A BRIEF REVIEW ON TWO PANDEMIC ZOONOSES

ZO 8091 Project report

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2006

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INTRODUCTION

Diseases transmitted between animals and humans are termed zoonotic diseases. More than 1400 human pathogens are known to medical science. Of these, approximately 64 % are of zoonotic origin (*Taylor et al. 2001; Woolhouse & Gowtage-Secueria 2005; Woolhouse et al. 2005*). Most of the zoonoses are, under certain environmental circumstances, capable of causing considerable mortality and morbidity among humans in all age groups and both sexes (*Pal 2005*). Wild animals are involved in the epidemiology of most zoonoses and serve as major reservoirs for transmission of zoonotic agents to domestic animals and humans (*Kruse et al. 2004*). Zoonoses with a wildlife reservoir are in most cases caused by various bacteria, viruses, prions, parasites and fungi (*Belay et al. 2004; Kruse et al. 2004; Stenseth et al. 2006*) and are considered as a major public health problem occurring on all continents. Public awareness of the human health risks regarding zoonotic infections has increased in recent years. The recent occurrence of the potential pandemic H5N1 avian flu, severe acute respiratory syndrome (SARS), Ebola-virus, West-Nile virus, bubonic plague and monkeypox with following human fatalities during the recent years led to an increased focus on zoonoses. Viral infections, such as avian flu and bubonic plague carry the potential of fatal impact on humans through epidemics and pandemics if the causative agents establish the necessary adaptations for efficient human-to-human transmission (*Heeney 2006*).

The aim of this report is to provide an updated and brief review on the arena of zoonoses, historic information on bubonic plague and avian-derived influenza.

THE ARENA OF ZOONOSES

Microbial pathogens target a limited number of animal species. Some pathogens can be transmitted to humans either directly (rabies and brucellosis) or through a vector (Lymes disease/borreliosis, West-Nile fever). Only very few infectious agents from animal reservoirs infect people, and even fewer are capable of further human-to-human

transmission. This is attributed to as a so-called ‘species barrier’. This concept involves a series of conditions for successful inter-species transmission. Thus, pandemic zoonotic agents have to break a complex barrier code to get access to a new host. The species barrier code will challenge the infective agent as follows;

1. The agent must get access to an infectable surface on the new host

2. The agent must be able to colonize and multiply on/in the host

3. The agent must be at least partly capable of fighting the hosts immune system (= resistance to innate and adaptive immune mechanisms performed by the infected host).

Each of these steps requires significant adaptation capabilities, such as receptor interactions. Efficient implantation of agents in new hosts requires genetic adaptation or reprogramming to eliminate all steps in the species barrier. These changes occur through mutations or genetic exchanges between species new to each other. The probability to break the species barrier code is proportional to the number of intermediate stays on different hosts with following genetic reprogramming. Further, to obtain the final human-to-human transmission capability some additional adaptive modifications are required. Thus, the risk of pandemics is very limited and dependent on host shifting (*Sansonetti 2006*).

Certain occupational groups are in particularly high risk of zoonotoc diseases. People working in meat industry, farmers, veterinarians, slaughterhouse staff, field- and laboratory biologists and hunters are predisposed to zoonoses (*Strangmann 2000; Deutz 2002, Noordhuizen & Metz 2005*). The prevalence of zoonoses among these occupational groups is closely linked to their behaviour, customs and attitudes on a variety of arenas. Other factors, such as climate and demographic changes, concominant alterations of the environment, technological development and agricultural changes seem to favour the emergence and spread of parasitic zoonoses (*Kallio-Kokko et al. 2005; Macpherson*

2005; Stenseth et al. 2006). The increasing frequencies of movements of people and their animals (and parasites) around the world may introduce new reservoir species, probability of gene mixing, cultural preferences, customs and behavioural patterns which are considered favourable for the prevalence of zoonoses. The increasing proclivity for eating raw, undercooked, smoked, pickled or dried meat from a variety of animal species facilitate zoonoses of different origin. Further, the increasing human population and the inability to keep adequate sanitary conditions and clean drinking water have increased the importance of waterborne zoonoses (*Macpherson 2005*). As a curiosity, traditional Chinese medicine has been practiced worldwide recently, recommending formulas containing animal tissue from tigers, buffalo, antelope, deer, rhino, bears and snakes which carries a significant risk of transmission of zoonoses (*Still 2003*). Thus, a cosmopolitan life style may involve severe public health considerations.

PANDEMIC ZOONOSES

Several pandemics of zoonotic origin are known from written records and other historic materials from the last centuries. The bacteria *Yersinia pestis* are responsible for three bubonic plague pandemics (*Cunha & Cunha 2006*) whilst avian-derived influenza A viruses have also caused three pandemics during the last century (*Hsieh et al. 2006*). These events had huge impact on human population structure by sweeping away millions of people over the centuries. The actuality of bubonic plague and avian influenza are still highlighted due to outbreaks with human fatalities and the awareness of the potential for pandemics, especially for avian influenza (*Ackerman & Giroux 2006*). Bubonic plague is still responsible for 1000-3000 human deaths each year worldwide, and is in fact an ongoing pandemic (*Keeling & Gilligan 2000*).

PLAGUE PANDEMICS

The Justinian Plague (42-590 AD)

This was the first definitely identified pandemic known in the human history. It occurred in Egypt and was caused by *Y. pestis* (*Drancourt et al. 2004*). It is estimated that this plague killed approximately 100 million people during six to eight centuries of duration (*Parkhill 2001; Kahn 2004*).

The Black Death/The Great Pestilence (1347-1351)

This pandemic is classified as the second one in the known human history. The highest impact was restricted to a 5-years period, but is recognized from the early 1300s to the late 1600s (*Cunha & Cunha 2006*). The disease was immediately recognized as a directly infectious disease upon its arrival at the port of Messina of Sicily in 1347 (*Duncan & Scott 2006*). The Black Death moved as a wave northwards through Europe at an average speed of 4 km x d^{-1} and reached the Arctic circle in 1350 (*Zeigler 1982; Twigg 1984; Scott & Duncan 2001*). The impact of the pandemic was on a scale never before experienced, and it is estimated that 40 % of the human population of Europe was killed (*Duncan & Scott 2006*).

It is believed that The Black Death was caused by bubonic plague. However, recent research has questioned whether *Y. pestis* was the causative agent (*Wood 2003*). Duncan & Scott (2006) present evidence that the disease probably was due to hemorrhagic fever, characterized by an incubation period of 32 days. The rapid spreading between localities was considered too fast to be a bubonic plague of zoonotic origin (*Wood et al. 2003*). This new approach fits better to the rapid and widely distribution combined and the limited transportation abilities in the Middle Ages. They suggests that hemorrhagic plague emerged from an animal host in Ethiopia and spread repeatedly through Asian and European civilizations before it appeared as The Black Death.

AVIAN INFLUENZA PANDEMICS

Three pandemic outbreaks are known from the 20th century in 1918, 1957 and 1968. In addition, three severe outbreaks, so-called pseudo-pandemics, occurred in 1947, 1976 and 1977 (*Kilbourne 2006*). Such major influenza A epidemics show no predictable pattern or periodicity and they perform very different impact on people. It is believed that virus-subtypes with human-to-human transmission capability arise from two mechanisms; genetic re-assortment with animal influenza A viruses or genetic mutations (*Kilbourne 2006; Lindstrøm et al. 2004*). Genetic analysis of the causative viruses from historic pandemics demonstrated that new strains emerged after re-assortment of genes of viruses from birds and humans in a permissive host. The leading theory is that pigs represent the so-called ‘mixing vessel’ where the genetic re-assortment may occur (*Capua & Alexander 2002*). The new avian influenza A virus (H5N1) has 3 of the 4 properties necessary to cause a pandemic outbreak: it infect people, most people are immunological naïve, it is highly lethal but lacks sustained human-to-human transmission capability. However, the capability for efficient human-to-human transmission only requires a single genetic re-assortment or mutation by this genetically unstable virus. Up to present time, most infected people acquire the illness through direct contact with poultry (*Bartlett 2006*).

Spanish influenza (1918-1919)

This pandemic is termed “The mother of all pandemics” (*Tautenberger & Morens 2006*) and the causative agent was H1N1-virus from birds (*Tautenberger et al. 1997*). The pandemic transversed the world in 3 months and caused an estimate of 30-50 million deaths (*Cox et al. 2003*; *Bartlett 2006*). In Norway, 15.000 people died from flu, especially young adults between 20 and 40 years of age. It is estimated that the severity of this pandemic flu was 10-15 times the impact of a normal seasonal flu occurring each year. This catastrophic event is a powerful reminder of the importance of zoonoses and public health (*Folkehelseinstituttet*).

Asian influenza (1957-1958)

This pandemic was caused by H2N2-virus which occurred after re-assortment between circulating human H1N1 and H2N2 from birds (*Hehme et al. 2002*; *Lindstrøm et al. 2004*). About 1 million people died throughout the world. In Norway, approximately 2000 people died. The mortality rate was highest among newborn and elderly people. The severity of this pandemic was about 3 times a normal seasonal flu (*Folkehelseinstituttet*)

Hong-Kong influenza (1968-1969)

This pandemic was caused by H3N2-virus which occurred after re-assortment of circulating H2N2 from humans and H3-virus from birds (*Hehme et al. 2002*). On a worldwide scale, between 1 and 4 million people died of this illness. In Norway about 3000 people died, especially elderly people and persons suffering from other chronic illnesses (*Cox et al. 2003*). The severity of the flu was about 3 times a normal seasonal flu (*Folkehelseinstituttet*).

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