries with intensive or semi-intensive rearing of sheep and goats, and has been reported in many papers (AMIN and WILSMORE: 1995; PAPP and SHEWEN, 1996). The infection in sheep and goats clinically results in premature births, still births and dead sucklings while adult sheep can be in poor condition (JUBB at al., 1991).

Other species from the genus Chlamydophila

In contrast to much better known species that can be transmitted from animals to humans such as *Cp. abortus*, *Cp. psittaci* and *Cp. felis* potentials of other species from the genus Chlamydophila are less known and are still being investigated (Fig. 1).

The species *Chlamydophila pecorum*

This species has only been isolated only from mammals such as cattle, sheep, goats, koalas and swine (STORZ, 1988). In the new classification the species *C. pecorum* was

renamed *Cp. pecorum*. The species displays serological and pathological diversities. The pathogenesis of this species was not confirmed in mice. In koalas *Cp. pecorum* causes reproductive disease, infertility and urinary tract disease. In other animals *Cp. pecorum* is associated with abortion, conjunctivitis, encephalomyelitis, enteritis, pneumonia and polyarthritis. Most *Cp. pecorum* strains have a low level of virulence. Such low virulence prevents the microorganism from penetrating into blood vessels and spreading. Localization in the placenta is also not possible. Therefore, there are mainly sub clinical intestine infections, local infections of epithelial cells and mucosal surfaces (RODOLAKIS et al., 1998). Some authors believe at least one strain of the bacteria *Cp. pecorum* appears within a flock of sheep as a ubiquitous microorganism (DOON et al., 1997).

The species *Chlamydophila pneumoniae*

It was formerly thought to be a specific human pathogen, but recently it has been isolated from koalas, horses and other animals. In humans *Cp. pneumoniae* is primary a pathogen of the respiratory tract, causing acute or chronic bronchitis and pneumonia. It has also been associated with obstructive pulmonary disease, arteriosclerosis, Alzheimer's disease and other acute and chronic respiratory diseases. GRAYSTON et al. (1986) recognized the bacteria *C. pneumoniae* (TWAR – Taiwan Acute Respiratory) as a new species in the genus Chlamydia which is only pathogenic for humans (MAFFEI et al., 1987). The contact of humans infected with the species *Cp. pneumoniae* with birds was not established, as was the case in infections of humans with the species *Cp. psittaci*. The bacteria *Cp. pneumoniae* is transferred only from human to human (BOURKE et al., 1989). A relationship between an infection with the species *Cp. pneumoniae* and arteriosclerosis, cardiac arrest and rheumatic arthritis was established. Seroepidemiological studies on infections with *Cp. pneumoniae* have shown that 40-50% of human population worldwide is positive (PEELING and BRUNHAM, 1996). CAMPBELL et al. (1998) describe *Cp. pneumoniae* as a ubiquitous microogranism of acute respiratory diseases with a potential role in heart diseases.

According to the new classification *C. pneumoniae* was renamed *Cp. pneumoniae* and it comprises three biovars: *Cp. pneumoniae* TWAR biovar, *Cp. pneumoniae* koala biovar and *Cp. pneumoniae* equine biovar (EVERETT et al., 1999). The structure of the elementary body of TWAR biovar differs from other elementary bodies of Chlamydia. The main extramembrane proteine (Major Outer Membrane Protein - MOMP) in koala biovar partly differs from the TWAR and equine biovars.

There is a growing number of reports on research and isolation of the species *Cp. pneumoniae* in amphibians and reptiles. At the same time there is more and more interest in research of potential hazards for human health (SOLDATI et al., 2004). *Cp. pneumoniae*

equine biovar currently includes only strain N16 which was isolated from the respiratory tract of a horse (STOREY et al., 1993). N16 has a plasmid which was not identified in other strains of *Cp. pneumoniae*. Inoculation of horses with isolates of the N16 strain was not successful (STOREY et al., 1993; HOTZEL et al., 2001). The increasing number of reports of the isolation of human strains of the pathogen *Cp. pneumoniae* from frogs (BERGER et al., 1999; REED et al., 2000b; HOTZEL et al., 2001).

The species *Chlamydophila caviae*

It includes isolates, pathogens of inclusion conjunctivitis in guinea-pig, which formerly belonged to the species *C. psittaci*. The first isolations of the guinea-pig inclusion conjunctivitis followed after the isolation of the pathogen from the mucous membrane of a guinea-pig (MURRAY, 1964). There are five known *Cp. caviae* isolates and immunogenetic research has showed that the ompA (omp1) sequences of these isolates are almost completely identical. The strain causing guinea-pig inclusion conjunctivitis (GPIC) contains an extrachromosal plasmid (pCpGP1) (READ et al., 2003). The presence of the *Cp. caviae* in high percentages corresponds to the findings in the infected mucosal epithelium and does not show a tendency to invade tissues and organs. The natural site of *Cp. caviae* infection is the conjunctiva, but there is a possibility for infection of the genital tract of guinea-pigs when the described symptoms of the disease are similar to those in human *C. trachomatis* infection (MOUNT et al., 1973). The guinea pig is an important experimental model of Chlamydial genital tract infection in humans (MOUNT et al., 1973). Guinea pigs with primary conjunctivitis develop immunity to reinfection of the eyes or the genital tract (MOUNT et al., 1973; AHMAD et al., 1977).

The families *Parachlamydiaceae*, *Simkaniaecae* and *Waddliaceae*

On the basis of the comparison of 16S rRNA the new group of unidentified bacteria has been classified as a member of the order Chlamydiales and belonging to the families Parachlamydiaceae, Simkaniaecae and Waddliaceae. The above mentioned families contain intracellular bacteria, most of which have a similar developmental cycle as the members of the Chlamydiaceae family. Electron microscopy was used to identify members of this family in amoebas (MICHEL et al., 1993), in contaminated cell cultures (Microorganism Z) (KAHANE et al., 1993) as well as in aborted bovine foetus (microorganism WSU 86-1044) (KOCAN et al., 1990).

Unidentified species from the *Chlamydiacea* family

Extensive morphological, physiological and genetic research has revealed new lines

within the order Chlamydiales, some of which have not yet been completely investigated. Chlamydias isolated from waste waters are known as "lines of Chlamydia environment" and are exterior members of the Chlamydiacae family. Their relevance for human health is yet to be studied (HORN and WAGNER, 2001).

A short survey of the bacteria from the genus *Chlamydia*

The species *Chlamydia suis*

This new species has only been isolated from swine with clinical symptoms of endemic enteritis and conjunctivitis.

The species *Chlamydia muridarum*

This new species which was formerly known as a *C. tachomatis* biovar was isolated from mice and hamsters. It can cause mild diseases or can be present in an asymptomatic state.

The species *Chlamydia trachomatis*

The genus Chlamydia has kept the old name of the genus as it contains a genus specific species, i.e. *Chlamydia trachomatis*. The species *C. trachomatis* is primarily a human pathogen. However, this microorganism has also been isolated from swine and mice (PUDJIATMOKO et. al., 1997). The bacteria *C. trachomatis* isolated from swine and a mouse differs genetically from the species *C. trachomatic* isolated from humans. According to the new classification these bacteria are assigned as a new species of C. muridarum and *C. suis*. *C. trachomatis* (11 immunotypes) causes sexually transmitted genital diseases in humans, inflammations of respiratory organs, eyes, genitals in new born babies and trachoma (4 immunotypes) caused by direct contact with infected humans (SCHACHTER and CALDWELL, 1980).

Reducing risks of infections in humans

Chlamydia infections of animals and humans that sporadically occur worldwide have no special importance. However, the new epidemiological facts shown through the relationship between pathogens and their hosts are worth pointing out. Also, the new microbiological classification is important especially on several occasions when the disease has proved to be very dangerous for humans and animals. Due to human susceptibility to bacteria from the genus Chlamydophila and the risk of infection from animals, the possible hazard for humans can be reduced by implementing tighter control and preventive measures. The known origin and health status of animals that could potentially transmit the pathogen will additionally lower the risk.

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SAŽETAK

Red Chlamydiales sastoji se od različitih skupina mikroorganizama značajnih za ljudsko i životinjsko zdravlje. Klamidioza je bolest od koje obolijevaju čovjek, većina domaćih sisavaca i ptice. Zaraze navedenim bakterijama proširene su po cijelom svijetu. Vrste *Chlamydophila psittaci*, *Chlamydophila felis* i *Chlamydophila abortus*, kao i druge bakterija iz roda Chlamydophila ustanovljene su u različitih vrsta domaćih i divljih životinja. Zoonoze uzrokovane ovim mikroorganizmima ishod su izravnog dodira s oboljelim ili uginulim domaćim, divljim i sinantropnim životinjama. Te spoznaje važne su za razumijevanje novih epidemioloških činjenica i mogućnosti prijenosa uzročnika sa životinja (posebice kućnih ljubimaca) na ljude. Prikazom literaturnih podataka o uzročnicima klamidijalnih zaraza u životinja i ljudi, cilj nam je pomoći u boljem razumijevanju

novog mikrobiološkog razvrstavanja klamidija s posebnim osvrtom na odnose između klamidija i njihovih domaćina.

Ključne riječi: klamidioze u životinja, zoonoze, patogenost, zaraza