Emerging *Bartonella* in animal and human in China

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**Objective:** To investigate the emerging *Bartonella* infections in animal and human for further research and public health response in China.

**Methods:** The authors have reviewed the Chinese literature of clinical diagnosis, and ecological and laboratory investigations on *Bartonella* infections in China between 1980 and 2006, analyzed the characteristics of *Bartonella* agents and the current situation of *Bartonella* infection in China.

**Results:** It was found that cat scratch disease (CSD) is the main bartonellosis diagnosed based on clinical manifestations and routine pathologic examination in China, and the surveillance studies mostly focused on pet animals, rodents and arthropods which might be determined to be the possible source of infection of *Bartonella*. Twelve isolates of *Bartonella* were grown from blood of 64 cats from Shandong Province. The seroprevalence of *B. henselae* antibodies in cats from Shandong and Henan provinces was 29.6%, including 19.3% in kittens that were younger than 6 months and these numbers doubled in older cats (>2 year old). Two isolates were identified as *Bartonella vinsonii berkholffii* from blood specimens of domestic dogs in urban areas of Shandong province.

Other research demonstrated the presence of *Bartonella* in a variety of rodents, such as the family Rattus, Apodemus and Eothenomys. Subsequent studies expanded further the list of rodents infected with *Bartonella* and extended the geography of their distribution. The data on association of *Bartonella* with *S. murinus* are particularly important since around 20% of small commensal mammals trapped in south-eastern China are *S. murinus*. Beijing is the most northern area where *Bartonella* were isolated from the blood of *Rattus norvegicus*. Preliminary identification of the *Bartonella* isolates from Chinese rodents established the presence of multiple genotypes based on differences in nucleotide sequences of the 325 bp fragment of the conserved gene encoding for citrate synthase (*gltA*). Most of the Yunnan isolates from *R. flavipes*, *R. norvegicus*, *A. chevrieri*, *A. draco*, and *A. latronum* are identified to be *B. elizabethae* and *B. grahamii*.

Some papers have reported the detection of *Bartonella* in association with fleas or ticks from dogs, cats or cows. And they may be potential vectors responsible for transmission of *Bartonella* in areas where infected animals are present in high prevalence.

**Conclusion:** The findings indicate the emerging *Bartonella* exists in animal and human in China mainland. This needs further assessment for public awareness and preparedness. The development and implementation of specific and sensitive diagnostic assays is urgently required for establishing a state surveillance and diagnostic capacity by the reference diagnostic laboratories. Further studies will be needed to establish the specific genotype of the Chinese isolates, and to understand their reservoir association, mode of transmission, spectrum of diseases, and pathological conditions they may cause in mammals. Current knowledge on *Bartonella* species and bartonelloses found in mainland China and their role as causes of febrile illness in China are presented as guides for local physicians in China and for travel medicine physicians and tourists abroad.

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More and more human and animal coronaviruses

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The recent SARS epidemic in 2003 has boosted interests in discovery of novel coronaviruses in both humans and animals. Two novel human coronaviruses, human coronavirus NL63, a novel group 1 human coronavirus; and human coronavirus HKU1, a novel group 2 human coronavirus; were reported in 2004 and 2005 respectively. As for animal coronaviruses, we and others have described the discovery of SARS-CoV-like viruses in horseshoe bats in Hong Kong and other provinces of China. In addition, numerous other novel coronaviruses in bats as well as other animals, such as giraffe, turkey and beluga whale, have been discovered. These discoveries and comparative genomics studies have led to proposal of novel subgroups of coronaviruses. Recently, we have also developed a comprehensive database, CoVDB (http://covdb.microbiology.hku.hk), of annotated coronavirus genes and genomes, for rapid and accurate batch sequence retrieval, the cornerstone and bottleneck for comparative gene or genome analysis. With these, we will be able to get a more in-depth understanding on coronavirus phylogeny.

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The interaction between M1 protein of influenza virus and host cell factors

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Influenza A virus matrix protein (M1) is the most abundant protein in the viral particle, consisting of highly conserved 252-amino acids. M1 is a multifunctional protein in the influenza virus replication. Several host cell factors have been identified possibly to be required for regulation of influenza virus replication through interacting with M1. The knowledge obtained from these virus-host cell interactions are continuing provide critical insights into the molecular mechanisms of the biology and pathology of the virus. In our study the yeast two-hybrid system was performed using M1 as the bait to search for possible counterpart host proteins. Several candidate proteins have been identified including cyclophilin A (CypA), specifically interacting with M1. We have demonstrated that CypA was able to directly bind to the M1 protein. The functional analysis indicated that CypA regulated the influenza virus replication.

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Structural study of RNA polymerase PA subunit from an avian influenza virus

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The recent emergence of highly pathogenic avian influenza A virus strains with subtype H5N1 pose a global threat to human health. Elucidation of the underlying mechanisms of viral replication is critical for development of anti-influenza virus drugs. The influenza RNA-dependent RNA polymerase (RdRp) heterotrimer, containing PA, PB1 and PB2, plays crucial roles in viral RNA replication and transcription. PB1 is known to harbour polymerase activities and PB2 is responsible for cap binding. PA is implicated involving in RNA replication, endonuclease and proteolytic activity, however, its functional mechanism remains elusive. Recently, we have determined the crystal structures of avian H5N1 influenza A virus PA protein. The structures of PA have provided detail information for the binding of PB1 to PA and implicated its previously unknown functional mechanisms. Our structure also reveals that PA is a significant target for novel anti-influenza therapeutics.