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Impact of zoonooses on human health

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Summary

By reviewing the most significant zoonotic disease outbreaks that have occurred mostly during the past ten years, the author provides a clear idea of how varied these diseases can be in regard to their aetiological agent, size and direct impact on public health. Most examples involve emerging zoonotic diseases caused by viruses and prions and transmitted to humans by a bite, close contact with affected live animals or carcasses, or through the consumption of their tissues. These outbreaks vary from very small and localised clusters of individual cases to millions of deaths, as reported during the past influenza pandemics. The author also shows that even for the larger outbreaks, the direct impact on public health measured by the morbidity and mortality of zoonoses is largely inferior to that of major communicable diseases that affect only humans, particularly human tuberculosis, malaria, HIV/AIDS. However, it is very difficult to predict the outcome on public health of these emerging zoonotic diseases since transmission patterns are not always sufficiently understood to assess this impact accurately. In addition, new modes of agent transmission may compound the initial impact on public health. Finally, the author indicates additional reasons that explain why these diseases are important by placing special emphasis on the financial losses recorded in both human and animal health and also the societal non-monetary losses these diseases can incur. Lessons learnt following major crises generated by the emergence of zoonotic diseases, such as bovine spongiform encephalopathy, severe acute respiratory syndrome and avian influenza, are provided.

Keywords

Animal diseases, Avian influenza, Bovine spongiform encephalopathy, Public health, Severe acute respiratory syndrome, Zoonoses.

L'impatto delle zoonosi sulla salute umana

Riassunto

Prendendo in esame i più significativi focolai di zoonosi manifestatisi soprattutto durante gli ultimi dieci anni, l'autore presenta una chiara opinione sulla variabilità di queste patologie in relazione all' agente eziologico , alla dimensione e all'impatto diretto sulla sanità pubblica. La maggior parte degli esempi è relativa a zoonosi emergenti, sostenute da virus e prioni e trasmesse all'uomo attraverso morsicature, contatto diretto con animali vivi infetti o carcasse, o consumo di loro tessuti. Questi episodi variano da clusters molto piccoli e localizzati di casi individuali a milioni di morti, come nel corso delle ultime pandemie di influenza. L'autore inoltre mostra che anche per gli episodi più importanti di zoonosi, l'impatto diretto sulla salute umana valutata come

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morbilità e mortalità è di gran lunga inferiore a quello delle maggiori malattie trasmissibili che colpiscono solo gli esseri umani, particolarmente tubercolosi, malaria e HIV/AIDS. Tuttavia, è molto difficile prevedere l'effetto di queste zoonosi emergenti sulla salute umana, considerato che i modelli di trasmissione non sono sempre compresi in modo sufficiente per valutare questo impatto in modo accurato. Inoltre, nuove modalità di trasmissione degli agenti responsabili possono potenziare l'iniziale impatto sulla salute pubblica. Infine, l'autore indica ulteriori ragioni che spiegano il perché dell'importanza di queste malattie, ponendo una enfasi speciale sulle perdite finanziarie registrate in sanità umana ed animale e, anche, sulle perdite non monetarie ma sociali che queste patologie possono comportare. Ci si sofferma su gli insegnamenti derivanti dalle maggiori situazioni di crisi causate dall'emergenza di zoonosi, come la encefalopatia spongiforme bovina, la sindrome respiratoria acuta grave e l'influenza aviaria.

Parole chiave
Encefalopatia spongiforme bovina, Influenza aviaria, Malattie animali, Salute pubblica, Sindrome respiratoria acuta grave, Zoonosi.

Introduction

Zoonoses are defined as those diseases and infections naturally transmitted between vertebrate animals and people. Domestic and/or wild animals play an essential role in maintaining and amplifying the infectious agent in nature and can transmit infection to humans and sometimes to other animals. These diseases have a variety of transmission mechanisms that may be direct, such as in rabies, anthrax or trichinellosis, or indirect via vectors, food, water and the environment, such as bovine tuberculosis and cysticercosis. Many, such as brucellosis, also have multiple routes of infection.

A large percentage of human pathogens (61%) are zoonotic and 75% of all emerging pathogens fall within this category (18). New emerging zoonotic diseases, of which severe acute respiratory syndrome (SARS) and avian influenza are the most recent examples, have mobilised human and animal health authorities at national, regional and international levels as epidemic-prone diseases affecting domestic and wild animals and the humans in contact with these animals or their products (30). Emerging diseases are discussed in detail by Brown in this journal (2). The vast majority of zoonoses are, however, not prioritised by health systems at national and international levels and are labelled 'neglected' or 'endemic' (29, 36, 37). Such neglected zoonoses include, among others, rabies, brucellosis, leishmaniasis, zoonotic sleeping sickness (*Trypanosoma brucei rhodesiense*), cysticercosis and echinococcosis. The significance of zoonotic diseases, whether they are emerging or neglected/endemic is increasing and many countries are experiencing the health and socioeconomic impact of these diseases more often, particularly developing countries, where they mostly affect the poorest segment of the human population (13, 22, 37). Zoonotic diseases continue to burden public health systems as well as undermine efforts to boost the livestock industry and production of safe foodstuffs of animal origin to satisfy national demand and exports.

Morbidity and mortality of new emerging zoonoses: from individual cases to the pandemic threat

Mortalities incurred by outbreaks of new emerging zoonoses recorded during the past 10 years have ranged from a very few to hundreds of deaths for a single event. These diseases have had a limited

direct impact, measured in terms of human mortality and morbidity, on human health (11, 12) compared to major strictly human contagious diseases and to certain endemic zoonoses (8).

For example, the 1997/1998 Hong Kong outbreak of avian influenza virus H5N1 involved less than 20 cases including 6 deaths (23) and the 1998/1999 outbreak of Nipah paramyxovirus responsible for the 'barking pig syndrome' in Malaysia involved 154 cases and 55 deaths confirmed to be due to the Nipah virus alone (25). In June 2003, monkeypox was reported in prairie dogs and humans in the United States. By 30 July, a total of 37 laboratory confirmed cases were reported by the Centers for Disease Control (CDC) (case count at www.cdc.gov/ncidod/monkeypox/index.htm). Ebola and Marburg haemorrhagic fever are febrile haemorrhagic illnesses which cause death in 50-90% of clinically ill cases. Their natural reservoirs, which are likely to be animals, are still unknown although frugivorous bats may be the reservoir of Ebola virus in Africa (9). In recent years, we have witnessed the emergence of the largest outbreak of Ebola virus infection ever reported (Uganda 2000-2001), with a total of 425 cases and 224 deaths, and the largest and deadliest outbreak of Marburg haemorrhagic fever (Angola 2005), with a total of 374 cases, including 329 deaths (case fatality rate: 88%) reported countrywide (33, 34). A variant form of Creutzfeldt-Jakob disease (vCJD), a fatal brain disease of humans, was first recognised in 1996 as a result of the bovine spongiform encephalopathy (BSE or 'mad-cow' disease) epidemic in the United Kingdom. Since the first reports, 161 cases of vCJD have occurred in the United Kingdom, 17 in France, 4 in Ireland, 2 cases in the Netherlands and the United States of America and single cases in Canada, Italy, Japan, Portugal, Saudi Arabia and Spain. Cases of BSE and vCJD have decreased in the United Kingdom in recent years, but both diseases have appeared in other countries. Until recently, all vCJD cases were attributed to the consumption of beef products contaminated with the infectious agent of BSE. Since December 2003, three individuals have been identified with vCJD infections probably acquired from blood transfusions. This may imply that other blood donors, who might currently be incubating the disease, would also be potential sources of infection for recipients. The possible extent of future blood-borne spread of vCJD infections is still unknown (39).

Other events, such as the West Nile virus (WNV) and the SARS epidemics, have had greater repercussions. The WNV epizootic that commenced in 1999 in New York State is still ongoing. According to the CDC, the 2002 WNV epidemic resulting in reports of 4 156 human cases of WN disease in the United States (including 2 942 meningoencephalitis cases and 284 deaths) was the largest recognised arboviral meningoencephalitis epidemic in the western hemisphere and the largest WN meningoencephalitis epidemic ever recorded (3). The first known cases of SARS occurred in Guangdong Province, China, in November 2002 and the World Health Organization (WHO) reported that the last human chain of transmission of SARS in that epidemic had been broken on 5 July 2003. The aetiological agent, the SARS coronavirus (SARS-CoV), is believed to be an animal virus that crossed the species barrier to humans when ecological changes or changes in human behaviour resulted in human exposure to the virus and the virus adapted to cause disease in people and enabled human-to-human transmission. By July 2003, the international spread of SARS-CoV resulted in 8 098 cases in 26 countries, with 774 deaths. In areas with sustained local transmission of SARS, the epidemic caused significant social and economic disruption. In addition, the disease had a direct impact on health services and on the international travel industry (31).

As a final example of a zoonotic disease outbreak, it should be stressed that the epizootic of highly pathogenic H5N1 avian influenza that affected domestic and wild birds and humans in South-East Asia in mid-2003 and then spread to Europe and Africa, is the largest and most severe on record, even though the currently reported cumulative number of cases and deaths in humans appears small compared to certain other diseases. Prior to the present situation, outbreaks of highly pathogenic avian influenza in poultry and wild birds were considered rare. Before the highly pathogenic H5N1 emerged in Hong Kong in 1997, reports of human infection with avian influenza viruses were extremely rare and usually resulted in mild disease. Since December 2003, nine South-East Asian countries have reported outbreaks. In late July 2005, the virus spread from its original Asian focus to affect poultry and wild birds in central Asia. From October 2005 to April 2006, the presence of the virus was reported in several European countries. The African continent was affected for the first time on 8 February 2006 and since then the virus has continued to spread among poultry to eight countries on this continent. At the end of February, India and Pakistan reported their first cases in domestic birds. Among other possible modes of transmission, such as national and international trade of live birds and derived products, migratory birds have also played a role in the geographic spread of the disease from its original South-East Asian focus and there has been one confirmed case of human-to-human transmission. Further spread of the virus along the migratory routes of wild waterfowl is still possible. The highly pathogenic H5N1 virus is of concern for human health for two main reasons. First, since December 1997, the H5N1 virus has caused human cases of very severe disease with a 55% mortality rate. Since early 2004 to June 2006, a total of 226 human cases have been notified with more than 129 deaths. Most of these reported human cases and human deaths have occurred in five Asian countries which were all linked to the original focus. In all other countries of Africa, Central Asia and the Caucasus, Europe and Middle East, cases were reported in domestic and/or wild birds, except in five countries (Azerbaijan, Djibouti, Egypt, Iraq and Turkey) where the disease was reported in humans with a total of 37 human cases and 17 deaths. The second implication for human health, of far greater concern, is the risk that the H5N1 virus – if given the opportunity – will develop the characteristics required to spark another influenza pandemic.

Assessing the public health risks of new emerging zoonoses in the short and long term: expect the unexpected

Assessing the public health risks when the communicable disease and causative agent are entirely new is often difficult and is further complicated in the case of new animal diseases as there is great uncertainty regarding how easily the agent will cross the human species barrier. In this respect, forecasting with some precision both the morbidity and death toll is difficult as relevant epidemiological or experimental evidence is usually missing or lacking. For example, during the late 1990s, various predictive models for vCJD provided very variable estimates of the impact of the disease in the United Kingdom, ranging from a total over time of a few hundred cases for the optimistic model to tens of thousands for the worst case scenario (17, 28). A recently published survey of kuru patients (4) indicates that incubation periods for human transmissible spongiform encephalopathies (TSEs) can exceed 50 years. Human infection with animal TSEs

such as BSE can be expected to increase the incubation period further. It is hypothesised that today, vCJD cases could represent a subpopulation with short incubation periods to the BSE agent, that the BSE epidemic may eventually prove to be multiphasic and that recent estimates of the size of the vCJD epidemic could be underestimated. Ten years after the notification of the first cluster of cases in the United Kingdom, the number of definite and probable cases of new vCJD is below 200 worldwide. In recent years, cases of BSE and vCJD have decreased in the United Kingdom. Both diseases have appeared in other countries, such as Japan and Italy, and although the number of BSE cases has decreased markedly in France since 2001, the notification rate for new cases of vCJD has increased in this country over the past two years.

It can be hypothesised that global trade of potentially infective material before effective bans were introduced at national and international levels may have led to the exposure to the BSE agent of other human populations than those living in currently known BSE-infected countries (14). Only reinforced surveillance in humans and animals may tell us in the future how widely the agent may have been exported, during the late 1980s and mid-1990s, from its original European focus. The recent identification of the three cases of vCJD associated with blood transfusion is of great concern as the disease might spread within the human population through the use of a life-saving health technology. It is clear that the blood of donors incubating vCJD might contribute to an unrecognised spread of the disease, especially in countries where surveillance and reporting systems are not established. In addition, results from a tonsil-appendix survey also suggest that a substantial number of individuals in the United Kingdom might be incubating vCJD – a mathematical analysis predicting that as many as 5 000 individuals in the total population (a rate of 237/million) might be infected. Some proportion of healthy individuals with subclinical or preclinical vCJD would presumably be blood donors. Transmission of infection by blood transfusion may have the potential to significantly increase the size and duration of the current vCJD outbreak in the United Kingdom. Risk of transmission of new emerging diseases, including zoonoses, through frequently applied health technologies, such as surgery, blood transfusion or organ donation, should be more systematically considered and mitigation strategies proposed according to the estimated level of risk. This was done in the United States for prevention of WNV transmission through blood donation (1). In addition, recommendations for the prevention of transmission of TSEs, especially vCJD, through medical interventions at home and in health care settings were proposed (28). Although not a new zoonosis, it should be remembered that for the first time ever, a cluster of cases in recipients of transplanted organs and in their common donor was reported in the United States in mid-2004 and in Germany in early 2005.

Viruses with a pandemic potential, such as the highly pathogenic H5N1 viruses currently circulating in birds, are a particular case in point. Most evidence to date indicates that close contact with dead or sick birds is the principal source of human infection with the current H5N1 strain of the virus. In most situations, risky activities were identified, such as the slaughtering, defeathering, butchering and preparation for consumption of infected birds. By mid-2006, H5N1 virus infection remains a rare zoonotic disease in humans. A first case of human-to-human transmission was however demonstrated recently in one family cluster in Indonesia in June 2006, but no effective human-to-human transmission chain has been demonstrated.

Today, the risk of an influenza pandemic has not materialised but the possibility that a H5N1 virus bird strain eventually mutates or recombines with a human influenza virus to acquire the characteristics needed for efficient human-to-human transmission remains. If this happened, future spread of the virus within the human population would no longer require contact with birds and the virus would lose its zoonotic origin in the same way that many other microbial agents have in the past. Influenza pandemics are remarkable events that can rapidly infect virtually all countries. The severity of disease and the number of deaths caused by a pandemic virus vary greatly and cannot be determined prior to the emergence of the virus. During past pandemics, attack rates have reached 25-35% of the total population. In the best circumstances, assuming that the new virus causes mild disease, the world could still experience 2 million to 7.4 million deaths (projected from data obtained during the 1957 pandemic). Projections of deaths from a more virulent virus are much higher. The 1918 pandemic, which was exceptional, killed at least 40 million people. In the United States, the mortality rate during that pandemic was approximately 2.5%. In addition, pandemics can cause large surges in the numbers of people requiring or seeking medical or hospital treatment, temporarily overwhelming health services. High rates of worker absenteeism can also interrupt other essential services, such as law enforcement, transportation and communications. As populations will be fully susceptible to a H5N1-like virus, rates of illness could peak fairly rapidly within a given community. This means that local social and economic disruptions may be temporary. They may, however, be amplified in today's closely interrelated and interdependent systems of travel, trade and commerce (32).

Comparing mortality data of emerging and endemic zoonoses with major communicable diseases of humans

The annual cumulative number of deaths due to major infections and parasitic diseases was estimated at about 15 million in 2002. Six diseases cause the majority of these deaths, as follows: respiratory infections (3.95 million), AIDS (2.8 million in 2005) (20), diarrhoeal diseases (2 million), tuberculosis (1.7 million) (38), malaria (1 million) (35) and major infectious diseases of children (1.3 million) (26). Six tropical parasitic diseases, including trypanosomosis and leishmaniasis, were estimated to be responsible for 1.38 million deaths during the same year. On the other hand, a classical zoonotic diseases such as rabies, which is the leading cause of reported deaths in the zoonoses group, is responsible for more than 55 000 deaths per year in Asia (31 000) and Africa (24 000) and 1.7 million disability-adjusted life years (DALYs) (8). DALY is defined as the health gap measure that combines both time lost due to premature mortality and non-fatal conditions. DALYs for a disease or a health condition are calculated as the sum of the years of life lost due to premature mortality in the population (YLL) and the equivalent 'healthy' years lost due to disability (YLD) for incident cases of the health condition (24). The total number of reported Ebola cases since the first identified outbreaks in 1976 to the end of 2005 was 1 860 cases with 1 296 deaths. Measuring the health impact of these new emerging or re-emerging zoonoses by using mortality data can be misleading as it is small compared to many other human infectious diseases. Only a pandemic, originating for example from a currently circulating H5N1 strain of virus, could lead to mortality figures (conservative estimates ranging from

2 million to 7.4 million deaths) that would be comparable to or exceed the annual mortality data of any one of the major killer diseases.

Why are emerging and re-emerging zoonoses important?

Livestock and other animals play a vital role in the economies of many countries and contribute in all sorts of ways to the well-being of their inhabitants. From the economic standpoint, livestock provides food or, more specifically, animal protein in human diets, income and employment. For low-income producers, livestock also serves as a source of wealth, provides draught power and organic fertiliser for production and a means of transport (6, 10, 37). Other animals, particularly dogs, play a role as guardians of livestock and households as well serving as companions to humans. In most places, livestock and other animals are very closely associated to human beings. Therefore, any contagious disease of animals that is transmissible to people represents a direct threat to human health and if the disease drastically affects the economy of the household, it can be an indirect threat to family survival. In these conditions, zoonotic diseases create permanent direct and indirect threats for livestock keepers, rural dwellers and consumers. Zoonoses have major socioeconomic implications through the direct impact of the disease and through the individual, collective and international costs incurred in preventing and controlling the disease in both humans and animals.

Besides the enormous direct financial losses associated with the BSE epizootic, in particular in Europe, or the SARS epidemic or the avian influenza panzootic, mainly in Asia, these diseases have had a significant impact on all facets of society and have incurred important non-monetary losses. For example, the BSE crisis led to a loss of consumer confidence in food of animal origin, in national food inspection services and in science and scientists. The scientific community was unable to clearly explain what prions were, how BSE crossed the species barrier and what the size of the vCJD epidemic might be. A number of social disruptions accompanied the SARS epidemic: internationally, the WHO issued advice discouraging travel to certain destinations and, nationally, human movement restrictions were restricted in certain affected areas of the developed and developing world. In China, the disruptions came from the closure of live animal markets, the ban on food originating from suspect animals and the mass culling of suspect animal reservoir species. Avian influenza also led to similar disruptions by halting the trade of fresh poultry products from Asia and any other affected country. The disease also led to the re-evaluation of traditional food production models, distribution means and marketing practices. It also lead to the questioning by the affected rural societies of the use of certain environments (wetlands) for the production of a variety of poultry species and the ancestral very close human-animal relationship.

The lessons learnt

The BSE crisis attracted the attention of the health sector to the not well-known but old practice of collecting and rendering carcasses of dead animals (particularly production animals, but also pets). In the rendering process, this material is ground and melted down using various techniques (different combinations of temperature and time with or without solvent.). The rendered protein fraction is further processed to produce meat-and-bone meal (MBM) which is used as a food supplement in feed rations of production animals (ruminants, poultry, swine and fish). The practice was considered

to be an efficient way of recycling nutritious materials and also an economical way of managing the disposal of very large quantities of animal by-products and waste (27). The health sector was the first to condemn the practice and to request that efficient safeguards be implemented to prevent the possible spread of microbial agents through the process to food animals and eventually to the plate of the consumer. In this way, the BSE crisis contributed to the recognition of the 'feed to food' or 'farm to table' continuum and the need for additional safeguards to ensure the safety of foodstuffs. Another lesson learnt from the BSE epidemic was that trade very rapidly adapts itself to changing regulatory environments. When, in 1991, countries of continental Western Europe stopped importing potentially infectious materials from the United Kingdom, new market outlets for these products were immediately found in other parts of the world, such as South-East Asia (19), confirming the validity of the decision later taken by the European Union (EU) to place a ban on the feeding of MBM to all mammalian species within EU member states as well as a ban on MBM exports outside of the EU.

The spread of SARS as a disease of those travelling at the speed of today's aeroplanes contributed to the understanding by the general public of the notion of 'global village' in relation to disease spread (7).

The panzootic of highly pathogenic H5N1 avian influenza virus has been instrumental in finally making clear to the world that human, animal and environmental health are interdependent. This message had been voiced by various groups many times previously but had not been heard (5, 12, 15). Largely as a consequence of the H5N1 avian influenza crisis, the concept of 'one world, one health', which expresses this interdependence (21), is now better understood and is shared by many international governmental and non-governmental organisations.

The impact of these new emerging zoonotic diseases on politicians and health professionals and public perception of their health significance, extend far beyond the actual numbers of cases and deaths induced (16). This is due to the fact that the disease agents responsible were new and their modes of transmission unknown, for the most part, at the outset (e.g. vCJD, Nipah) and for some agents as not confirmed even after the epidemic died out (e.g. SARS) or to the horrific nature and almost invariably fatal outcome of some of these diseases (Marburg and Ebola haemorrhagic fever, vCJD) or to the usually high case fatality rate (55% for avian influenza, 50% for Nipah and 50-90% for Ebola outbreaks). Furthermore, these new emerging diseases remind us of the catastrophic potential of new infectious agents and diseases and of their capacity to occur unexpectedly in new places and animal species. They stress the need for reinforced international cooperation and better local, regional and global networks for communicable disease surveillance reporting and pandemic planning. They contribute to the definition of new paradigms in relation to food production and food safety, agriculture practices and environmental protection, international trade of live wild animal species, disease spread and especially, to the impact of human activities on public health. Finally, they remind us of the importance of interdisciplinary collaboration for disease containment and of the value of interdependence of regional interests and transparency when managing health risks.

Conclusions

Although history shows that the cascade of events leading to the emergence of a new disease is different each time, several factors are known to favour such emergence. These include microbiological adaptation; environmental changes; globalisation of agriculture, food production and

trade; and human behavioural factors. The decline of public health systems in many countries and the increasing number of people who are potentially more susceptible to opportunistic infection by agents of animal origin are also important. It is difficult to predict from which geographic areas or animal reservoirs the greatest risks to human health might originate, the main risk factors involved, and exactly how these risks develop. Nevertheless, a careful review of past events could help to identify key trends and provide guidance for the future. Effective surveillance, prevention and control of newly evolving threats from animal reservoirs require that strong links between the different sectors involved be established. International organisations and their partners need to strengthen the capacity of countries to face these events and the international community to share information across disciplines and sectors. This will contribute to minimising the impact of such threats on public health.

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