

## ***Chlamydia (Chlamydophila) pneumoniae* in animals: a review**

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**ABSTRACT:** An important discovery in the last couple of years is that humans are not the only natural hosts with which *C. pneumoniae* is the primary cause for the disease. Successively, the *C. pneumoniae* strain was isolated from horses, koala bears affected by ocular and genital infection, Australian and African frogs, from a Tanzanian chameleon, a green sea turtle living in the Cayman Islands, an iguana, puff adders and a Burmese python. All of the animals in which the *C. pneumoniae* was confirmed, were suffering from some form of illness that is also typical in humans when affected by this chlamydial species. All strains also showed a high similarity with the human *C. pneumoniae* strain (up to 100%).

**Keywords:** epizootology of chlamydia; free-ranging animals; laboratory and domestic animals

*Chlamydia (Chlamydophila) pneumoniae* (*C. pneumoniae*) is a primary pathogen with humans. The present state of knowledge indicates that it plays the most important role in human pathology out of all chlamydia species. It is the most frequent cause of respiratory infections. It is also one of the agents in the pathological processes in other organs (joint inflammation, genital infection and consequent fertility disorders etc.) and it is very likely that it is one of the factors leading to atherosclerosis, a co-factor of bronchopulmonary carcinoma and also of some disorders of the central nervous system. According to present taxonomic criteria the family *Chlamydiaceae* contains only one genus *Chlamydia* which involves the four following species: *C. trachomatis*, *C. pneumoniae*, *C. psittaci* and *C. pecorum*. Natural hosts are: for *Chlamydia trachomatis* and *Chlamydia pneumoniae* humans, for *Chlamydia psittaci* birds and some mammals, for *Chlamydia pecorum* mammals (above all pigs and cattle). *C. trachomatis* and *C. pneumoniae* are primary human pathogens, the transmission of *C. psittaci* to humans is possible as a rare occurrence like ornithosis and psittacosis.

The transmission of *C. pecorum* to humans has not occurred or has not been proved yet.

According to a newly proposed classification (Everett and Andersen, 1997; Everett *et al.*, 1999) the family *Chlamydiaceae* is divided into two genera: *Chlamydia* (includes the species *C. trachomatis*, *C. muridarum*, *C. suis*) and *Chlamydophila* (includes the species *C. pneumoniae*, *C. pecorum*, *C. psittaci*, *C. abortus*, *C. caviae* and *C. felis*). This opinion of these authors is in correspondence with the opinion of other authors (Meijer *et al.*, 1997; Pudjiatmoko *et al.*, 1997; Hartley *et al.*, 2001). However, the older *Chlamydia* nomenclature is still being used more often than the newly designed one. A final agreement should therefore be reached in order to prevent the indiscriminate use of both nomenclatures often leading to unnecessary confusion.

*C. trachomatis* and *C. pneumoniae* have the most relevant importance in human pathology. While in the last two decades the highest attention has been paid to *C. trachomatis* as the germ causing genital chlamydiosis, dominating among the sexually transmissible diseases (Black, 1997; Korych, 1998),

recent research indicates that it is *C. pneumoniae*, which occupies the most important position in human pathology out of all chlamydia species (Veznik and Pospisil, 1997; Zampachova, 1998). The reason for this assertion is that *C. pneumoniae* is not only the germ causing the frequent respiratory infections, but that it can bring about processes which originally used to be attributed solely to *C. trachomatis* (reactive arthritis, ocular, genital and dermatologic infections) (Peeling and Brunham, 1996; Thomsen *et al.*, 1996; Bernhard *et al.*, 2001; King *et al.*, 2001). Furthermore the *C. pneumoniae* infection represents another risk factor for the development of atherosclerosis and also its destabilization, and because it can be a co-factor of the origin of the bronchopulmonary carcinoma and some other chronic diseases of the central nervous system (sclerosis multiplex etc.) as suggested e.g. by Gran *et al.* (1993), Wimmer *et al.* (1996), Wollenhaupt and Zeidler (1997), Wong *et al.* (1999), Sriram *et al.* (1999), Paavonen (2000).

*C. pneumoniae* was obtained for the first time in 1965 out of a conjunctiva of a Taiwanese child; the strain was marked TW-183. The second isolate from the throat of a student with pharyngeal inflammation took place in 1983 and was marked AR-39. The original name for *C. pneumoniae* was TWAR agent and was formed by the connection of the names of the first two isolates (Kuo *et al.*, 1986; Grayston *et al.*, 1986). The *C. pneumoniae* infection is cosmopolitan. The majority of the world population usually catches the infection more than once in a lifetime (Sodja, 1998; Sodja *et al.*, 1998). The increase of prevalence of antibodies against *C. pneumoniae* with age proves this (1–4 years of age 22.2%, >20 years 63–79%, >60 years 97.1%). Respiratory infections caused by *C. pneumoniae* are usually mild. Nevertheless in a significant amount of cases they can develop into a more serious form of disease (sinusitis, bronchitis, complicated pneumonia) (Grayston *et al.*, 1993). Another important discovery in recent years is that humans are not the only hosts, with whom *C. pneumoniae* causes primary disease. Its presence at infections (with *C. pneumoniae* as the primary factor) occurring with various animal species is reported in an increasing number of cases.

### ***C. pneumoniae* occurring with domestic and wild animals**

One of the first studies proving the existence of nonhuman *C. pneumoniae* with horses in Great

Britain was published by Storey *et al.* (1993). They characterized and taxonomically ordered one of the 15 isolates of chlamydia (N16) from the conjunctiva and throat swabs, which were carried out with 300 horses (*Equus caballus*) affected by epizootic (Wills *et al.*, 1990).

Glassick *et al.* (1996) isolated from koalas seven chlamydial strains, which had been divided into two genetic groups. The koala group A omp 2 sequence is 93% similar to the human *C. pneumoniae* and also 99% similar to the horse strain (N16). The koala group B omp 2 sequence is only 71% similar to the koala group A strains. Later Jackson *et al.* (1999) published an epidemiological study on chlamydia infections in two koala colonies (*Phascogaleus cinereus*) living in a free range koala population. The prevalence of *C. pneumoniae* was being identified by a genus specific PCR in combination with a species-specific DNA in a process of hybridization. In a population of koala bears of the first colony the prevalence of a chlamydia infection was 85% (out of which *C. pecorum* was 73% and *C. pneumoniae* 24%). In the second group the prevalence was only at 10%, while the presence of both chlamydia species was approximately balanced. It is necessary to mention that 5 out of 24 koalas infected by *C. pecorum* had clinical signs of the disease (ocular, genital), while 7 animals infected by *C. pneumoniae* did not have any. The incidence of the *C. pecorum* infection increased with age (from 58% with young individuals to 100% in an older age group). In this case sexual transmission was undoubtedly a crucial factor. On the other hand, *C. pneumoniae* was affecting only young sexually inactive individuals.

According to a number of authors the *C. pneumoniae* biovar isolated from koalas is different from the human biovar (Jackson *et al.*, 1999; Wardrop *et al.*, 1999). Bodetti and Timms (2000) compared the abilities of the “human” and “koala” biovars of infecting mononuclear cells of the peripheral blood stream (as an important factor of the infection’s dissemination from the respiratory ways) and they found out that this ability is not typical only for the biovar of human origin but also for the “koala” biovar and they claim that it is a typical quality of this particular chlamydia species.

Another comparison of the *C. pneumoniae* “koala” biovar was carried out by Coles *et al.* (2001). They carried out research on the ability of infecting Hep-2 and human monocytes and also on the influence of the infection on the formation of foam cells. “Koala” biovar creates big inclusions in human and koala

monocytes and in Hep-2 cells. “Koala” *C. pneumoniae* induces the formation of foam cells without the addition of lipoprotein of a low density (LDL).

The occurrence of *C. pneumoniae* with giant barred frogs (*Mixophyes iteratus*) was identified by Berger *et al.* (1999) again on the Australian continent. Reed *et al.* (2000) published a study on chlamydial epizootic in a colony of African clawed frogs (*Xenopus tropicalis*) brought to the USA, out of which 90% died. The use of electron microscopy and cultivation on tissue cultures proved the presence of *C. pneumoniae*.

The genetic characterization of *C. pneumoniae* isolated from the African frog was carried out by Hortzel *et al.* (2001) and they compared it with the commonly accepted biovars. They sequenced the isolate DE 177 from frogs identified as *C. pneumoniae* in five genomic regions. The comparison with corresponding sequences of a horse, human, and koala biovar of *C. pneumoniae* showed that koala strains are a closely related taxon with slight variations.

Bodetti *et al.* (2002) describe six cases of disease or death of animals of different species as a consequence of the *C. pneumoniae* infection, which indicates the fact that the reservoir of this microbe in the natural environment could be mammals, amphibians, reptiles and other animals. The animals came from different (and often very distant) parts of the world (Europe, Africa, Australia, Central of America and USA). The samples of their tissues were examined histopathologically, electronoptically and also with PCR.

In the first case, the heart tissue of two puff adders (*Bitis arietans*), out of four deceased during four months, was examined. At a necropsy of all the snakes a pericardial exudate was found, in two cases a multiplex granulomatous foci in the livers containing chlamydia-like organisms.

The second case was a chameleon (*Chameleo dilepsis*) from Tanzania. It had intracytoplasmatic inclusions in circulating monocytes. Similar inclusions were found in the macrophage of the spleen and liver at the histological examination. Transmission electron-microscopy proved the presence of chlamydia particles.

The third case was a green sea turtle (*Chelonia mydas*) from the Cayman British West Indies. It was a member of a group of turtles epidemically affected by lethargy, anorexia and inability to digest the nutriment. Necrotic foci of the myocardium and liver were found at a necropsy of the deceased animals. *Chlamydia* was proved in the macrophages in the heart, liver, and spleen.

Another case was an iguana (*Iguana iguana*). It was imported from Central America to Florida in 1996 together with a whole group of individuals of the same species, which had a high rate of mortality preceded by lethargy and anorexia. Chlamydia-like organisms were identified in the cells of a mucosal epithel of the respiratory tract of the individual at the necropsy.

The fifth case was represented by two Burmese pythons (*Python molurus bivittatus*) (3 and 5 years old, kept in the USA and suffering from suppurative pneumonia) that were also examined with positive results.

Finally, the sixth case was two Australian Blue Mountains tree frogs (*Litoria citropa*) with chronic nephritis. The cells of the endocardium and the mononuclear of the renal interstium contained intraplasmatic inclusions of chlamydia.

Chlamydia-like organisms found in these animals were further identified by a molecular biological method (detection of the DNA including PCR with genus specific 16S rRNA gene and species-spe-

Table 1. Molecular evidence of Chlamydia proved in different animals and their similarity with human genotype of *C. pneumoniae* (according Bodetti *et al.*, 2002)

Animal species	<i>Chlamydia</i> genus-specific 16SrRNA gene ( <i>Chlamydia</i> species similarity)	<i>C. pneumoniae</i> -specific ompA gene (% similarity to human genotype)
Puff adder	<i>C. abortus</i> , <i>C. pneumoniae</i>	100
Chameleon	not specified	99.7
Green turtle	<i>C. abortus</i>	100
Iguana	<i>C. felis</i> , <i>C. pneumoniae</i>	100
Burmese python	<i>C. abortus</i>	100
Blue Mountains tree frog	<i>C. pneumoniae</i>	100

cific ompA gene). The above described strains of chlamydia were qualified by chlamydial PCR and genotypic analysis as follows (Table 1).

It is important to add that the above mentioned strain of chlamydia N16 isolated from a horse and originally named *C. psittaci* (Wills *et al.*, 1990) showed 94.5% similarity with the genotype of the human strain *C. pneumoniae* (or more precisely TWAR as it is presented by Storey *et al.*, 1993). Likewise, the “koala” strain isolated in Australia was showing a 98.8% and a strain from the giant Australian frog 98.3% similarity with *C. pneumoniae* (Wardrop *et al.*, 1999; Berger *et al.*, 1999).

Sako *et al.* (2002) successfully proved the *C. pneumoniae* antigen (immunohistochemically, electronoptically and PCR) in atherosclerotic lesions of the aorta, coronary and splenic arteries of seven dogs suffering from atherosclerosis. Similar infection of chlamydia was proved with dogs with similar changes on the arteries already in 1970 and 1983 Liu *et al.* (1986) and Kagawa *et al.* (1998).

Natural co-infection of *C. pneumoniae* and *Mycoplasma pulmonis* can occur in laboratory rats and is associated with histopathological and functional compromise of many organs. Specific pathogen-free animals are necessary to prevent the influence of co-infection on the results of experimental studies with rats (Damy *et al.*, 2003).

It is surprising that we have not yet managed to find a report on the proof of *C. pneumoniae* with a pig in the literature so far, because in pigs *C. suis* and other species of chlamydia were identified (*C. trachomatis*, *C. pecorum*, *C. psittaci*; Schiller *et al.*, 1997a,b).

### ***C. pneumoniae* with animals in the experiment**

The center point of this article is the occurrence of *C. pneumoniae* with animals, and because this *Chlamydia* species is often an object of research on the animal model, we think that it is useful to mention the problematic. For further details on animal models and *C. pneumoniae*, see Shor (2000) and Campbell and Kuo (2002). The most frequent topic of present experiments with *C. pneumoniae* on animals is a highly current problematic of its co-influence on the development of atherosclerosis and the possibility of its prevention by antibiotics. In these studies rabbits and pigs are used as experimental animals (Coombes *et al.*, 2002; Liuba *et al.*, 2003; Pislaru *et al.*, 2003), while earlier it used

to be laboratory rodents (Yang *et al.*, 1993; Moazed *et al.*, 1998; Saikku *et al.*, 1998; Rothstein *et al.*, 2001; Blessing *et al.*, 2002).

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