A Brief History, Modes of Spread and Impact of

Fowl Plague Viruses

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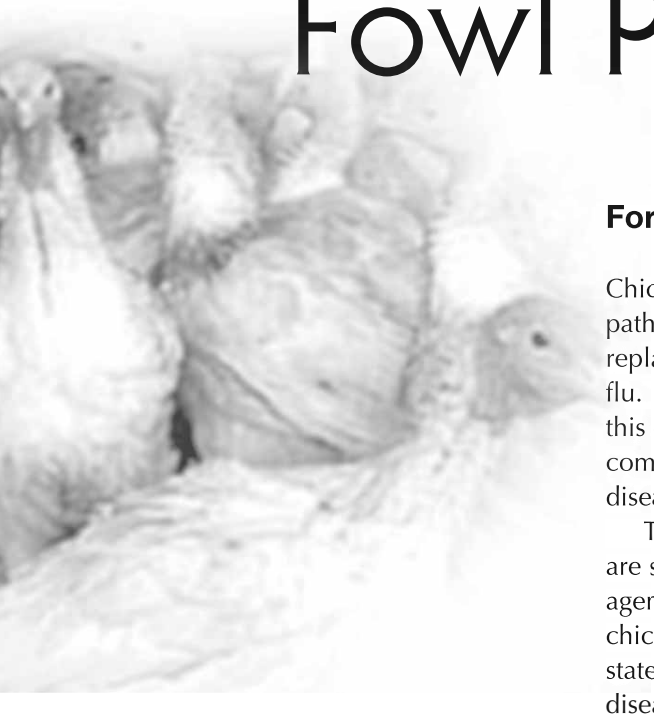

Foreword

Chickens and turkeys suffer most severely from infections due to highly pathogenic avian influenza viruses (HPAIVs), a term which is seemingly replacing the traditional names fowl plague, Lombardic pest, and bird flu. Numerous names were given and used as synonyms in the past for this disease with its dramatic devastating nature. The author prefers in this communication the term fowl plague. This term denotes the severity of the disease and gives honourable credit to the historical authors.

The original homeland of chickens and their place of domestication are southern China and north-east India. It is very likely that all infectious agents are the result of co evolution of contemporary vertebrates including chickens, turkeys, and many other avian species. However, if these two statements are true, the very first cases of fowl plague (and also likely other diseases) should have occurred in these countries. Unfortunately, the author of this contribution is not able to locate such descriptions, nor is he able to read and understand the languages that are used in these countries. Since translations are not available to him, the author is left with the sad feeling that he has missed major scientific contributions from early and contemporary China and India.

This contribution provides a brief review of the history of fowl plague with a special focus on outbreaks in European countries. Preliminary attempts are made to draw some conclusions from outbreaks and their management by veterinarians, governmental authorities, and farmers.

Early Records on Poultry

Written historical records in Europe state that chickens have been bred for more than 2000 years and turkeys for approximately 500 years. The antique Greek (e.g. Aristotle) and Roman (e.g. Columella, Plinius, Varro) writers describe in detail good husbandry conditions, behavioural characteristics, and versatile utilization of various breeds of chickens and their eggs. However, these authors remain silent on topics like diseases and losses.
Coloured paintings, belletristic books, and naturalistic sculptures that go back to the Middle Ages prove that the chicken was a frequent part of rural and urban life. Again, the topics of diseases and their control are not mentioned. This situation changed gradually after the time of Napoleon Bonaparte some 200 years ago. Voluminous books were published in Dutch,

English, French, German, Italian, and other languages on good housekeeping practice, care for farmed animals and their versatile use. Unfortunately, these books focus on horses, cattle, and to some extent on pigs, dogs, and cats. Little if any space was left in these books for poultry. Consequently, only marginal information is available on any of the likely ailments of domestic birds. To my knowledge, the first text book that is entirely devoted to diseases of poultry was published in 1882 by F. A. Zürn in the city of Weimar, Germany.

The Italian Chicken Disaster That Started in 1877

Today, it is generally accepted that the very first description of a gravissima malattia ("most severe disease") was provided by Professor Edoardo Perroncito. He was a highly appreciated member of the University of Torino in northern Italy.In 1877 Perroncito observed a highly lethal disease in chickens, turkeys, and birds of prey; and termed the disease "Epizootia tifoide nei gallinacei" in his article which was published in the highly respected journal, Annali della Reale Accademia d'Agricoltura di Torino (1878) 21, 87—126. His long and detailed report of forty printed pages and two colored illustrations provides insight into the type of small-scale, extensive poultry holdings, trade in live birds, the clinical signs and short duration of the course of the disease, and gross lesions of succumbed chickens and other birds. Professor Perroncito also pointed out that the true origin of the disease could not be determined – a remarkable point which is made quite frequently today as well.

In the following years, additional reports appeared in Italy that confirmed the observed characteristics of the "epizzootia tifoide" as a transmissible disease and its local spread. The new disease was highly contagious and losses were extreme leaving some villages in northern Italy without any chickens. Maggiori and Valenti published in 1901 and 1904 the results of numerous transmission experiments and found that many different bird species were susceptible, whereas rodents were resistant and did not develop obvious signs. Unlike the current outbreaks in some Asian countries, the involvement of mammals and humans was never reported during the early cases of fowl plague in Europe.

Search for the Causative Contagion

Perroncito was convinced that a very poisonous virus caused the outbreaks. At the time, details on viruses were not known, but within a very short period of time many major discoveries were made. Indeed, during the relatively short period between the years 1870 to 1914, a tremendous number of discoveries were made in several European countries. To name a few as examples of scientific

progress in relation to fowl plague and other diseases, a look at this fruitful period of science is presented.

Due to the pioneering works of Louis Pasteur in France, bacteria were cultured for the first time in human history in bottles, while Robert Koch in Germany discovered that bacteria grow in single Colonies on agar plates. Simultaneously, Petri, a co worker of R. Koch in Berlin, invented a glass plate which is suitable for the culturing of bacteria and is now well known as the "Petri dish." Pierre Emile Roux assisted L. Pasteur by providing a specially designed glass flask for culturing bacteria in bouillon medium that is still in use under the name "Roux bottle." Gustav Giemsa – working in the Institute for Tropical Diseases in Hamburg – published his work in 1904 on a staining procedure for flagellates, blood cells, and bacteria that is now almost ubiquitously used as the "Giemsa stain." This stain was soon commercially available by the company Merck in Darmstadt. The visualization of bacteria was made possible better than at any time before due to the development of powerful microscopes by the two companies Carl Zeiss in Jena and Ernst Leitz in Wetzlar, both of which still exist in Germany.

Unfortunately for the brilliant researchers at that time, all attempts to visualize the virus of fowl plague met with complete failure, and the isolated different bacteria were not able to induce a disease that would be similar to the spontaneous cases of fowl plague. The huge amount of work that was devoted to attempts to culture virulent bacteria from succumbed birds provided firm evidence that the new disease was clearly distinguishable from fowl cholera, another severe disease affecting all domestic bird species. Although many bacteria were cultured and described none of them were able to induce fowl plague following the infection of chickens. The discrepancy between various cultured bacteria and the failure to associate disease manifestations with them prompted Jakob Henle and Robert Koch to formulate the "Henle-Koch postulates."

Circumstantial evidence indicated quite clearly again and again that the newly appearing disease outbreaks that were predominantly seen in chickens and other gallinaceous bird species could be transmitted by direct contact between birds and indirectly by materials that were in close proximity to diseased or dead chickens. The attempts to visualize and culture the virus continued. However, for the time being, the contagiousness of the disease had to be demonstrated by transmission experiments using tissues, blood, faeces, or swabs from affected chickens as an inoculum, and healthy-looking chickens and other birds as recipients of the inocula.

Breweries regularly and successfully used keramic filters to remove yeast (Saccharomyces cerevisiae) from the produced beer. The application of such filters to remove bacteria and yeasts from tissue homogenates provided strong evidence that the causative virus did pass these bacteria- and yeast-proof filters, and that the filtrate was still powerful enough to cause a disease indistinguishable from spontaneous cases of fowl plague. This major achievement was obtained by Centanni and Savonuzzi in 1901, who were probably aware of the filtration experiments that were published by Loeffler and Frosch in 1898 with the virus of foot and mouth disease in bovines. Consequently, the virus of fowl plague became the more precise term "ultra visible and filter-passing" agent.

National and International Spread

Local spread within a farm and also from village to village was already a well-proven factum for Perroncito in his first and subsequent publications. The spread of fowl plague along trade and migration routes was also seen. Due to the increasing human population in northern Italy, many young people crossed the Alps and found work and subsistence in southern Germany. These migrating workers carried not only bread and Parmesan cheese as daily food, but also live chickens to sell in Germany. Italian chickens were highly sought after because they were excellent layers. As a result, the fowl plague was unwittingly transported unnoticed across the mountains of the Alps.

In 1901, the Federation of German Poultry Breeders held a large exhibition of poultry in the city of Brunswick in northern Germany. Chickens from all parts of Germany and from surrounding countries including Italy were presented at this poultry fair. Unfortunately, chickens started dying soon after their arrival. The organizers of the fair decided – in an attempt to prevent further spread among the exhibited poultry – to finalize the fair and to send all exhibitors with their birds back home. This decision created a huge disaster. Quite a number of birds were already infected at the site of the exhibition and became sick during railroad travel to their home cities. After arrival in their poultry houses, transmission continued to resident chickens and reached unbelievable proportions. Both, the accumulation of many birds of different origin on the fair grounds and the sudden finalization of the poultry fair resulted in the spread of the disease over Germany and neighbouring countries. This event is a convincing example for measures that should never be taken again.

Modes of Spread

In spite of the drama in Brunswick, rumours from northern Germany about the appearance of the excellent Italian layer chickens reached farmers in France, the Netherlands, and Belgium. Very soon thereafter, Italian layers were exported from Italy to these countries and as a fatal consequence new cases of fowl plague were seen in these countries. These observations indicate that healthy-appearing chickens can serve as infected carriers and can transport the disease-causing agent over long distances.

In the following years until 1925, spontaneous and mostly single outbreaks in different European countries were observed and described in the literature. The losses were high for the individual farmer, but of little significance for the national economy of these countries. Chicken meat and chicken eggs were at that time a rather

seasonal food, and losses in chickens were easily compensated by pork and beef meat or vegetarian food. During 1925 to 1927, a large epidemic of fowl plague started again in northern Italy and spread with the commercial trade in live chickens to many European countries. After this episode, fowl plague was virtually absent in European countries. Simultaneously, regional outbreaks were located in live bird markets in New York City, USA, in the years 1924-1925. The virus probably originated from AIV that was imported from Europe for scientific purposes. No information is available from the African continent.

Irrespective of the distance, the transport of live infected chickens, turkeys, and other birds are the primary and most frequently seen mode of spread. Second in frequency of spread is frozen poultry and poultry by-products. All influenza A viruses are relatively sensitive to inactivation of their infectivity at room and higher temperatures, and freezing does stabilize the infectivity. Frozen carcasses and unheat-treated meat remain infectious for a very long time. Consequently, imports of untreated, unheated, or otherwise processed meat, organs, and feathers are banned by EU authorities. As a third possibility, untreated trophies (feathers, stuffed birds, toys of avian origin, etc.) are considered as a means of spread. However, no direct evidence is available that could prove unequivocally that these materials can be contaminated with an infectious virus and remain infectious over a prolonged time. Our studies on experimentally contaminated Peking duck feathers prove that the virus remains infectious for about four days at room temperature. A fourth means of spread could be realistic if people (tourists, journalists, etc.) return in airplanes to Europe after visiting from infected farms. The infectious virus may persist on clothing, shoes, equipment, etc. and may reach a poultry farm. Direct evidence is not yet available for this theoretical possibility.

The Appearance of Newcastle Disease in Europe

In 1927, T. M. Doyle described outbreaks of a "hiherto unrecorded disease of fowls due to a filter-passing virus" that he studied in villages close to the city of Newcastle upon Tyne, a city with major industry and an international harbour in the north-east region of England. Confusion arose as to whether this disease was identical to fowl plague or whether Doyle's disease was something new and different. Clinical signs and gross lesions were quite similar for both diseases. Additional information on a disease similar to Doyle's descriptions came from Indonesia and in more detail from India. Indian researchers, especially Dr. Ganapathy Iyer, studied the disease in great detail the Imperial Veterinary Research Institute in Muktesvar. They coined the term Ranikhet disease. This disease was also seen in Korea, Japan, and the Philippines among other countries, and was frequently confused with fowl plague and fowl cholera. It was not until 1955 that Dr. Werner Schäfer at Max-Plack-Institute in Tübingen, Germany, was able to demonstrate unequivocally that fowl plague and Doyle's Newcastle disease were indeed two etiologically different disease entities but with similar signs and gross pathology.

Doyle's disease spread all over Europe during World War II as a result of movements of livestock, troops, civilians, and after the war of refugees. Newcastle disease remained the dominant severe infectious disease in Europe until about 1960. At that time, vaccination was introduced to protect chickens and turkeys against the devastating losses. US researchers (Stan B. Hitchner and many others) postulated successfully that a targeted infection of chickens with a mild to avirulent live virus conferred protection against disease and losses. For the first time a safe vaccine was available that could be swallowed by chickens without any harm. In fact, the application of live Newcastle disease vaccine is of paramount importance for general vaccination methodology, as oral application of a vaccine was later mimicked in humans for polio and other vaccines.

Few and Limited Cases of Fowl Plague Between 1930 and 1999 in Europe

Coming back to fowl plague, between 1930 to 1999, no large epidemic forms of fowl plague were seen in Europe with the exceptions of some localized outbreaks. All these outbreaks came – as it appeared to the farmers – out of the blue. Interestingly, all these single, localized cases were seen close to open waters such as rivers, lakes, and ponds. This happened in Scotland in 1959 in two small chicken flocks due to a H5N1 virus. These cases were the first that were caused not by a known H7 virus but by a H5N1 virus. Since then it became clear that fowl plague could be caused by AIV of the H7 and H5 subtypes. In 1963, cases were recorded in England of turkeys being killed due to a H7N3 virus. In 1979, a large number of layers and geese were killed in Saxony, Germany and again in England in turkeys. Both outbreaks in the UK and Germany were due to a H7N7 virus. A case in Ireland in 1983 affected turkeys due to a H5N8 virus, and again in England in 1991 in turkeys due to a H5N1 virus.

All of these European outbreaks seem to suggest an association with the proximity to open waters namely an association with (latently) infected and virus-shedding free-living waterfowl, particularly mallards and swans. Additional lateral spread from the index case to other premises was not documented.

Worldwide Situation Since 1994

The fowl plague scenario has changed world wide in the last fifteen years. Major outbreaks were recorded in Mexico (1994-2005), Pakistan (beginning 1995) and Hong Kong (1997). In addition, several devastating outbreaks occurred in Italy in 1999 due to a H7N1 virus that caused the death (spontaneous mortality and

culling) of 14 million birds. In 2003, the Netherlands, Belgium, and Germany were hit by a H7N7 virus that resulted in the death of 30 million birds. In parallel to these European fatalities, additional outbreaks occurred in Chile in 2002 due to H7N3, Canada in 2004 due to H7N3, Texas in 2004 due to H5N2, and the Republic of South Africa in 2004 due to H5N2.

Many theories have been generated to explain the reasons for occurrence and modes of spread. Obviously, differences do exist between the outbreaks that occurred during the time of Perroncito and in the following decades. One hundred years ago, fowl plague behaved similarly to a caterpillar that moved from farm to neighbouring farms and from one village to the next village. Local transport of live affected chickens and movements of people and materials can convincingly explain the spread of the disease in early days. However, such modes of spread do not explain the single cases in the years 1930 to 1999. One might argue that rapid detection of the causative virus, the containment of affected farms, and the complete culling of all birds prevented further spread. However, these measures do not help to explain the unexpected introduction of the virus in hitherto free and healthy populations that were far away from index cases.

The Postulated Role of Wild Migrating Birds

Detailed surveillance of free-living birds–especially anatiform birds and gulls–yielded in the last two years numerous influenza virus isolations in several European countries. For example, from late 2004 to May 2005, approximately 40 000 samples (tissues from dead birds and some swabs from live birds) were tested in state-operated veterinary investigation laboratories in Germany by real-time reverse transcriptase polymerase chain reaction (RRT-PCR) of the matrix gene, and 431 tissue samples yielded various influenza A subtypes, including avirulent viruses of the subtypes H5 and H7. It is concluded from these studies that currently a large proportion of free-living waterfowl is currently infected with these viruses. The conclusion goes further in stating that, occasionally and unforeseeably an overspill of still avirulent virus from wild birds to domestic chickens and turkeys occurs. During serial continuous virus passages in farmed, densely kept poultry occur random point mutations occur and therefore result in the production of highly virulent fowl plague-causing viruses.

Indeed, numerous avirulent influenza A viruses of 16 hem agglutinated and 9 neuraminidase subtypes were obtained from free-living, predominantly aquatic birds. The theory of spread from these birds to poultry is convincing. However, it has to be admitted that straightforward confirmation in individual cases is difficult to obtain.

Conclusions

In reviewing the current situation in Europe and in particular in Germany, the following observations are made and have at least in part been experimentally confirmed:

(1) all virus detections of the H5N1 subtype were obtained from single dead waterfowl, birds of prey, and gulls;
(2) so far, only one case in a commercial turkey flock was detected in southern France and in one large flock of turkeys in Saxony. The case in Saxony is very close to the location in which the outbreak in 1979 due to H7N7 occurred;
(3) the screening of live birds that were caught at the same location in which dead virus-positive birds were found yielded no isolations;
(4) several thousand trapped healthy birds were found to be free of the detectable (RRT-PCR) virus;
(5) a few virus isolations were obtained from free-living carnivorous cadaver-consuming mammals;
(6) surveillance studies in the vicinity of dead virus-positive mammals yielded no isolations; (7) much discussion arose following the detection and experimental reproduction of the disease and the successful horizontal transmission of a H5N1 subtype to domestic cats. Earlier studies had already shown that cats are also susceptible to the H7N7 subtype and react with severe disease. However, these data were published in Japanese with a summary in English (Yoshihiro Kawaoka, personal communication), and so were not really noticed by the scientific community;
(8) unprotected people who collected dead virus-positive birds or mammals remained healthy and free of the detectable virus and antibodies to the H5N1 subtype; and
(9) so far, accidental infections of laboratory personnel are absent.

All these observations seem to suggest that the wild population of water-associated birds is the actual source of viruses. Therefore, the most reasonable protective measure would be to keep the highly susceptible chickens and turkeys in bird-proof premises that are far away from open waters on which virus carriers aggregate. Most European countries now have regulations at work that require in-house keeping of domestic birds during the migration season and at other times, depending on the risks of open waters with resting places of migrating birds that are located in the vicinity of poultry farms.

A review of the time span between 1878 and 2006 illustrates that fowl plague has periods of frequent occurrence followed by years of almost complete absence. If waterfowl is the only source of viruses, than the incidence of viruses in these birds must be of an undulating nature. The mechanisms that control the fluctuating presence of influenza viruses in wild bird populations are largely unknown. An answer seems likely if the isolation frequencies are maintained over longer periods of time and if the results of these studies are related to environmental alterations such as changed migration routes, alterations of climatic conditions, and possibly other environmental determinants.

Responsible veterinarians in Europe and elsewhere maintain fears of further cases of fowl plague from four sides. First, it appears to be likely that domestic poultry acquires influenza viruses from indigenous and migrating free-living waterfowl; secondly, further spread of the so-called Asian H5N1 virus will find its way into poultry farms and will destroy not only poultry, but possibly also companion animals such as cats; thirdly, virus-containing raw poultry meat may enter the food chain and cause a spread to humans and farm animals; and fourthly, virus spread from infected indigenous waterfowl to terrestrial free-living birds might endanger the life of these populations.

Responsible physicians in Europe and elsewhere are indeed concerned of a possible chain of events that begins with

(1) further westbound spread of the Asian H5N1 virus in Europe,
(2) the infection of mammals (in particular domestic cats) during feeding on dead virus-positive birds,
(3) the transmission of the virus from contaminated (or infected) outdoor roaming cats to owners who care for returning cats in their living rooms which could finally (after mutation and / or restoration) cause disease in human.
(4) Logically, physicians advocate the continuation of surveillance of the free-living bird populations, the collection of all dead birds for virus assays (or incineration of the cadavers), and the simultaneous removal of these infectious cadavers from the environment as a significant source of virus for other birds and mammals. Most importantly, rapid and well-sponsored research is needed for both new and better vaccines for prophylaxis and chemotherapeutics for the effective treatment of established diseases due to influenza viruses.

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