Emerging or re-emerging bacterial zoonoses: factors of emergence, surveillance and control

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Review article

Emerging or re-emerging bacterial zoonoses: factors of emergence, surveillance and control

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Abstract – Surveillance and control of emerging bacterial zoonoses is essential in order to prevent both human and animal deaths and to avoid potential economic disorders created by trade barriers or a ban on free circulation of human or animal populations. An increased risk of exposition to zoonotic agents, the breakdown of the host's defenses, the emergence of bacterial strains resistant to antibiotics and their widespread distribution as well as conjunctural causes associated with the action or inaction of man have been identified as the main factors leading to the emergence or re-emergence of bacterial zoonoses. After an in-depth review of these various factors, the present manuscript reviews the main components of detection and surveillance of emerging or re-emerging bacterial zoonoses. A description of the systems of control and the main obstacles to their success is also presented. Detection and surveillance of emerging zoonoses have greatly benefited from technical progress in diagnostics. The success of detection and control of emerging bacterial zoonoses is largely based on international solidarity and cooperation between countries.

emerging bacterial zoonoses / control / surveillance / factors of emergence

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1. INTRODUCTION

At times when basic rules of hygiene were not properly applied and vaccines nor antibiotics had been discovered yet, bacterial zoonoses such as bubonic plague, glanders, bovine tuberculosis and brucellosis caused more human deaths than they ever will again. However, the incidence and impact of some bacterial zoonoses appear to have been increasing over the last several decades and new bacterial zoonoses could arise.

It is this latter possibility that is discussed in most of the articles included in this special edition. However, in order to better understand these analyses, it is important to set these emerging or re-emerging zoonoses within their historical context, to explain what are the factors favorable to the emergence or re-emergence of bacterial zoonoses and how they are currently surveyed and controlled, as well as the strength and weaknesses of these surveillance systems. Despite the considerable technological progress made during the last thirty years, there is still a risk of emergence of new bacterial zoonoses, notably those that are foodborne. Food-borne zoonoses account for most of the emerging bacterial zoonoses due to the globalization of food resources and their worldwide distribution, which can be illustrated by the emergence of *Escherichia coli* O157:H7 [10] or *Salmonella* Enteritidis [54]. In addition, new bacteria have recently been identified, giving a precise etiology to diseases that were already known or whose zoonotic characteristics were discovered or validated recently. This is the case for numerous rickettsial infections (see [46]) or for the identification of the agent of cat-scratch disease, *Bartonella henselae*, and other pathologies associated with this bacterium (see [7]).

2. HISTORICAL CONTEXT

In October 1347, human plague was imported to Europe from the Orient during the siege of Caffa (Crimea, Ukraine) by the Mongolians, when plague entered into the port of Messina, Sicily. It then spread to most of Occidental Europe, where 25 million people died in less than five years, that is one death for every three or four inhabitants [58]. In contrast, 36 876 cases of human plague (with 2 847 deaths) were officially reported in 24 countries (11 in Africa, eight in Asia and five in the Americas) for the period 1987–2001. Although, since the beginning of the 1990s an increase in the incidence of human plague has been observed, especially in Africa, none of these sporadic cases has caused a serious epidemic in these regions, or even a pandemic [25, 59].

The reason for this progress is that current methods of rapid specific diagnosis, the establishment of a world epidemiological alert system, modern hygiene measures and the availability of efficient antibiotic treatments have completely modified the conditions of development of bacterial zoonoses. The three following examples are an illustration of these changes:

– In 1887, Bruce was able to isolate in goats raised on the Island of Malta the agent that causes Malta fever (also known as brucellosis) in man, a disease which was widespread in the region at that time [43]. This discovery led to the prohibition, in 1905, of the consumption of raw goat's milk. The role of other animal species in the contamination of man was shown later on, due to progress in bacteriology and serology. The sanitary or medical control of animal brucellosis, according to the epidemiological conditions and the resources of the infected country, has allowed to control or even eradicate the pathogenic agent reservoir in many parts of the world [15]. This incontestable success of veterinary services has led to a major reduction in the number of human cases in most countries, even if brucellosis is still a very common bacterial zoonosis in many parts of the world.

– In 1890, the discovery of tuberculin by Koch, its use for the diagnosis of bovine tuberculosis in cattle by Guttman and the generalization of the method led by Bang, Nocard or Johne were the basis for the eradication of the disease in Europe within a half a century [5]. Even before antibiotics became available, this eradication had efficiently reduced the risks of human tuberculosis of bovine origin. However, a non-negligible number of cases are still caused by bovine bacilli excreted in the milk of infected cows, since 5 to 10% of human cases are caused by *Mycobacterium bovis* [19, 45]. In a recent review of tuberculosis (TB) in 563 children living along the United States/Mexico border for the period 1980–1997, *M. bovis* caused 10.8% of all TB cases [18]. The yearly incidence of pediatric tuberculosis cases began rising in 1989 and peaked in the mid-1990s, with Hispanics constituting 78.9% of the patients. Amongst the 180 patients with positive culture results, *M. bovis* accounted for 33.9% and *M. tuberculosis* for 66.1% of the cases. This high percentage of *M. bovis* infection was largely attributable to its contribution to extra pulmonary TB (55.2% of all culture-positive specimens). Of course, most human cases of tuberculosis are essentially due to *M. tuberculosis* which caused the death of 30 million humans between 1990 and 1999, mainly in developing countries where access to treatment is difficult due to limited human and financial resources [17]. In 2001, the incidence rate of tuberculosis in the world was still increasing at about 0.4% per year, but much more rapidly in sub-Saharan Africa and in the ex-Soviet Union countries [60].

– In 1890 again, the systematic use of mallein was a revolution in the fight against equine glanders [3]. Discovered by Helmann and Kalning (who died of the disease), the bacilli extract plays the same role in the sanitary prophylaxis of glanders as tuberculin for bovine tuberculosis control. Its use allowed detecting and slaughtering infected animals before they could contaminate other equines and/or humans. This short historical background emphasizes the considerable progress that has already been made in the fight against bacterial zoonoses and the uncountable number of human lives saved or protected due to such progress [6].

The "resistance pockets" of bacterial zoonoses appeared therefore very reduced. However, over the last thirty to twenty years we have been observing the emergence or re-emergence of several bacterial zoonoses [8, 56]. In most cases, these diseases are the ones that humans have contracted either when ingesting contaminated foods or by exposing themselves to wild bacterial reservoirs or their vectors. Fortunately, these infections produce fewer victims than in the past. The availability of antibiotic treatments has made their prognosis much less severe than that of zoonoses due to viruses or non-conventional transmissible agents, such as transmissible spongiform encephalopathies.

3. FACTORS OF EMERGENCE OR RE-EMERGENCE OF BACTERIAL ZOONOSES

The conditions for the emergence or re-emergence and spread of bacterial zoonoses still seem to be present at the beginning of the XXIst century, even if the severity of such infections seems to be less serious than for many emerging viral zoonoses. Many national sanitary statistics have reported an increase in the prevalence and the incidence of some bacterial zoonoses [11, 37, 38, 52], and the specific causes of such an increase are discussed by several authors in the present issue [7, 10, 25, 46, 48, 54]. Indeed, an ensemble of causes favorable to the multiplication and diffusion of zoonotic bacteria exist that can be identified for most of these zoonoses, as previously reported [8, 13, 26, 28, 38, 41, 52, 53]. However, it is useful to list them again for a better surveillance and control of the diffusion of the diseases that they cause.

3.1. An increased risk of exposition to zoonotic agents

One of the principal causes of emergence or re-emergence is an increased risk of exposure to certain pathogenic bacteria, depending on different factors, such as:

– Animal and human diet changes: thus, the number of human food-borne infections due to the ingestion of pathogenic bacteria, such as *Campylobacter*, enterohemorragic *Escherichia coli* (including *E. coli* O157:H7) or *Salmonella* (in particular *S.* Enteritidis or *S.* Typhimurium DT104) has considerably increased with the development of large scale industrial food processing and the development of fast-food restaurants. Food-borne infections caused by zoonotic agents have become more frequent throughout the last decades [53]. As far as animal food is concerned, the same is true for *Listeria monocytogenes* carried by cattle ingesting contaminated silage [61].

– Increased densities of production animal or wildlife populations, associated with modern breeding methods for domestic animals: this has naturally favored the development of some pathogens such as *Mycobacterium bovis*, *Brucella* spp. or *Francisella tularensis* [20, 21, 64]. In addition, the increase in the number of pets in developed countries and the increased interest for exotic pets has led to the emergence of new viral and bacterial infections or parasitic infestations. The recent tularemia epidemic detected in prairie dogs sold as pets underlines such an emerging risk [48, 49].

– Human or animal population displacement (voluntary or not, notably following socio-economic disorders) or translocation (game release, zoological Parks, wildlife safari Parks), as well as changes in the activity period of wild animals (diurnal/nocturnal) under the pressure of hunting [20, 40, 42] have direct effects on the emergence of bacterial zoonoses. Increased contact between human and livestock populations in Africa have led to major health problems [32]. As reported by Kock et al. [32] "in recent years, the growth in livestock populations has slowed, owing to a cycle of degradation and disease, affecting especially traditional pastoral systems with a close physical association between people, livestock, and wild animals". The recent outbreaks of *M. bovis* in wildlife in the Kruger National Park were likely the consequence of initial infection via an infected cattle herd [51]. A similar hypothesis was raised for the presence of tuberculosis in wildlife in the Donana National Park in Spain, since no cases of tuberculosis were detected before the uncontrolled increase in the cattle population [1].

– Increased contacts with a wildlife reservoir, associated with the development of various outdoor leisure activities, such as hunting, fishing or tourism, especially ecotourism may expose humans to bacteria excreted by healthy animal carriers, such as *F. tularensis*, *Leptospira* spp. and *Bartonella* spp. [14, 48], or with arthropods that are vectors of bacteria, such as *Borrelia burgdorferi*, responsible for Lyme disease or

Coxiella burnetii, the agent of Q fever [24]. For instance, a high seroprevalence was detected for several zoonotic agents among hunters in Austria when compared to non-hunter controls [24]. The high seroprevalence especially to *Borrelia burgdorferi* s.l., *Ehrlichia* spp., *Leptospira interrogans*, *E. granulosus*, *E. multilocularis*, encephalomyocarditis virus and Puumala virus demonstrated that hunters are particularly exposed to zoonotic pathogens. This may also be the case with *Mycobacterium bovis*, which is spreading to new wildlife reservoirs, including wild carnivores, deer or wild boars [20, 42]. Ecotourism can also be a contributor to the emergence of new zoonotic diseases. Ecotourism has been one of the fastest growing sectors of the tourism industry with an annual growth rate of 10–30% and comprises about 20% of the world travel market (The International Ecotourism Society (TIES): Ecotourism statistical fact sheet presented in: USDA-APHIS: Nature and Ecotourism: Animal and Human Health concerns: October 2001. 10 pages. http://www.aphis.usda.gov/vs/ceah/cei/ecotourism.pdf). It can be a source of human exposure to zoonotic agents [62]. The increasing popularity of foreign travel and ecotourism places travelers at increased risk for some tick-borne diseases. During the last decade, some 400 cases of tick-borne rickettsioses have been reported in international travellers, the vast majority being African tick bite fever caused by *Rickettsia africae* and Mediterranean spotted fever caused by *Rickettsia conorii*. [31, 46]. From 1999 through 2002, 31 cases of imported spotted fever-group rickettsioses (SFGR) in United States residents reporting travel to Africa were confirmed by laboratory testing at the Centers for Disease Control and Prevention [35]. Nineteen patients (61%) reported visiting South Africa prior to onset of illness [35]. Expansion of ecotourism-based industries, changes in land-use practices, and escalating competition for resources have increased contact between free-ranging wildlife and humans [2]. Although human presence in wildlife areas may provide an important economic benefit through ecotourism, exposure to human pathogens may represent a health risk for wildlife, as illustrated by outbreaks of *M. tuberculosis*, a human pathogen, in free-ranging banded mongooses (*Mungos mungo*) in Botswana and suricates (*Suricata suricatta*) in South Africa, which were recently reported for the first time [2].

– Accelerated degradation of the natural environment, notably in developed countries (by deforestation, building of dams, land consolidation) may cause wildlife species to move to new areas, favoring their relocation in suburban zones, therefore entering into contact with humans [12, 28, 40, 41]. This risk may also be created by humans, when translocating some species in order to populate or repopulate a territory for fauna diversity or hunting purposes [42]. All species translocation (sometimes between continents) is accompanied by the stirring of infectious agents, which may lead to unexpected exchanges of genetic material. It seems that following such a stirring, in the 1980s, a commensal *E. coli* of the human intestine acquired an aggravated pathogenic power therefore becoming verocytotoxic (*E. coli* O157:H7), by exchanging genetic material with a bacteria from the *Shigella* genus [53]. The same type of risk can exist on farms, where the coexistence of different animal species can facilitate the development of severe *Salmonella* and *Campylobacter* infections [53].

– Global warming caused by human activities is also a cause of concern in the emergence of viral and bacterial vector-borne diseases. For instance, outbreaks of plague have been associated with increased rainfall in both Africa and North America (see [25]). Similarly, an association was reported between plague outbreaks and the El Nino southern oscillations effect (see [25]).

3.2. Breakdown of the host's defenses

The second cause of the emergence/re-emergence of bacterial zoonoses is the breakdown of the host's defenses. This breakdown of the host's defenses can be associated with an immunodepression, either following medication or infection caused by pathogenic agents capable of weakening the host's immune defenses allowing infection by opportunistic organisms. The best known example is that of the acquired Immunodeficiency syndrome (AIDS) during which certain bacteria, for which humans are usually healthy carriers, multiply to a level such that they lead to the death of their host [57]. This may explain in certain cases the re-emergence of *M. bovis* or *L. monocytogenes* infections. Out of 225 cases of listeriosis reported in France in 1997, 73% were observed in immunodepressed individuals, who for the most part were AIDS victims [33].

3.3. Emergence of bacterial strains resistant to antibiotics and their widespread distribution

Another cause of the increased incidence of bacterial zoonoses is the appearance of bacterial strains resistant to antibiotics and their widespread distribution, following an excessive usage or misuse in both human and veterinary medicines. The existence of these multi-resistant strains considerably hinders the control of certain infections. They are often the consequence of an increase in the number of these infections (largely nosocomial), which offer many occasions for the appearance of resistant mutants amongst zoonotic bacteria. This is certainly one of the explanations for the emergence or re-emergence of food–borne pathogens such as *Salmonella* Enteritidis or Typhimurium or by certain colibacilli.

A recent report indicated that compared with both control subjects and patients infected with pansensitive strains of *Salmonella* Typhimurium, patients with multidrug-resistant (MDR) *S.* Typhimurium infection were significantly more likely to have received an antimicrobial agent, particularly an agent to which the *Salmonella* isolate was resistant, during the four weeks preceding onset of illness [29]. These authors concluded that prudent antimicrobial agent use among humans and among veterinarians and food-animal producers is necessary to reduce the burden of drug-resistant salmonellosis in humans.

3.4. Conjunctural causes associated with the action or inaction of man

At last, other conjunctural causes associated with the action or inaction of humans exist.

– Humans could have contributed, and could still contribute to the re-emergence of certain zoonoses. Zoonotic agents may be considered for deliberate release to cause harm, since they can simultaneously and adversely affect human and animal health [44]. Such attempts have been made or projected during the last two World Wars, but without any harm. For glanders (caused by *Burkholderia mallei*), the horses willingly infected to cause an epizootic were not able to infect the opposite army's horses, and for anthrax (caused by *Bacillus anthracis*) the people responsible for the attack finally did not dare to use the five million "anthrax cakes" they had prepared [4]. However, *Bacillus anthracis* was recently used in the United States of America, but without serious dispersal. The attack was mainly aimed at specifically chosen persons, to whom a letter was sent; but unfortunately some postal workers were also infected.

– The industrialization of food production for animals and humans followed by its worldwide distribution can also increase the risk of contamination. In humans, the number of infections due to food-borne zoonotic agents has increased and has been maintained since the end of the last century, despite the considerable progress in hygiene made during this period. For instance, in 1997, 730 cases per one million inhabitants per year of salmonellosis were accounted for in the countries of the European Union, as well as 300 cases of campylobacteriosis, 20 cases of yersinosis, 10 cases of brucellosis and 2 cases of listeriosis [53]. However, even if it is impossible to obtain statistics as precise for the previous decades, it is probable that despite the lower number of reported cases, their prognostic was then much more serious. Thus in France, 124 persons died of bacterial gastro-intestinal infections in 1995 (to be compared with 23 513 deaths caused by alcoholism!), whereas a century earlier, 4 000 people died of "typhoid fever" infection [39]. However, several of these so-called "typhoid fever" cases could have been unrecognized cases of zoonotic *Salmonella* infection [39].

– In some countries, the re-emergence of bacterial zoonoses may be due to a lack of surveillance or a lack of appropriate control measures associated with the breakdown of public services [41]. This is caused more often by a lack of financial and human resources, which may be the consequence of economic crisis, social uprising, wars or natural disasters. The re-emergence of some zoonoses, especially water or food-borne zoonoses, is very often associated with an influx of refugees or insalubrity of poor districts in which the sanitary services can no longer exercise a control. For instance, a large outbreak of tularemia was reported in Kosovo in the early postwar period, 1999–2000 [50]. Environmental circumstances in war-torn Kosovo led to epizootic rodent tularemia and it spread to resettled rural populations living under circumstances of substandard housing, hygiene, and sanitation. Professional risks also increase as soon as governments lack resources to enforce hygiene or security standards in places such as slaughterhouses or shelters, leading to an increase in cases of brucellosis, Q fever or anthrax among professionals during certain periods or in specific countries.

Environmental pollution may expose wildlife species to causal agents of diseases that they can then disseminate: open-air landfill sites, manure dispersal and more recently the supplementary costs for breeders for the destruction of the carcasses of their animals after the "Bovine Spongiform Encephalopathy crisis", are good opportunities for foxes, stray dogs, prey birds as well as marauders, especially seagulls to pick up and disperse pathogenic enterobacteria or the agents of tuberculosis or brucellosis [28]. For instance, the recent outbreaks of *M. tuberculosis* in free-ranging banded mongooses and suricates in southern Africa, as previously mentioned, were related to the proximity of garbage pits, where banded mongooses were observed feeding regularly [2].

– The lack of coordination or harmonization of control systems, when two neighboring countries practice different methods of prophylaxis, can be a factor of re-emergence. Thus a country practicing a rigorous stamping-out strategy that succeeds in eradicating a zoonosis may have that zoonosis reappear at its border with a neighboring country that practices only limited sanitary prophylaxis or no prevention at all. The case is well known for tuberculosis and brucellosis.

Another factor in the emergence or reemergence of bacterial zoonoses is the impoverishment of some human populations amongst which all zoonoses can find suitable hosts due to poor hygiene. In developing countries, this impoverishment forces some of these populations to move further into areas where animal reservoirs of potential zoonotic agents exist, as reported for retroviruses [63] or the Ebola virus [55]. As mentioned by Wolfe et al. [63]: "Contact with non-human primates, such as happens during hunting and butchering, can play a part in the emergence of human retroviruses and the reduction of primate bushmeat hunting has the potential to decrease the frequency of disease emergence".

– Paradoxically, in other cases the risks are associated with the financial ease of upper social classes, which makes hobbies easier to practice, such as tourism, hunting, or fishing. By practicing these hobbies, people may come in contact with potentially infected wild animals. The risk is even greater when new "exotic pets" are brought into their home. The danger of *Salmonella* being carried by reptiles has still not discouraged owners of turtles, iguanas or snakes [12, 28]. As reported by Mermin et al. [36] in two case-control studies of human salmonellosis occurring during 1996–1997 in the USA, "the population attributable fraction for reptile or amphibian contact was 6% for all sporadic *Salmonella* infections and 11% among persons < 21 years old". It is therefore estimated that reptile and amphibian exposure is associated with approximately 74 000 *Salmonella* infections annually in the United States.

– For food-borne infections, the most unfavorable factor is the integration and globalization of food treatment chains, which multiply the risk of contaminations in an exponential way [53].

4. SURVEILLANCE SYSTEMS

4.1. National or regional systems

The organization of regional or national surveillance systems for bacterial zoonoses is based on the analysis and synthesis of information usually collected by official public health or animal health systems. Data may be provided to health authorities through partnership and networks organized with the help of medical practitioners, veterinarians, animal health and wildlife specialists or livestock breeders grouped together for the sanitary defense of their livestock (for example, "Groupements de Défense Sanitaire"(GDS) in France), as developed in many countries by commodities, such as cattle farmer associations, egg producer associations. Such networks usually receive some financial aid form their government for setting prevention measures.

In some countries, this surveillance system may also be completed by the development of some more confidential (and sometimes competing) networks, led by different animal production sectors. These networks provide the collection and diffusion of information on animal diseases, some of which are zoonotic, affecting poultry, horses, fish or wildlife. Their main objective is to protect this type of commodity against the dispersal of contagious diseases by providing the professionals with all useful information on the situation of these diseases at national or international levels. The access to these networks is generally restricted to professional members of that commodity and sharing with public health services is seldom done, since they usually do not contribute financially to their start-up funding or to their regular activities.

Since the recent occurrence of several severe sanitary crises (notably associated with bovine spongiform encephalopathy (BSE) in Europe), the necessity of a territorial "web" that allows rapid alert of national health authorities, has become evident to the government of most countries. In response, most of them have created agencies or institutions that are specifically dedicated to setting up a specific surveillance network that reinforces or coordinates the action of the already existing services. However, the efficacy of such surveillance systems may be hampered by various obstacles. For instance, one limitation of such systems can be the increasing disinterest of medical practitioners (both veterinarians or physicians) for practicing in rural areas, which deprives national authorities of a precious sanitary observatory. Similarly, the disengagement of the government (sometimes recommended or requested by world financial organizations) in some developing countries has also led to the accelerated and counter-productive privatization of health professionals.

A good example of annual surveillance of zoonotic diseases, including bacterial zoonoses, at the national level is given by the Swiss Zoonoses report 2003 (accessible on the Web at: http://www.bvet.admin.ch/info-service/e/publikationen/magazin/2004/3_gesamt.pdf).

However, only a limited number of Web sites are available for surveillance systems of bacterial zoonotic diseases and most of them relates to food-borne zoonoses. Here are some examples of such sites.

United Kingdom: the Health Protection Agency has a specific section on zoonotic diseases (http://www.hpa.org.uk/infections/topics_az/zoonoses/menu.asp) and zoonotic surveillance at its web site: http://www.hpa.org.uk/infections/topics_az/zoonoses/zoo_surveillance.htm

Ireland: http://www.fsai.ie/surveillance/human/surveillance_human_zoonoses.asp Netherlands (Netherlands Institute for Scientific Information Services): http://www.niwi.knaw.nl/en/oi/nod/onderzoek/OND1287428/toon

France: http://www.invs.sante.fr/publications/2002/def_priorite_zoonoses/ Within the European Union, recent directives have also been set to establish Zoonotic diseases surveillance, especially for bacterial food borne pathogens (see Web site: http://europa.eu.int/scadplus/leg/fr/lvb/f83004.htm).

In the United States of America, different networks are also available for bacterial zoonoses surveillance either at the state level (for example for California: http://www.dhs.ca.gov/ps/dcdc/disb/disbindex.htm) or at the federal level, mainly within the US Public Health Services or the US Department of Agriculture. Specific sites for food-borne diseases, including bacterial zoonoses (http://www.cdc.gov/foodnet/) or vector-borne bacterial zoonoses have been developed by the federal Centers for Disease control and Prevention (CDC) (http://www.cdc.gov/ncidod/dvbid/misc/bzb.htm). Specifically, the Foodborne Diseases Active Surveillance Network (FoodNet) is the principal foodborne disease component of CDC's Emerging Infections Program (EIP). FoodNet provides a network for responding to new and emerging foodborne diseases of national importance, monitoring the burden of foodborne diseases, and identifying the sources of specific foodborne diseases. However, this system is based only on active surveillance for laboratory-diagnosed illness. Similar sites have been developed in Europe for foodborne diseases, such as the Salm-net network for human salmonellosis (http://www.eurosurveillance.org).

4.2. The world system

The value of a worldwide network for zoonoses surveillance can only be the result of that of national networks, since any interference into the zoo-sanitary information of a country is currently impossible without the agreement of this country. The establishment of such worldwide networks has still to overcome several obstacles. However, such systems are important to be set in a more and more interdependent economy and are usually a booster for improving national systems. At the global level, there are a number of recognized surveillance systems, including the World Health Organization (WHO)-Global Outbreak Alert and Response Network (GPHIN). The surveillance systems for food-borne diseases include Global Salmonella Surveillance (Global Salm-Surv), the SIRVETA system (diarrhea syndrome surveillance) coordinated by INPPAZ (Pan American Institute for food protection and zoonoses) which include countries from South America and the Caribbean) (see web sites: www.panalimentos.org and www.PAHO.org) or the EnterNet System from WHO. For instance, Global Salm-Surv is a global network of laboratories and individuals under the WHO coordination involved in surveillance, isolation, identification and antimicrobial resistance testing of *Salmonella*. The methods used by these different surveillance systems may vary from laboratory-based sentinel surveillance to active and intensive epidemiological investigations, with sometimes an overlap in these various systems.

Indeed, some countries have not been able to or have not shown the willingness to set-up a regular surveillance of zoonoses, and animal diseases in general. Others do have such a network, but screen the information collected, publishing only those that have no risk to penalize their international trade or their tourism industry. This strategy may lead them to sell their animal products at low cost to countries whose food shortage or political pressure forces them to take sanitary risks. Over recent years, a considerable effort has been made to improve the passive system of collection of world zoo-sanitary information, in particular by developing an active system of collection at the Office International des Epizooties (OIE) (www.oie.int), at the World Health Organization (WHO) (www.who.int) or at the Food and Agriculture Organization (FAO) (www.fao.org) of the United Nations. For instance, FAO started in the mid 1990s the surveillance system *Empres* early warning system (http://www.fao.org/ag/AGA/AGAH/EMPRES). Specific agreements have been signed between these organizations (for example http://www.oie.int/eng/OIE/accords/en_accord_fao_2004.htm). Some of these systems are shared between these international institutions, such as the FAO-OIE-WHO initiative called GLEWS (Global Early Warning System for trans-boundary animal diseases). The sources of information developed by these organizations are not systematically and mandatorily validated by national authorities (e.g. the *Empress* bulletin of the FAO). Other sources of information include the *Promed* network developed in the United States, networks of specialized information per region, by animal sector production (in particular in aviculture and aquaculture) or by disease. The reports of non-governmental organizations (NGO) or laboratories in the private sector, as well as articles published in the local press, can also be very interesting and useful information, even though these data are not always validated.

Once the data are collected, they must be used and diffused by competent and motivated persons. This is not always the case, and it is not rare, in some countries, to observe a pile of reports on animal diseases that have never been read. The exploitation of original data should be given to competent epidemiologists, equipped with an efficient computer and networking system.

The diffusion of such data should first be performed at a local level, in order to permanently motivate the people responsible for their collection. But they should also be assured at the national level and beyond the national borders, in order to inform the international community of the evolution of the zoo-sanitary situation in a specific region and demonstrate the capacity of that country to follow the sanitary situation.

The "need" to sometimes keep under control (often delayed reporting, sometimes lack of reporting, especially to international organizations) the diffusion of information by health authorities can be explained by the political and financial consequences that can be attached to the announcement of the first appearance of a deadly zoonosis. Without willingly hiding the truth, some governments delay the first official report of this appearance on their territory, to the detriment of the general interest. They thus leave themselves the time to set-up a plan for the control of the disease, to modify their trade networks or to prepare their constituents to such devastating news.

5. METHODS OF CONTROL

Current methods used to control bacterial zoonoses are mainly aimed at reducing the burden of the zoonotic agent in its animal reservoir, or eradicating it, using the classical methods of sanitary or medical prophylaxis.

5.1. Current methods

5.1.1. Sanitary prophylaxis

Sanitary prophylaxis of zoonoses, which consists in slaughtering and/or destroying all infected or contaminated animals (stamping-out method), has largely been proven useful for the control of bovine tuberculosis. Therefore, in many countries, humans are safely protected from any risk of contamination by *M. bovis*. This same method has succeeded or is in the process of succeeding to also eradicate *Brucella bovis* or *B. melitensis* in many parts of the world.

However, this method reaches its own limits when wild animal reservoirs are concerned or when a disease is spread all over the world. All hope to one day eliminate the animal reservoirs of anthrax, tularemia, leptospirosis, or any other ubiquitous disease seems vain.

5.1.2. Medical prophylaxis

Medical prophylaxis of zoonoses, based on either parenteral vaccination of animals or on chemoprophylaxis, is usually more expensive than sanitary prophylaxis on the long run and also prevents to achieve the eradication of the pathogen from its animal reservoir, since some vaccinated individuals can remain healthy carriers. Furthermore, it is often very difficult to differentiate antibodies produced by naturally infected animals and vaccinated animals based on most serodiagnostic tests used for the detection of bacterial diseases. It is thus reduced to a minimum in many industrialized countries (e.g. control of brucellosis), but it is still practiced in some developing countries where vaccination campaigns using inexpensive vaccines are still organized in order to reduce the burden of zoonotic diseases such as brucellosis, anthrax or animal erysipelas, since financial efforts required for eradication cannot be sustained.

5.2. Obstacles for controlling zoonotic bacterial infections

5.2.1. Main obstacles

The main obstacles that are encountered in the control of bacterial zoonoses are the same as those opposed to the control of any infectious disease, that is most often financial and human obstacles rather than technical limitations.

The financial resources needed to efficiently fight against zoonotic agents are not available for all countries. Only the international community's financial support, could, notably, allow developing countries to organize a proper control of zoonotic diseases, but it is rare that this is materialized as a financial gift and mobilization of specific funds, even by well-known international organizations (such as WHO, FAO, OIE), is limited for such diseases. Due to all these difficulties, many sanitary authorities of these countries have given up the establishment of such prevention programs. Others manage, with a lot of perseverance, to elaborate complicated multilateral financial arrangements. This allows punctual projects to be realized, but rarely to establish the long-term prophylaxis plans that they really need.

When financial and material problems are supposedly solved, human-related difficulties should not be underestimated. These difficulties can originate within the services in charge of applying the national prophylaxis plans, when these services are not themselves convinced of the good use of these plans, or when they do not seem to get specific benefits from it. The obstacles sometimes result from a lack of cooperation between specific professional categories, amongst which figure breeders, as well as livestock brokers or even veterinarians bothered by the application of certain programs of control or the limited incentive given by the health authorities for performing prophylaxis tasks. Finally, the obstacle to such plans may be caused by the active opposition of the public opinion to certain methods of control. This is notably the case for the hostility of some groups to the mass slaughtering of animals during epizootics, or to the use of vaccines issued from genetic engineering. By lack of an appropriate consensus, the control of some zoonotic diseases may simply be impossible in some countries.

5.2.2. Some more specific difficulties

Some more specific factors can also hamper an effective control plan, such as,

– The availability of treatment for humans. The fact that, on the contrary to zoonoses due to viruses or non-conventional transmissible agents, bacterial zoonoses can be cured with an appropriate antibiotic treatment can represent an obstacle to their control. Indeed, in many countries, health authorities are not giving a high priority to the control of such zoonoses, since they know that infected people can be treated. These same authorities will, at the same time, pay less attention to prevention programs or to public information on the risk of zoonotic bacteria. The overall result will be that deaths due to some bacterial zoonoses may be higher than those due to some viral diseases.

– The existence of a wildlife reservoir. Many pathogenic bacteria may find a refuge in wild species, in particular when their domestic hosts are protected by vaccination or chemo-prophylaxis. The control of the zoonoses that they cause immediately becomes more difficult, since the species are generally inaccessible to human interventions. The strategies of sanitary prophylaxis, founded on the limitation of these populations, encounter technical and even more ethical problems. Oral vaccination strategies, which were able to eradicate wildlife rabies in many European countries [47] and in North America [34], are only at the development stage for two bacterial zoonoses: tuberculosis [9], especially in badgers [23], possum [16] and deer [30] and brucellosis, in bison, elk or wild boars [22].

– A new emerging difficulty is becoming apparent: the progressive unavailability of some veterinary drugs illustrated by the progressive disappearance, due to the lack of a profitable market, of some drugs intended for the prevention or treatment of existing diseases in some domestic animal species living in developing countries (camels or goats, for example). In some of these countries, the development of a wide fraud on veterinary pharmaceutical products can also worsen this problem.

– Administrative difficulties. Finally, some purely administrative difficulties can also complicate the control of some zoonoses. This is the case for the control of zoonotic diseases whose consequences are very severe for humans, whereas they have only a very negligible impact on animal husbandry or are considered as phenomena of natural regulation of wild populations. If the Ministry of Health requires the Ministry of Agriculture (or Environment) to cover in their own budget the expenses for a control program, it may become very difficult to find the resources necessary to conduct the prophylaxis programs, since these programs will never be a priority within these administrations. In several occasions, some programs for zoonosis control (e.g. rabies, brucellosis, tularemia) have been abandoned or severely reduced because the prophylaxis of foot and mouth disease was absorbing most of the budget allotted to the veterinary services. Controlling the existing zoonoses, in some regions of the world, can also be added to these difficulties, as it does not allow to investigate and to financially support programs on new and emerging zoonoses. The programs of control may be hindered by the existence of civil or military insecure zones, which prevent proper management and the eradication of a zoonosis in the territories where their risks of development are at the highest. In other regions, the failure results from a disagreement on the choice of the prophylaxis method to be adopted, notably when a choice must be made between a sanitary prophylaxis and a medical prophylaxis. The wealthy countries within a given region generally prefer the former strategy, which costs more but is more rapid and radical, whereas their neighbors with lower income can only afford the latter.

6. CONCLUSION

All political analysts agree today that the big challenge of the XXIst century will be to reduce the gap which is increasing between the rich and poor countries of the planet in the interest of everyone. This seems to be especially true for the health sector. Hopefully, favorable factors for the development of a better surveillance and more efficient control of zoonotic diseases, including bacterial zoonoses, currently seem to override many unfavorable factors. Notably, two of these favorable factors allow much optimism concerning the prevention and control of bacterial zoonoses.

6.1. Technical progress

The surveillance of bacterial zoonoses has been facilitated and boosted by the development of many biological tests and benefited from the molecular biology revolution, which has successively made tests, such as ELISA serology, the use of monoclonal antibodies, and finally gene amplification, using the polymerase chain reaction (PCR) available to health authorities. The introduction of these techniques has made diagnostics become more rapidly available at a lower cost and with a higher accuracy and precision. They also allow, in many cases, the traceability of contamination, thus avoiding new outbreaks. Such progress allowed, during the last decade, in association with standard virus isolation, the very rapid identification of very severe viral zoonoses, such as the Hendra virus in horses in Australia, Nipah virus in humans and pigs in Malaysia or the severe acute respiratory syndrome (SARS) in the People's Republic of China and the recognition of the emergence of bacterial zoonoses such as Lyme disease [27] or rickettsial zoonoses [46].

Similarly, the control of such zoonoses has benefited from very important technological progress that has been made in recent years. Vaccines with serological markers distinguishing between infected and vaccinated animals have been developed, mainly for viral infections, but are starting to emerge for bacterial infections. The use of such vaccines allows to combine the sanitary and medical methods of prophylaxis for some zoonoses, such as brucellosis. Research on oral vaccination methods against zoonoses carried by wildlife has already allowed obtaining spectacular success in the eradication of rabies, and they are promising for the control of tuberculosis and brucellosis in wildlife.

In the field of food hygiene, a more rigorous control of production chains or transformation of food based on the Hazard Analysis Critical Control Point (HACCP) method has considerably reduced the risk of food-borne bacterial infections. More in-depth genetic analysis of bacterial isolates also allows tracing back the origin of these infections, sometimes avoiding their diffusion from a common source.

6.2. Solidarity and international cooperation

An international concerted control has better chances to succeed than when organized only at regional or national levels, since it reduces prophylaxis costs, and specifically improves the overall results by avoiding new contamination of one country by another. In addition, international cooperation programs may more easily receive financial, material or technical aid than with national programs and they can benefit from the advice of the best international experts. Their existence largely encourages all participating countries, which are much more active in this collective work since the results are better recognized, or even rewarded, at the international level.

As we stated in the introduction, it is clear that bacterial zoonoses do not present the same danger today as they did a century ago. The development of hygiene and asepsis and then the discovery of vaccines, and later of sulfones and antibiotics, have ended the ancestral scare of bubonic plague, or more insidious dangers such as glanders, tuberculosis or brucellosis, despite some recent fears from bioterrorism threats.

Even though the emergence factor that is to be the most feared today for bacterial zoonoses is the resistance of bacteria to antibiotics, medical and veterinary authorities should remain extremely vigilant concerning emerging bacterial zoonoses.

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