Available online at www.sciencedirect.com

ScienceDirect

Current Opinion in Virology

Cross-species transmission and emergence of novel viruses from birds

Jasper Fuk-Woo Chan[1], Kelvin Kai-Wang To[1], Honglin Chen and Kwok-Yung Yuen

Birds, the only living member of the *Dinosauria* clade, are flying warm-blooded vertebrates displaying high species biodiversity, roosting and migratory behavior, and a unique adaptive immune system. Birds provide the natural reservoir for numerous viral species and therefore gene source for evolution, emergence and dissemination of novel viruses. The intrusions of human into natural habitats of wild birds, the domestication of wild birds as pets or racing birds, and the increasing poultry consumption by human have facilitated avian viruses to cross species barriers to cause zoonosis. Recently, a novel adenovirus was exclusively found in birds causing an outbreak of *Chlamydophila psittaci* infection among birds and humans. Instead of being the primary cause of an outbreak by jumping directly from bird to human, a novel avian virus can be an augmenter of another zoonotic agent causing the outbreak. A comprehensive avian virome will improve our understanding of birds' evolutionary dynamics.

Addresses
State Key Laboratory of Emerging Infectious Diseases, Department of Microbiology, and Research Centre of Infection and Immunology, The University of Hong Kong, Hong Kong Special Administrative Region

Corresponding author: Yuen, Kwok-Yung (kyyuen@hku.hk)
[1] These authors contributed equally to this work.

Current Opinion in Virology 2015, **10**:63–69

This review comes from a themed issue on **Emerging viruses: interspecies transmission**

Edited by **Antoine Gessain** and **Fernando Garcia-Arenal**

For a complete overview see the Issue and the Editorial

Available online 31st January 2015

http://dx.doi.org/10.1016/j.coviro.2015.01.006

Introduction

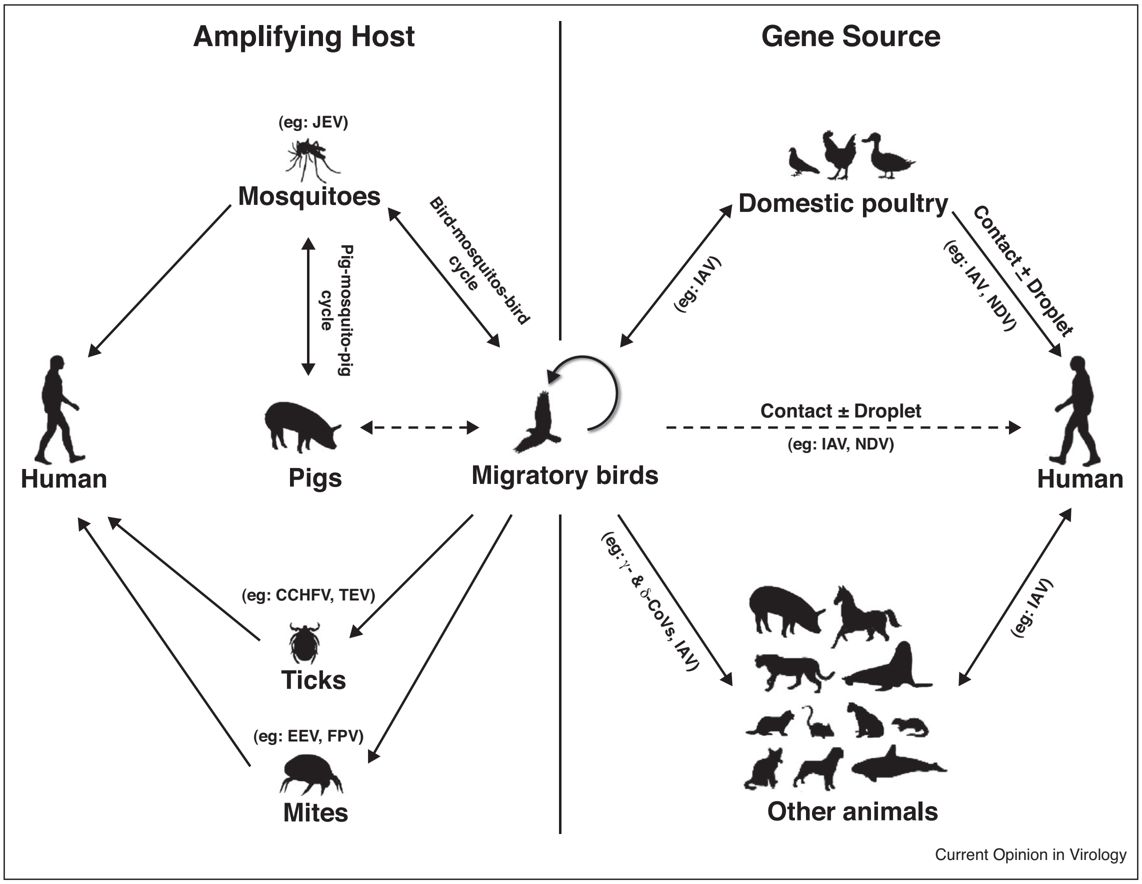
Birds are flying warm-blooded vertebrates of the class *Aves*. They are the most highly biodiversified tetrapods with about 10,000 species. The evolution of birds from bipedal carnivorous dinosaurs through sustained miniaturization and anatomical innovation over approximately 160 million years is one of the most compelling examples of macroevolution [1••]. Modern-day birds are believed to be the only living members of the *Dinosauria* clade. Their unparalleled biodiversity and length of evolution among animals have provided abundant opportunities for virus acquisition from various sources. Their unique adaptive immune system allows asymptomatic infection and virus co-evolution to occur [2•]. Their global distribution, annual long distance migrations, and habitual roosting in environments shared by other animals further enhance the mixing and dissemination of viruses to and from other species.

These biological, immunological, and ecological characteristics have given birds distinctive roles in the emergence of novel viruses and their cross-species transmission [2•]. Birds may act as a vehicle for vector dissemination, an amplifying host in bird–vector–bird cycles, or the gene source of emerging viruses in cross-species virus transmission (Figure 1). Transmission of tick-borne viruses such as Crimean-Congo hemorrhagic fever virus, tick-borne encephalitis virus, and louping ill virus is facilitated by migratory birds which carry infected ticks especially of the genera *Ixodes*, *Hyalomma*, and *Haemaphysalis* [3]. Mesostigmatic mites such as *Dermanyssus gallinae* which are found in birds are implicated in the transmission of various human and avian pathogens including equine encephalitis viruses, Fowlpox virus, Newcastle disease virus, and hantaviruses [4]. Flaviviruses such as West Nile virus, Japanese encephalitis virus, and St. Louis encephalitis virus are amplified by birds in bird–mosquito–bird cycles and then transmitted to dead-end hosts including human. Avian influenza viruses are classical examples of viruses emerging from birds through the reassortment of different gene segments [5•]. In this article, we use the novel avian influenza viruses as examples to illustrate the role of birds in the cross-species transmission and emergence of zoonotic avian viruses, and discuss on the types and significance of other non-zoonotic avian viruses identified in the past two years.

Avian influenza viruses: the role of birds in cross-species transmission and emergence of novel viruses

Birds have had a close relationship with human throughout history. The intrusions of human into the natural habitats of wild birds, the popularity of rearing pet birds in developed countries, pigeon racing and the increasing consumption of poultry in developing countries may have facilitated the emergence and dissemination of novel avian influenza viruses that cause zoonosis [5•,6]. Avian influenza viruses have been known to cause human diseases since 1959 [7]. In 1997, A(H5N1) virus caused the first large human outbreak in Hong Kong [8••]. Other

Figure 1



Birds as the gene source and amplifying host in cross-species transmission and emergence of novel viruses. *Abbreviations*: CCHFV, Crimean-Congo hemorrhagic fever virus; CoV, coronavirus; EEV, equine encephalitis virus; FPV, Fowlpox virus; IAV, influenza A virus; JEV, Japanese encephalitis virus; NDV, Newcastle disease virus; TEV, tick-borne encephalitis virus.

avian influenza viruses causing human disease between 1998 and 2012 include A(H7N2), A(H7N3), A(H7N7), A(H9N2) and A(H10N7) viruses [7]. In the past two years, four novel avian influenza viruses have emerged to cause human infections confirmed by genome sequencing of the virus isolates (Table 1) [9,10•,11,12]. Among these four viruses, A(H7N9) virus poses the most severe threat to humans, causing over 450 human cases with a case-fatality rate of about 30% [5•,13].

Sixteen of 18 hemagglutinin (HA) subtypes and nine of 11 neuraminidase (NA) subtypes of influenza viruses can be found in birds, especially waterfowl and shorebirds [2•]. Out of a possible 144 HA and NA combinations, 112 were identified in wild birds, including 49 that were also found in domestic birds [14]. Since most of these avian influenza viruses are of low pathogenicity in birds, infected migratory birds can carry different influenza virus subtypes for long distances. Mixed infection is also commonly identified [15]. Therefore, waterfowls remain the most important source of genetic diversity for influenza viruses.

Although wild birds harbor the most diverse subtypes of influenza viruses, reassortment and amplification events of avian influenza viruses affecting humans most likely occur in live poultry markets (LPM) where there are high densities of poultries [16,17••]. Surveillance studies showed that avian influenza viruses were found more commonly in poultry samples collected in LPM than in wild bird samples or backyard poultry samples [18]. Next-generation sequencing showed that mixed infection of different subtypes is common among poultries in LPM [19]. Phylogenetic studies suggested that A(H7N9) and A(H10N8) viruses are reassortants with internal genes originating from A(H9N2) viruses that are circulating in poultries [16,17••,20]. Unlike A(H5N1) virus which is highly pathogenic for poultries, A(H7N9) and A(H10N8) viruses tend to cause asymptomatic avian infections, and therefore widespread circulation of A(H7N9) and A(H10N8) viruses