

Responding to new severe diseases – the case for routine hospital surveillance and clinical networks in Europe

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Any review of the emergence of the more important infectious disease threats in the past few decades will note how many of them were first detected, or recognised as being serious, through unusual patterns of severely ill people appearing in hospitals (Table 1).

That was also the case for the 2009 influenza A(H1N1) pandemic: While the first detected cases were mild infections in children in the south-west of the United States, it was severe disease in Mexico City that led to the appreciation of the potential seriousness of the threat [8,10]. In this issue of *Eurosurveillance* a series of articles describes the initial surveillance in the European Union (EU) [11], how new comprehensive surveillance was developed in Iceland [12], the response in Italy [13], the form that detected mortality took in Germany [14] and clinical surveillance for severe cases in Denmark [15]. The Danish paper notably describes successful efforts to mount surveillance in intensive

care units. It is striking that at a time when there was infection and disease in the community, it was the hospitals, and their paediatric services and intensive care units in particular, that were most under pressure [16-18]. It is a truism that the severe cases are to be found in hospital. However, that is where some of the most important information on this pandemic was found, i.e. data and analyses that were needed to guide the countermeasures. A number of the analyses that filled in the gaps for ECDC's *Known Unknowns* (the important features that vary between pandemics and need to be known for control activities) eventually had to come from hospital sources [19]. It is therefore logical to make an effort to gather the early clinical, virological and epidemiological information during a pandemic from hospitals and clinicians in general and intensive care units in particular.

TABLE 1

Examples of important emerging infections detected through hospital observations since 1981

New condition or threat (year)	First appreciation of emergence and severity	References
Human Immunodeficiency virus (HIV) (1981)	Severe and unusual opportunistic infections in men who have sex with men in Los Angeles and then New York, United States	[1]
Escherichia coli O157 causing haemorrhagic colitis and renal failure (1982)	Haemolytic uraemic syndrome causing acute renal failure in children presenting to paediatricians and other physicians in the United States	[2]
Avian influenza A(H5N1) in humans (1997)	Severe respiratory infections in hospitalised patients in Hong Kong	[3]
Emergence of new variant Creutzfeldt-Jakob disease (CJD) and eventual indication that bovine spongiform encephalopathy (BSE) was transmissible to humans (1996)	New variant CJD recognised by neurologists in the United Kingdom	[4]
Deliberate release of anthrax (2001)	Severe or unusual infections seen in hospitals and emergency rooms in the United States	[5]
Severe acute respiratory syndrome (SARS) (2003)	Severe infections spread nosocomially in hospitals in Hong Kong and then in other countries	[6]
Multidrug-resistant <i>Acinetobacter</i> causing severe infections (2004-5)	Observations in injured military personnel in the United States with severe infections of the extremities	[7]
Pandemic influenza A(H1N1) (2009)	Severe respiratory infections seen in hospitals in Mexico City	[8]
Highly drug-resistant <i>Klebsiella</i> with a new mechanism of resistance (2009)	Identification and detailed microbiological investigation following diagnosis by hospital physicians of a resistant urinary tract and other infections	[9]

At the same time, hospital surveillance for severe acute respiratory infections (SARI) was one of the two most obvious weak links in the European strategy of surveillance in a pandemic [20] – the other weak link was delivering timely population-wide serological data and analyses [21]. These are not so much issues on a European level as weaknesses in the national systems. There are very few formal systems for hospital-based clinical surveillance in the EU. Neither ECDC nor the World Health Organization (WHO) can ask the Member States for additional analyses and data that they do not routinely collect. Collecting detailed clinical data in real time while clinicians are busy dealing with an outbreak remains a challenge. Even if the rapid collection of data is completed, e.g. via web-based tools, there also needs to be a rapid analysis fed back into the outbreak response.

These reasons alone make a strong case for establishing routine hospital-based clinical surveillance at least in sentinel settings and for linking clinical-microbiological services in international networks that collaborate with public health services and the authorities. However, there are other reasons why clinical networks should be there and function in emergencies (Table 2): The main aim should always be to improve patient care, to ensure that the care given is as safe as possible and that appropriate infection control measures are taken. The clinical lessons learned should ideally be captured in real time and linked with the microbiological and epidemiology results. Rapid analyses should be fed back into the response, providing for instance revised case definitions and improved clinical care [22].

These are not new observations. In 2003, the WHO rapidly set up a clinical network to respond to the epidemic of severe acute respiratory syndrome SARS [25]. It consisted of clinicians from as many as 10 countries

discussing case management issues in real time, sharing experiences that were invaluable for the front line clinicians and ultimately improved patient care. Efforts were always made to have an epidemiologist and a virologist on the calls to ensure a more coherent and cross-disciplinary approach [25].

Of course there is a plethora of existing clinical networks and societies in Europe, including ones that deal with intensive care, clinical virology, respiratory disease and infections. However they are not usually structured to respond to emergencies, their links to the public health authorities tend to be unclear and they do not receive enduring official funds. It is also asking a lot of the voluntary officers that run these networks in their spare time to do more in a crisis when individual members are already stressed by an increased workload. However the example of the one international emergency clinical network set up during the 2009 influenza pandemic by the Health Protection Agency (HPA) in the United Kingdom (UK) is encouraging [25]. Similar networks were active or formed de novo in France (REVA-GRIPPE-SRLF), Spain and the Ukraine, and there are undoubtedly others [26].

Following the admission of the first severe cases of pandemic influenza A(H1N1) into intensive care units in the UK, the HPA facilitated and coordinated discussions between intensive care clinicians from a wide range of fields, including specialists in intensive care, paediatrics, thoracic medicine, virology, epidemiology, and infectious diseases [22], including also the UK Department of Health and the WHO (Europe Regional Office and HQ Geneva). Disease experts and clinicians from outside of Europe were included from the beginning to ensure that the experiences made in Mexico and the rest of North America with 2009 pandemic influenza A(H1N1) and in the Far East with avian

TABLE 2
Potential purposes of clinical networks linked with public health in Europe

Activity	Benefit
Empower clinicians at a local level, allowing for detection, early warning and alerting of new threats	Essential for the implementation of the International Health Regulations 2005 [23]
Share clinical experience and provide support to other teams for challenging clinical decisions	Particularly important when dealing with a novel disease and limited information in the literature
Respond rapidly with evidence-based clinical advice where possible	Evidence readily available to help with decision making
Collect clinical data in real time linked to laboratory and epidemiological data	Data analysed and fed back into the system promptly will help the clinical response
Coordinate and contribute to the writing of guidance, in cooperation with relevant stakeholders, notably professional societies	In a novel disease scenario it is important to capture evidence of best practice
Agree on a platform to disseminate the guidance	Readily accessible guidance
Provide early warning from the first affected localities for other European countries	Countries have the opportunity to prepare for a new threat and to fulfil the obligations of EU Decision 2119 to disseminate information that benefits other European Countries European [24]
Provide training for clinicians in basic principles of outbreak response, personal protective equipment, epidemiology, laboratory test limitations and interpretation of result	Continue to strengthen the clinical frontline, so that when the next novel disease emerges it will be easier for them to manage
Assist the Global Outbreak Alert and Response Network (GOARN) and European authorities such as the Humanitarian Aid department (ECHO)	Opportunity to support other countries and foster international relations; experience gained abroad could be fed back into national plans

influenza A(H5N1) did not have to be relearned. They followed a format similar to the traditional clinical 'Grand Round' with treating clinicians seeking peer review of their proposed clinical management programmes. The Practice Notes for the care of critically ill adults and children were disseminated via the websites of relevant societies and the HPA [27,28]. Dedicated teleconferences examined particular elements of care including infection control in intensive care, paediatric care, and pregnancy. This was a demanding process requiring the time and efforts by clinicians and experts in many countries as well as the HPA itself.

It is striking how well the initial impressions from these networks held up to the evidence that eventually appeared in the peer-reviewed literature, for example the early observations regarding differences to seasonal influenza (children being relatively overrepresented and older people underrepresented), special challenges in managing the profound hypoxaemia, groups at higher risk of severe disease (the very obese, pregnant women, asthma patients, certain ethnic groups), and the benefit of higher than normal doses of oseltamivir [22].

Particularly valuable for the early risk assessments was to combine the hospital experience with that in the community. It was apparent early on that severe as the cases seen in hospital were, they were uncommon compared to the many infections known to have occurred in places with good surveillance affected early (New York and parts of the UK)[21]. This allowed ECDC to be cautiously optimistic in its risk assessments in early 2009 [29].

The first HPA teleconference call took place in early June and the first practice note that the UK clinicians could look to for guidance was published in August on the professional websites [27,28]. However the formal dissemination of much of that information was a problem. Publication of most clinical observations proceeds slowly and those with the information did not always appreciate the obligation to disseminate their core messages through rapid systems like the Early Warning and Response System (for Europe) and the International Health Regulations alerting system (global). In a novel situation there will be a lag time as information is collected prior to wider dissemination.

A number of lessons can be learnt from the experience with the 2009 pandemic. Firstly, there is a need for routine surveillance of severe infections in hospitals. This could be in sentinel hospitals or for some conditions at a population level (in the United States all childhood deaths associated with influenza are notifiable to the Centers for Disease Control and Prevention) [30,31]. Secondly, the surveillance activities should be overseen by interdisciplinary groups of clinicians and microbiologists as well as public health institutes. Thirdly, the specifications for hospital information systems should facilitate this kind of work. And fourthly,

when emergencies arise, these surveillance systems should be reinforced with people and resources. These lessons need to be acted upon now as there are indications in Europe of disinvestment in the surveillance systems established during the pandemic at a time when early information on severe cases remains of high importance in Europe [32]. Table 2 highlights the benefits of operational clinical networks. Ideally a framework should be built prior to an outbreak, bringing together the multi-disciplinary groups for training and preparedness. The network would be activated by agreed triggers and contain a core group to facilitate its functions and outputs.

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