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Meeting report

Proceedings of the 4th School of Val-de-Grâce's seminar on emerging infectious diseases. Current trends and proposals, March 2015, 25th☆,☆☆

Actes du 4e séminaire maladies infectieuses émergentes de l'école du Val-de-Grâce. Actualités et propositions, 25 mars 2015

1. Abbreviations

ACO	allied command operations
DHSC	deployment health surveillance capability
CNRS	Centre national de recherche scientifique
IMS	international military staff
INRA	French National Institute for Agricultural Research
MILMED COE	NATO Centre of excellence for military medicine
NATO	North Atlantic Treaty Organization
UPD	Paris-Diderot University
UPMC	Pierre and Marie Curie University
WHO	World Health Organization

2. Introduction

If prior editions of the emerging infectious diseases (EID) School of Val-de-Grâce' seminar described EIDs as humankind's lifelong "travel companions", the flare-up of the Ebola virus which occurred in March 2014 in West Africa confirmed the existence of a significant connection between EIDs and our own history, and reinforced the interest of bringing together, for this fourth edition of the seminar, all those implicated in the stakes involved. Imagining many possible scenarios, and being capable of avoiding or defusing a crisis: such is the never-ending challenge of EIDs. The EIDs' seminar seeks to pursue and perpetuate the development of a body of expertise and a prospective reflection among the actors on the problem. The debates, which were centered around the knowledge shared among decision-makers, clinicians, scientists and the media, seek to contribute to the diminishing of uncertainty and ignorance about EIDs. Public online access to the seminar knowledge and argumentation presented therein, proceedings (see at: www.malinfemerg.org) serves the goal of bringing to the general public's attention the knowledge and argumentation presented therein, with the goal of better understanding the risks connected with EIDs.

3. Current topics: presentations and debates

3.1. Oceans, climate and health: the role of public-private partnerships in meeting the challenge of emerging infectious diseases

Moderators: Jean-François Guégan (IRD), Sylvie Briand (WHO).

Presenter: Pr. Rita Colwell (University of Maryland and Johns Hopkins Bloomberg School of Public Health, USA).

More than ever, drinkable water represents a crucial health issue. Diseases linked to water quality represent around 2 to 2.3 million recorded cases yearly, and cause no fewer than 2 million deaths. Cholera counts among these disease-related illnesses. Found in China in epidemic form as of the VIIth century, and in Northern India as of the XVIth century, the illness spread around the globe from 1831 onwards, and since 1961 has been in its seventh pandemic cycle. It particularly strikes parts of the world in which hygiene, sanitation and access to drinkable water are little or not at all guaranteed (primarily in Africa and in Asia). As of 1850, the development of urban sanitation policies has enabled many countries to reduce the incidence and to eliminate cholera in their territory. Nonetheless, Rita Colwell states that management measures for the disease are not synonymous with the definitive elimination of the bacteria which causes cholera (*Vibrio cholerae*). This bacterium is naturally present in the environment and plays an ecological role in the coastal marine ecosystem. Under the compound effect of certain factors, the presence of *V. cholerae* in the environment can generate a stage which is infectious for humans, and can favor the development of epidemics.

Through a study conducted in the Bay of Bengal, Rita Colwell and her collaborators at the International Centre for Diarrhoeal Disease Research (ICDDR) in Dacca, Bangladesh, have succeeded in demonstrating a link between the presence of the pathogen in the aquatic environment, and water surface temperature, precipitation levels, sea and river levels, and also water salinity. The discovery of the natural presence of the bacteria in the aquatic ecosystem (particularly in the plankton which functions as a reservoir) as well as the influence of environmental factors (described above) upon the density of the bacteria in the

☆ The 4th seminar on emerging infectious diseases took place on March 2015, 25th at the School of Val-de-Grâce, Paris.

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environment, tend to demonstrate that environmental factors and climate play an essential role in the emergence and the dynamics of the disease in humans. The use of spatial long-distance detection has played a major role in the discovery of these results, as it makes it possible to follow the evolution of climatic conditions and the evolution of aquatic reservoirs of *V. cholerae* in the Bay of Bengal. Notably it has made it possible to show that the coastal and estuary regions, subject to climatic variations (water temperature, precipitation levels) and to atmospheric influences on the ocean's surface, are more greatly affected by the endemic presence of cholera. Host-pathogen exposure therefore is the result of complex mechanisms, with ecological, environmental, climatic and societal dimensions.

As is the case with many pathogens at the origins of infectious diseases, the *V. cholerae* bacterium is transmittable from one environment to another by way of human activity. The work carried out by Rita Colwell and her collaborators thus has shown the probable introduction of *V. cholerae* in Haiti coming from South Asia, which was at the origin of the cholera epidemic in the country a few months after the earthquake of January 2010. However, the introduction of this new cholera strain to Haiti does not in itself explain the cholera epidemic which struck. Other factors which favor the emergence of the disease must also be taken into account: in 2010, Haiti had its hottest summer in 60 years, and recorded the highest precipitation levels for that same period. A joint study by the Haitian Ministry of Public and Population Health (MSPP) and the American Center for Disease Control and Prevention (CDC) has shown that in 2010 only 17% of the Haitian population had access to permanent sanitation facilities, and 69% to drinkable water. The earthquake largely contributed to the disorganization in a large part of the country and to the development of even more precarious hygiene conditions. Rita Colwell thus demonstrates that the structure which favors the development of a cholera epidemic, as described in the Bay of Bengal, equally applies in the explanation of the emergence of the cholera epidemic in Haiti. The use of high-speed sequencing, using intestinal samples taken from the Haitian population in the two years prior to the epidemic, has notably revealed the presence of strains of *V. cholerae* of the same type as that which was considered responsible for the 2010 epidemic. While the widely-accepted hypothesis of the introduction of the *V. cholerae* strain by Nepalese UN forces was broadly communicated in the press, an alternative hypothesis seems to be that of a persistence of the strain in human intestinal microbiome without the cholera having manifested itself prior.

Faced with the threat of infection, tools have been developed to help understand and better manage these phenomena. Rita Colwell has contributed to the creation of the software program GENIUS, capable of cross-referencing high-speed sequencing data on bacteria, viruses, parasitic fungi, etc., as well as data concerning antibiotic resistance and other virulence factors. Thanks to the use of powerful algorithms, the cross-analysis of these data makes possible in a few minutes the identification of the different strains of a (sub)species of bacteria and their characteristics, notably in terms of antibiotic resistance, exchange of genetic material, or virulence factors. From a practical standpoint, the research presented by Rita Colwell has allowed the development of effective methods of fighting and eradicating the scourge of cholera in this Asian part of the world. Using a sari folded over in several thicknesses, the population can filter water, thus eliminating bacteria and especially its carriers such as copepods. This example illustrated the ingeniousness of a translational process using today's most sophisticated technology to solve management issues in ways that are extremely simple, practical and affordable for even the most needy populations.

3.2. Foresight horizon scanning – the example of antibiotic resistance

Moderators: Henri Bergeron (Chaire Santé de Sciences Po), Didier Che (InVS).

Presenters: Cécile Wendling (research associate, Centre for organizational sociology, French National Science Research Council [CNRS Sciences Po]), Jean-Claude Desenclos (InVS), Vincent Jarlier (UPMC), Nicolas Fortané (INRA), Antoine Andremont (UPD).

This session took place within the context of the publishing of the report "antimicrobial resistance, global report on surveillance" [1]. Many of the stakes associated with antibiotic resistance justify a global reflection on this theme. First, resistance of bacteria to existing molecules, along with a critical lack of availability of new molecules, poses a certain number of therapeutic challenges which can only be expected to increase. In addition, the costs connected to antibioresistance (to antibiotic treatment as well as to the loss of labor productivity of individuals with infections due to multiresistant bacteria) are particularly high, comparable to those associated with Alzheimer's disease in the United States [2]. Finally, antibioresistance presents a problem of surveillance; many countries have not yet precise epidemiological data on antibiotic resistance, despite this information's being essential in the fight against its propagation. Antibiotic resistance remains in this regard a major international public health issue.

3.2.1. Foresight horizon scanning: an anticipatory strategic tool

Cécile Wendling began with a reminder of the distinction between "prospective/foresight" and "prevision/forecast", in that the former includes uncertainty, discontinuity and the unexpected as fundamental principles in its process, whereas the prevision/forecast focus on continuity. Forecast places the future in a continuum with the present, whereas the foresight supposes discontinuity and non-linearity in envisaging different possible futures. (Re)emerging infectious phenomena are difficult to predict, while their occurrence can have social and media consequences, and weigh heavily on the organization of public institutions as well as on private enterprise. Using foresight to anticipate infectious diseases makes it possible to understand major trends and to pick up on signals likely to have a future impact. Having appeared following the economic crisis of 1929 in the United States, with the goal of finding solutions to get the country back on its feet, foresight was then developed by the military before being adopted by the private sector. Today it is of interest for all kinds of organizations (international

organizations, national institutions, public and private entities) and concerns all types of sectors – economy, defense, insurance, environment, energy, health. Foresight horizon scanning does not enable one to predict a phenomenon but to adopt a proactive approach, in order to better grasp the uncertainty of the complex environment in which it may occur. Its practitioners seek to identify those factors which may induce a future change (which can be regulatory, technological, financial, environmental. . .) in order to be better prepared to meet it.

In order to do this, foresight horizon scanning rests upon a rational methodology, specifically suited to those who carry it out. It is a collective and transversal exercise. To grasp the complexity of future uncertainty it is in fact preferable to "get everyone around the table". This common vision facilitates the building of resilient strategies which are more robust, be they for an organization or a country. The practice of the prospective approach follows several steps:

- the defining of a temporal horizon: the future into which it is preferable for the organization to project itself. The temporal horizon depends on the type of activity engaged in, and the given objective;
- the actors' prospective analysis of the environment (understanding how other actors stand relative to one's own position), and what are considered to be determining factors for the future, be they constraints or "aspirations" (opportunities);
- the defining of exploratory scenarios (raising the possibility of different futures); aspiratory scenarios (the actors build their own prospective scenario(s) based on their own preferences); the stress scenario (drawing up the worst-case scenarios, and testing them out through crisis exercises, taking into account weak points in the system as well as the quantity of capital and human resources available);
- the creation of a foresight horizon-scanning cell to analyze major trends and weak signals, and compile a catalogue of innovations (technological or societal, for example). The work carried out by research laboratories which develop knowledge and tools based on "emerging" subjects for society, should be able to assist the foresight horizon scanning cell in picking up weak signals, also including "disruptive signals".

The French public health surveillance institute (InVS) invested in such an approach in 2014 with the goal of improving the anticipatory dimension of its actions. With the recognition that health surveillance focuses on short-term threats to health, on a daily or weekly schedule and in reaction mode, the InVS sought to reinforce its competencies in the reading and analysis of weak signals. It defined a mid-length temporal horizon (5 to 10 years) with the goal of better interpreting signals generally considered to be anecdotal, unusual or poorly explained, but likely to have a future impact. According to Jean-Claude Desenclos, the prospective approach makes it possible to escape the circle of urgency, to step back in order to better identify, on a daily basis, the germinal health safety questions to come, thus going beyond the reactive mode, and allowing the promotion of an anticipatory perspective. While the setting up of a foresight horizon scanning strategy necessarily takes time, it provides a useful framework for reflection. This field is become institutionalized through methods and tools which are more and more widely documented and recognized. Training in the prospective approach is expanding, and it is no longer rare to encounter public and private institutions having a "prospective director" within their human resource or strategy departments.

3.2.2. Reflections around the stakes of a prospective approach applied to antibiotic resistance

The prospective approach aims to establish a strategy based on the circumstances which are likely to present themselves in the future. Unlike the provisional approach which rests upon the principle of continuity and the permanence of change ("tomorrow will differ from today exactly as today differs from yesterday") [3], the prospective approach includes not only the dimension of a longer timeframe, past and future, but also the phenomena of rupture and discontinuity. In contrast to the sector-based approach of provisional reasoning, the prospective approach is global. When the antibiotic "miracle" appeared in the 20th century, it promised to improve the health status of populations. It in fact contributed to the significant increase in life expectancy over a period of nearly forty years. Nevertheless, one question emerges: was it possible to anticipate the "catastrophe" represented by antibiotic resistance nowadays? Has the arrival of antibiotics been perceived only from the angle of therapeutic progress? It very quickly became apparent that collective emulation gave way to the first signs of resistance. The lauded miracle was thus of short duration. Vincent Jarlier bases his presentation on two telling examples: on one hand, that of antibioresistance connected to the bacillus responsible for tuberculosis, and of enterobacteria on the other hand.

Concerning resistance linked to tuberculosis bacilli, it has undergone a progressive and dramatic accumulation of resistance mutations to a whole series of antibiotics: (isoniazide [INH], rifampicin [RIF], fluoroquinolones [FQ], aminosides [AMI]). Resistance to INH and RIF, the two major antituberculous drugs, developed into multiresistance. Next, treatments based on so-called second-line antibiotics (FQ and AMI) have not proven effective due to inoculation of additional mutations to quinolones and aminosides, which resulted in a situation known as "ultra-resistant XDR".

Today the WHO estimates that out of 9 million cases of tuberculosis diagnosed yearly, around three hundred thousand are due to multiresistant bacteria (MR-TB) – with considerable variation according to country. For example, around fifty thousand cases of MR-TB originate every year in Southeast Asia (China and India) and twenty to fifty thousand in the ext-Soviet Union; thirty thousand cases are likely due to an ultra-resistant bacteria (UR-TB). In France, on average five thousand cases are reported each year, of which one hundred and twelve MR-TB cases in 2014, with one-quarter being XDR cases. These cases primarily originate in the ex-Soviet Union – mostly in Georgia – and less so in Africa and Asia. The question of tuberculosis bacilli resistance remains limited in France relative to the limited number of cases. For this author, the development of a drastic increase

in the number of cases in our country is unlikely. However, those countries already reporting a high number of resistant cases, capable of using second-line antituberculous treatments despite an inadequately organized health system, risk seeing an increasing number of ultra-resistant cases.

Successive recourse to new-generation antibiotics has also concerned the treatment of enterobacteria, since in approximately forty years they have developed resistance to three successive generations of ß-lactamines, the primary family of antibiotics in human medicine (ampicillin in the 1960s, third-generation cephalosporins [C3G] by extended-spectrum β-lactamases in the 1980s, and carbapenems [from the year 2000]). The breadth of this phenomenon has proved highly variable from one country to the next: between 25 and 65% for ampicillin resistance; from 1 to 10% for third-generation cephalosporin resistance in *Escherichia coli*. This phenomenon markedly illustrates the weight of permanent interactions between the human and bacterial worlds. Among those factors which favor resistance, the author particularly points out the role of emunctories and wastewater from the human and livestock populations, as well as a strong link to stays in foreign countries (and particularly hospitalization). The consequence of this evolution is an increase in mortality through serious infection due to more resistant bacteria, because of the more and more limited number of antibiotics available to heal patients. The author draws the conclusion that antibiotic resistance is a true question of scientific ecology and sustainable development, requiring a persistent multisectorial approach, as limiting its consequences will take time.

Considering antibiotic resistance from the point of view of the animal world, livestock raising and veterinary medicine contribute keys to understanding, particularly because of the large degree of responsibility of this sector in the global phenomenon of antibioresistance. For Nicolas Fortané, it is necessary to avoid pitting the responsibility of animal and human medicine one against the other, in order to better focus on the problem of antibioresistance as the fruit of a collaborative design between two social universes (current One World – One Health approach). Early on, antibiotics were used as a form of an agricultural biotechnology toward the goal of productivity. This practice contributed to the transformation of the miracle which penicillin represented in the 1940s into a growing threat to public health as of the 1960s. If the scientific and medical milieu began to take the question seriously in the 1970s and 1980s, it was not until the following decade that the problem drew increasing attention from the authorities. The debate came to a head around the avoparcin crisis, in which human medicine held agricultural practices responsible for the development of resistant bacteria which could be transmitted from animals to humans. In 2003, the use of antibiotics as a growth additive in livestock was banned in Europe (measure applied as of January 1st, 2006), embodying the will to control the use of antibiotics in the animal world.

Any prospective exercise in the area of antibioresistance should thus be distinguished from a purely medical concept of bacterial resistance to antibiotics (an interpretation which long dominated the debate), in order to see it more as a multifaceted problem. In other words, the immediate response to problems linked to antibioresistance probably lies less in the production of new antibiotics, than in measures which would act upon the ways and means of using antibiotics. Such policies abound on the monitoring and control of antibiotic use, be it in human or veterinary medicine. The author proposes exploring the structural issues underlying the phenomenon of antibioresistance in livestock, and raises the question of regulation and a new socioeconomic model for the veterinary profession. He also comes back to the idea of disconnecting prescription and delivery in veterinary medicine (as exists in human medicine) which, according to him, masks deeper issues such as triangular relationships between farmers, veterinarians and cooperatives, or that of the organization of health aspects of livestock raising.

He emphasized the interest of orienting veterinary medicine more towards a prevention and hygiene advisory model, and points up the importance of developing new agricultural models, in which the use of antibiotics would be strictly limited to cures, and would no longer constitute the adjustment variable in the poorly-controlled health situation also constrained by technical and economic productivist imperatives.

While initially a medical concern, the problem of antibiotic resistance also covers an array of political issues, both national and international. The WHO is aware of this, and complements its expertise with that of the World Organization for Animal Health (OIE) and the United Nations Food and Agricultural Organization (FAO). This political and administrative coordination was also initiated in France through colloquia organized conjointly by the Ministries of Agriculture and Health. Today it must necessarily include the Ministry of Ecology. The question of antibioresistance calls for a shared ownership of the problem, and a common defining of solutions, in order to encourage innovation.

Antoine Andremont proposes an overview of the history of antibioresistance through three key points: the role of generic drugs, North-South relations, and the millennium event of the increase in selective pressures exerted by the environment. In his opinion, no simple solution will succeed in resolving the antibioresistance problem. It is a social issue which calls for extraordinary innovation.

Since the 1980s, the production of antibiotics has steadily decreased, and today no new molecule is being produced to respond to the most problematic cases of resistance. At the same time, although the phenomenon is gravely underestimated, the increase in antibiotic resistance is concomitant with the marketing of generic drugs which favor the consumption of antibiotics all around the world. Studies have in fact demonstrated the link between decreased cost, increased consumption and resistance development. Seen in the context of North-South relations, the development of antibiotics implies increasing exchanges likely to influence the phenomenon of antibioresistance. Currently most antibiotics are produced no longer in Northern countries, but in developing countries. There is in return a risk of a multiresistant bacterial invasion from the South to the North. Since the mid-2000s, extended-spectrum β-lactamase producing *Enterobacteriaceae* (EBLSE) epidemics have for the first time proved

to be beyond the control of hygiene practices, as they occur not in hospital but in the community (in connection with the food chain). The antibiotics were produced and used extensively in developing countries, generating an environmental contamination around farms through animal waste. Under pressure from environmental selection, these bacteria which are naturally resistant to C3G were able to multiply and transfer the resistance to *enterobacteria* present in the digestive tract, most likely first in livestock in contact with the environment. The transfer to humans then took place via the food chain.

In this context what innovations might limit, or eradicate, this phenomenon, and how best to communicate about the subject? The primary question is not the production of new antibiotics, but knowing how to use them. The author suggests rather favoring the production of niche antibiotics. However, he points out that lacking a business model, their production remains unattractive for the industry. Several proposals were made: phages (viruses which only infect bacteria); immunotherapy, development of preventive measures... All these ideas recall the necessity of cultivating innovation in the hope of harvesting a solution. More surprisingly, global solutions can also take the form of managing corruption. On this last point, the author mentions an article by Collignon et al. [4] in which he and his collaborators show that neither the consumption and use of antibiotics by the population, nor the level of economic development explain in themselves the multi-factored reality of antibioresistance. In fact, other variables (political or socioeconomic) are likely to influence this phenomenon. The quality of the system of governance in a country (which for the authors is synonymous with the capacity of the government to control corruption) constitutes a major socioeconomic factor among the principle determinants of antibioresistance.

The term "antibioresistance" covers a multi-factor reality which is complex and fragmented: it concerns a number of infectious agents, which cause numerous diseases, and variable types and levels of resistance, and implies the responsibility of actors with divergent interests. Communication on antibioresistance should therefore address the problem as the expression of a social complexity in which the role of human behavior in the environment is core. Antibioresistance should be defined as an issue which is ecological in the broad sense. This implies putting communication strategies in place which refresh both the content of the message (by developing for example information on the direct and indirect victims of antibioresistance), but also the means of broadcasting the message – using social networks, education through play techniques, "entertainment education".

3.3. Emerging infectious diseases: the NATO military approach

Moderators: MC Xavier Deparis and MC Rémy Michel, French Armed Forces Centre for Epidemiology and Public Health (CESPA).

Presenters: MC Jean-Baptiste Meynard (CESPA), MGA Gérard Nédellec (COMEDS), Lt-Col Anne-Marie Fenger (IMS), MC Patrick Malaguti (ACO), MC Benjamin Queyriaux (MILMED COE, DHSC).

3.3.1. Health in NATO

Created on April 4, 1949 following the signature of the Treaty of Washington, NATO currently includes twenty-eight Member States who are politically and militarily allied. The fundamental objective of "The Alliance" is the protection of the freedom and security of all members, through political[1] and military means[2]. NATO is a place of decision-making and consultation on a wide range of security issues. A "NATO decision" is an expression of the collective will of the totality of the twenty-eight members: all decisions are taken by consensus. Each member state is represented by delegations (civilian bodies) and military representatives. Whether preparing a military operation, planning for crisis scenarios, issuing strategic advice toward a decision, encouraging knowledge sharing, savoir-faire or experiential feedback between Member States and partner countries/organizations etc., the military entities contribute their expertise in crisis management. Each of the principle military structures within NATO (see Fig. 1 below) includes a medical branch entrusted with the task, within the specialized domain of each, of analyzing the medical implications raised by certain military questions.

3.3.2. NATO facing the risk of occurrence of an international epidemic crisis

Historically, NATO has always considered that health issues remain the responsibility of Member States, with support from international organizations (such as the WHO). For a long time the Alliance had no high-level medical authority. However, the development of conjoint military peacekeeping operations, as well as catastrophe humanitarian relief and rescue have led Member States to coordinate their actions in the medical area as well. Important work around data collection, information sharing and experiential feedback between Member States has been carried out to allow NATO to better assess the health of the Alliance's armed forces, before, during and after a NATO operation. The Alliance has developed its own expertise on questions of health, with goals resembling those of civilian society: surveillance and anticipation of a crisis to the greatest possible extent. However, these competencies developed by the Alliance are also and primarily developed for it as well: they should be considered primarily in the military sense.

How far can civilian and military cooperation be expected to go in the surveillance of and response to the global epidemic threat? The session drew heavily on an article published on April

[1] NATO's goal is to promote democratic values and to encourage consultation and cooperation on questions of defense and security in order to develop trust and, over the long term, prevent conflict (http://www.nato.int).

[2] NATO is committed to the peaceful resolution of differences. In the instance of failure of diplomatic means, it possesses the military capacity necessary to undertake crisis management operations. These are conducted under the title of Article 5 of the Treaty of Washington – NATO's founding treaty – or under the mandate of the UN, by NATO alone or in cooperation with other countries or international organizations (http://www.nato.int).

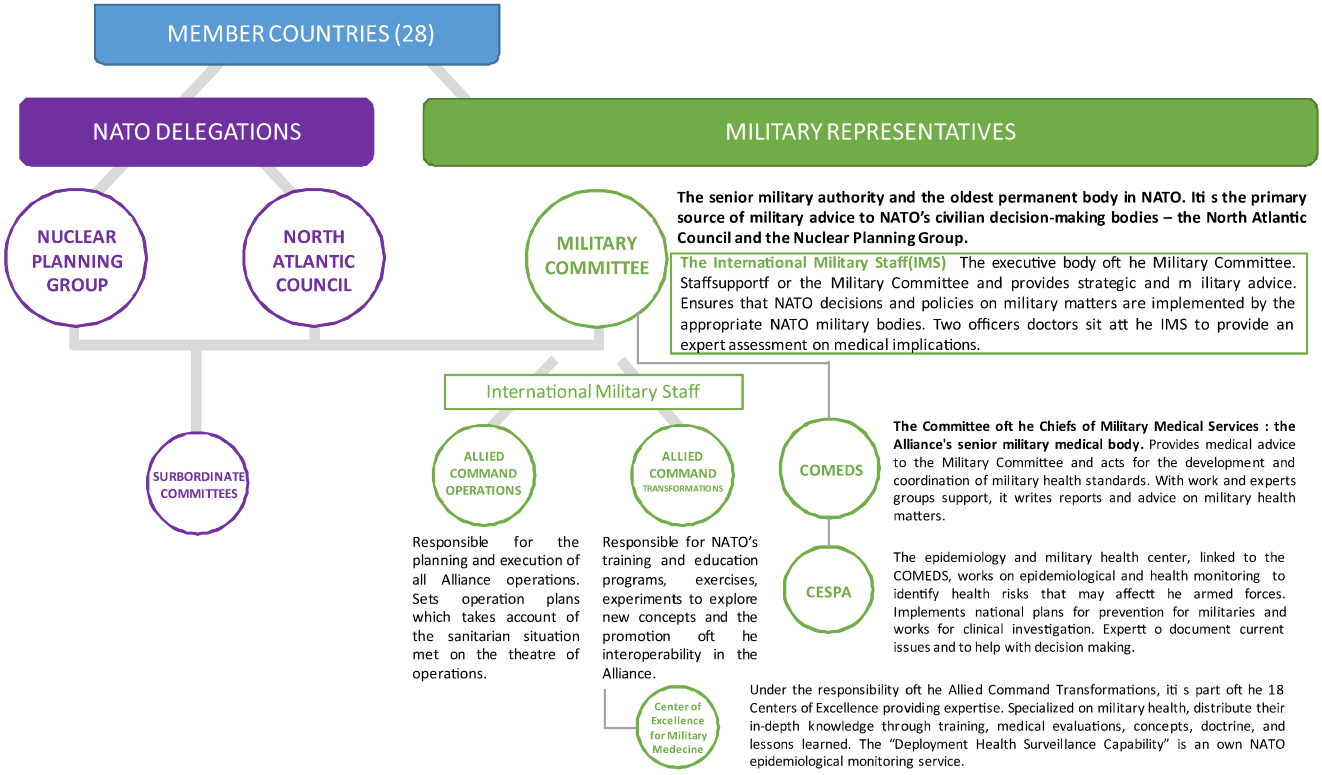

Fig. 1. NATO Military structures and their medical involvement. Source: organizational chart "working structures" (NATO), available at http://www.nato.int/nato-welcome/index_html. Modified by Pilot Committee of EIDs seminar (2015).
Les structures militaires de l'OTAN et leur implication médicale. Source : organigramme « structures de fonctionnement » (OTAN), disponible sur http://www.nato.int/nato-welcome/index_fr.html. Modifié par le Comité de pilotage du séminaire MIE (2015).

9 2015 in *The New England Journal of Medicine* ("The next epidemic – lessons from Ebola") in which Bill Gates emphasizes the need to put in place a global system for surveillance and management of epidemics. This system should be embodied by a leading international institution (such as the WHO), capable of reacting rapidly, of applying its decisions and mobilizing personnel trained in crisis management without delay; of investing continuously in research and development, and utilizing a global surveillance and alert network in real time. If, for Gates, the WHO should be reinforced in all aspects and become the international institution of reference in terms of warning and response to the epidemic threat, it cannot do so in isolation, but must coordinate with other organizations, be they political (the G7), economic (the World Bank) or military (NATO). The Alliance exhibits technical know-how (development of surveillance and warning tools such as MEDICS software), as well as operational (health crisis simulation exercises) and strategic expertise. On this last point, NATO has, for example, included in its doctrine the concept of "Smart Defense". In the context of economic recessions and reduction of national expenditure on defense budgets, cooperation becomes central to the Alliance doctrine in order to acquire, develop and preserve the military capacity and means necessary for the security of Member States. Cooperation for the purpose of reactivity and efficiency perhaps constitutes the primary advantage likely to improve health security, be it military or civilian. The NATO experience could be a helpful source of wisdom in the preparation of epidemic response.

3.4. Crisis management in health policies

Moderator: Patrick Zylberman (EHESP).

Presenter: Didier Tabuteau (Health Chair, Science-Po Paris).

"Governing in a stable environment is essentially programming", posits Didier Tabuteau. It involves projecting into the future, planning, anticipating. Crisis, on the contrary, upsets established programs and requires reactivity, immediate action and even sometimes improvisation. Patrick Lagadec defines crisis as "urgency plus destabilization". It is the inevitable moment of decision-making in face of the unknown. The health incident (in its epidemic proportions alone) does not suffice to make a crisis. The turning point at which a health incident becomes a crisis also takes into account the political and socio-cultural context in which it takes place.

Beginning in the 1990s, and especially since the "contaminated blood affair" which caused a veritable collapse of trust in medical progress, as well as a change in vision in the health system, leading to the 2002 law on patient rights, healthcare scandals have multiplied, and with them a true change in the health crisis paradigm has occurred. If until that time, healthcare "accidents" were attributed to fate, ever since there has dominated a much more determinist approach founded on causality. The *Legionella* example is particularly enlightening, since after its identification a policy to combat the legionellosis disease was implemented, based on technical norms (relative to hot water, water intake systems, organizational systems for group care centers, monitoring systems, investigations, and even

reimbursement procedures). A public health risk suffered through was transformed into a public health risk produced by society and regulated by the community. A crisis has its causes and "responsibilities", which should be identified in order to better master the risk involved. In just a few decades, as public health episodes followed one on another, the French health system, through complementing its legal and institutional arsenal, has acquired the capacity to identify risks and organize community response, which enables it to act on the causes leading to crises. Finally, public health crises manifest as powerful public health policy levers and a source of considerable change, because it is inherent in a democracy to identify its weak links and to correct them in order to better protect the population. The creation of agencies has emerged as a model of institutional guarantee of public health safety. The contaminated blood incident also led to the creation of the French Blood Agency in 1992, and the Drug Agency in 1993; the "mad cow" crisis helped spur the creation of the French Agency for Food Safety (AFSSA)[3]. Most importantly, the institutionalization of agencies in the health administration landscape has made it possible to identify the guarantor authorities, for evaluation purposes as well as for those of risk management, and to thus establish frontline responsibilities.

The emergence of new legal concepts, such as the notion of "serious health threat", in the French public health code of 2004, and the multiplying of health norms, illustrates a tendency to build up a legal arsenal, sometimes through improvisation, in reaction to a crisis. This also reflects a clear will to preserve community health safety. Therefore, in the case of a "serious health risk", the minister responsible for health is invested with the powers which enable him to decree any measure necessary to fight "against the propagation of diseases", including imposing quarantine. Extraordinary policing measures are authorized by law, and the management of a crisis appears to justify the existence of and recourse to this exceptional power held by the authorities. Similarly, the French Constitutional Council, in a decision dated March 20 of 2015, reaffirmed that measures related to mandatory vaccinations (diphtheria, tetanus and polio) for minor children are constitutional, despite their imposed character, in order to "fight against three very serious and contagious, or impossible to eradicate, diseases".

The obligation to react when faced with an identified risk requires management of human and material means. In 2007, a health reserve was created, and a structure for preparing for and responding to health emergencies (EPRUS) was put in place. Strategic health product stockpiles were accumulated by the State, to allow it to handle exceptional health emergencies [5]. It is also the responsibility of health authorities to seek out the risks, anticipate the crisis occurrence, and to limit the public health consequences. The implementation and reinforcement of monitoring, surveillance and also "health intelligence" are applications of this obligatory vigilance.

[3] This structure merged with the French Agency for health safety, environment and labor (AFSSET) to make up what is today the National Agency for health safety, food, environment and labor (ANSES).

The status of information and communication was also reinforced within public health institutions and health safety agencies, each of which is competent, and indeed mandated, to inform the public.

According to the author, all of these elements represent an evolution in the organization of the health system in anticipation of risk and in view of the capacity for real-time adaptation. Risk should not be suffered through, but sought out and mastered as far as the community can do. The more means the health safety authority has at its disposal, the more it detects risks. However, paradoxically, the improved response capacity of a society is accompanied by the multiplication of health safety alerts, with the risk of increasing the feeling of a diffuse and insufficiently controlled health threat.

Moreover, the identification of new risks, which science struggles to home in on and analyze, places political structures once again in the forefront, to whom it falls to organize the health response, whatever the scientific uncertainties involved. Finally, the management of health crises is deeply affected by the evolution of information systems and the media. Non-stop news channels and social networks make it possible to follow the crisis "live". Governmental authorities are thus faced with a new challenge, that of organizing and directing a crisis management system in the moment, but also that of tracking down health risks over the medium and long term.

4. Synthesis and proposals

EIDs raise a plethora of issues at the crossroads of a vast range of queries and reflections covering the fields of healthcare, politics, law, ethics... From a scientific viewpoint, they invite an understanding of the origins and means of existence of these emerging diseases. From a political standpoint, these questions force societies to imagine action capable of controlling them. One risk preparedness technique among others, the prospective approach seeks to establish a bridge between the understanding of the phenomenon of emergence, and the implementation of measures to handle it. This fourth seminar intended to once again bring together the actors of these different fields of reflection and action, in order to better define the conceptual issues and concrete realities of these diseases.

This day of presentation and debates has been the occasion to illustrate the notion of risk preparedness, drawing upon concrete examples implemented by public, private, civilian and military entities. Using the example of antibiotic resistance, presenters have had the opportunity to underscore the contribution of risk preparedness, as well as the issues and limits it entails, and to elucidate pathways for future reflection and action in order to meet the challenges posed by EIDs.

4.1. For a coordination of actors – at the national and international levels – around EIDs

EIDs are unpredictable, and have sometimes unexpected, if not paradoxical, effects. They can manifest as local or international, rural or urban public health incidents, having a medical impact, but also a political and media impact... Thus

antibioresistance, defined in turn as a public health issue, or as a veterinary problem linked to agriculture livestock raising. Another example: in 2014 and 2015, the Ebola virus shook public health authorities around the world, whereas in the 1970s this disease involved only a few isolated villages in Central Africa. Finally the political and media impact of the H1N1 flu virus in 2009 was unequalled in its influence on the number of deaths. These three examples illustrate well the plural and temporal, but also uncertain, nature of EIDs. They are in fact plural, and implicate, from the understanding of the diseases to their treatment, numerous actors with sometimes divergent interests. Considering the issues involved in EIDs requires taking on the problem and defining solutions shared by all sectors, disciplines and actors concerned. Risk preparedness should enable us to come to a common vision and, to this end, bring together all actors in an integrated approach. This is why the creation of foresight horizon scanning cells within organizations is essential to the operation of such a network. Moreover, their position in the organizational chart of the institution is strategic, as they require a multiplicity of competencies within the organization.

At the supra-national level, within structures such as NATO, when an EID emerges on the international scene, in regions of the world which may be theatres of operation or of a simple military presence, decision-making procedures sometimes may encounter a refusal by the States to surrender sovereignty. When, in 2014, the Committee of military healthcare unit heads (COMEDS) took up the subject of Ebola to generate recommendations for NATO authorities and its member countries regarding behavior in response to the risk of epidemics links to infectious diseases, certain countries considered that these civilian problems lay outside military jurisdiction. Faced with this "breaking of silence" or expression of reservations on the part of certain Member States, the recommendations generated by COMEDS were not adopted. This example perfectly illustrates the difficulty in coming to a common vision – particularly beyond a national level – among institutions composed of such diverse entities, actors and interests. Nevertheless, experience tends to show that the issues raised by EIDs extend beyond national borders, and precisely invite a redefinition of the position of all actors, not only public and non-governmental, but also military, in order to arrive at a coordinated interpretation and response to these global health threats. Given the unpredictable nature of infectious phenomena, as well as their diversity, no single crisis management model or "standard response" can prevent the risk of new emergence.

Risk preparedness and its tools, such as the foresight horizon scanning approach, reflect the need for exchange and sharing of experience among actors within a network, rather than a "turnkey" response. Such an approach seeks to promote better coordination of action in the case of a public health alert.

4.2. Escaping the circle of emergency

Monitoring is a warning device, inviting rapid response, whereas risk preparedness focuses on the mid and long term. Risk preparedness invites actors to step back, to escape the circle of emergency, to put back into context a sign which may appear anecdotal and therefore low-priority, yet which is likely to have a future impact. Risk preparedness is not driven solely by epidemiological data or a public health incident, but by the totality of contextual elements influencing it. This is why it implies not only working transversally, but also "in-depth", in that the solution to a problem or a crisis leads not only to an immediately visible reactivity (communication and crisis meetings), but also (and especially) to structured-decisions makings.

As for antibiotic resistance, the response cannot be restricted to the search for new molecules which are effective against resistant bacteria. The biomedical approach must be complemented by a reflective intention which extends to all the determining factors (structural, psychosocial. . .) which influence antibiotic use. This presupposes, for example, a line of questioning regarding the possibility of reforming procedures for prescription and delivery of antibiotics, and comparing and contrasting developmental models and regulatory systems of veterinary and human medicine. At the national level, interministerial coordination (Health, Agriculture) is necessary albeit difficult, and should be pursued with the inclusion of the Ministry of Ecology. As a general rule, antibioresistance should be thought of as a medical and political problem, of which infra- and international governance issues have repercussions on antibiotic treatment use and monitoring and, consequently, on the risk of propagation of resistant bacteria. Antibioresistance is not necessarily linked to the socioeconomic level of a state, nor only to the use made of antibiotics in the population. The quality of political systems and their general effectiveness in fighting corruption (surveillance of actors involved in the use of antibiotics, monitoring of quantities of antibiotics used and the duration of prescribed treatments) also influence the antibioresistance level in a country. These pathways for action cannot do without communication on the correct use of antibiotics. On this point, the use of digital information (smartphones, tablets), new channels of communication (social networks) as well as the evolution of message content, deserve to be further explored.

Mobilizing a network of actors who share the common will to prepare for the risk of emerging infectious diseases, beyond a state of emergency, could take the form of concrete exercises which would enable all concerned to test out crisis scenarios and their practical solutions.

4.3. Systematizing exercises

In order to become more efficient, risk preparedness should be able to find continuous support in experiential feedback from actual health incidents, and to be made concrete through drills. It is in this direction that, following on the publication of the information report by French Senator Fabienne Keller, on new threats by EIDs (under the auspices of the Senate Delegation on preparedness, January 2013), the French Health Minister, Marisol Touraine, was asked in a public debate to "organize an annual drill to prepare for an eventual major public health crisis, as is the case in numerous foreign countries" [6].

Experiential feedback can provide a host of lessons. This methodology is implemented and mastered particularly in the military sector, under the sometimes very constraining

conditions of theatres of operation, where the demands and rigor of analyzing the situation prove highly strategic. Setting up, or even systematizing, such experiential feedback could benefit civilian society in drawing from military experience, especially that of NATO.

Based on predefined scenarios, transversal warning and crisis simulation exercises would allow the different participants to better know each other (be they decision-makers, scientists or other experts), to share available knowledge, to learn how to better communicate (with health professionals, the public. . .), to better prepare together for a crisis' occurrence. Opening up such exercises to the society and to politicians, on a national and international scale, would facilitate the encounter of many attitudes and types of knowledge, and to identify potential difficulties in the management of a major crisis. The preparedness exercise illustrates the idea of risk pedagogy, and allows actors from different horizons to share a global vision and to develop reflexes for handling a common problem in a concerted manner. By targeting a specific theme, the exercise could also allow the drawing of useful analogies with other social questions. The question of antibiotic resistance could, for example, echo that of the resistance of insects to pesticides. In order to become operational, the promotion of these exercises (high command or full-scale exercises) applied to the EIDs question could also be codified by legislation. They should be accompanied by new objectives and be developed within institutions, as well as addressing socio-economic and educational sectors. Conducting frequent, regular exercises with the participation of expanded panels including key sectors of society would contribute to the promotion, in France, of a risk culture which to date has remained too theoretical.

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