French Republic

PARLIAMENTARY OFFICE FOR SCIENTIFIC AND TECHNOLOGICAL ASSESSMENT

MUTATION OF VIRUSES AND THE MANAGEMENT OF PANDEMICS

Summary of the final report

Since last year, Mr Jean-Pierre Door, a deputy, and Mrs Marie-Christine Blandin, a senator, co-rapporteurs of the OPECST study on the mutation of viruses and the management of pandemics, have heard more than 150 persons, organised two public hearings on the A(H1N1) virus, and published an interim report in February 2010.

Their final report draws a first appraisal of a crisis which has largely unfolded in an unexpected manner and which has been managed by applying a plan defined for another, far more dangerous virus, the H5N1 virus. It presents the results of investigations at the WHO, European agencies tasked with health surveillance and the authorisation of drugs, and the P4 laboratory in Lyon, while comparing the French situation with that which prevailed in Sweden, England, Germany and China.

The report takes up the highly detailed answers sent by the Director-General for Health in March this year and advocates a strengthening of research on viruses in order better to combat them. It also recommends international coordination between world, European and national authorities, and in-depth analysis on the public management of pandemics.

I. HAVING A BETTER UNDERSTANDING OF VIRUSES TO BETTER LIMIT THEIR DAMAGE

A – FINDINGS BASED ON COMMON DATA

Some viruses affect only animals, others men. They do not all have the same impact. Viruses recently discovered are known as emerging ones. The cause of their appearance or spread can be related to climate factors, the development of transport, or the extension of areas under irrigation.

Viruses are constantly mutating in an unpredictable manner. True mutations must be distinguished from genetic accidents which result from mixes of viruses. These accidents are random, which forces those devising plans to combat pandemics to work on the basis of hypotheses and scenarios.

Some viruses are harmless, others extremely dangerous. The latter must be studied in specific conditions in special, so-called P4, laboratories. These are viruses for which there is no vaccine or treatment and which are highly transmissible. The possibilities are studied there of the appearance of a virus combining the danger of H5N1 and the contagiousness of H1N1. Researchers then wear a protective suit in an enclosed, protective atmosphere placed under a negative pressure.

Research on viruses is diversified. Several research topics are prioritised such as the development of a long-lasting vaccine protecting against several flu viruses, the discovery of new antivirals, optimal organisation of the fight against a pandemic, and the definition of new policies for health risk management and crisis communication. The funding of research in emergency situations must be ensured, in accordance with procedures to be defined before new crises. Pluridisciplinarity must be encouraged, as should better knowledge on the acquired immunity of the population.

B – THE STUDY OF SPECIFIC VIRUSES DEMONSTRATES THE VERY GREAT DIFFERENCE OF ACTUAL SITUATIONS

Over the past few years, new, highly worrisome viruses have appeared.

SARS was the first serious virus which led to changing the approach in the public health policy field. It revealed the transmission of an animal virus to man.

H5N1, or the avian flu virus, has led to the death of one out of two of the infected, but has remained barely contagious. It led to the definition of pandemic plans.

Chikungunya is due to a virus whose mutation has facilitated its spread by mosquitoes. Participatory and imaginative methods have been used in Réunion

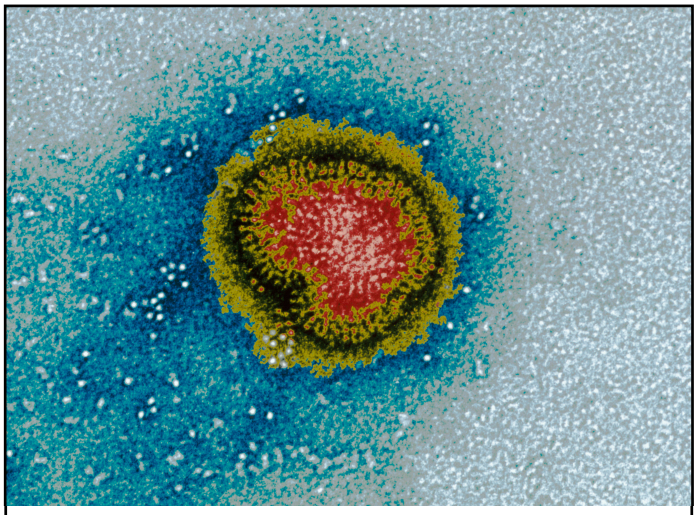
to combat it. But it is presently reappearing and could develop in the Camargue if the average temperature rises. This virus has revealed an interesting research potential on the island which could have an impact on all the Indian Ocean.

Hand, foot and mouth disease has already caused 250 deaths in China in the first quarter of 2010. This virus, which attacks more specifically young children, will have to be monitored very closely in the months and years ahead.

A(H1N1) has proven to be different from what was expected.

This situation has highlighted the relativity of scientific knowledge: it is is still not known how A(H1N1) came into being. It can merely be observed that it is circulating at the same time as other flu viruses like H1N1 or H3N2, which it has sidelined. Its low initial pathogenicity did not exclude a mutation. It is merely known that some people were already immunised against it, which has largely distorted the surveillance instruments.

Political decisions were taken in a climate of feverishness and uncertainty: this was the case for orders of vaccines, implementation of the pandemic plan and the organisation of vaccination. These decisions, which must be assessed on the basis of the information available to the decision-takers, were later criticised. For instance in July 2009 it was not known how many persons would have to be vaccinated and how many vaccine doses would be necessary.



Virus A(H1N1) © Institut Pasteur

Some choices could have been different. Health professionals could have been involved in the vaccination, which would have avoided certain denial or rejection reactions. The contracts could have included conditional phases and renegotiation clauses. Take-up of the vaccine would have been better if clearer answers had been given to the population's concerns.

The vaccines could have been packed as unidoses.

II. INTERNATIONAL COORDINATION, A NECESSITY

A – GLOBALLY, TWO ORGANISATIONS PLAY A VITAL ROLE : THE WHO AND THE IOE

The WHO is facing new challenges.

The WHO monitors the spread of a virus globally, chooses vaccine strains which will help to effectively combat a new virus, and manages assistance to the poorer countries. Today it faces new challenges:

- The circulation of viruses has speeded up from one region of the world to another and their surveillance must be made with greater coherence;
- The expectations of emerging countries have changed. Their demands go beyond assistance of the humanitarian type, and concern the definition of new intellectual property rules on medicinal drugs;
- Public opinion does not understand the highly restrictive definition which the WHO has given of a pandemic since May 2009. The lack of taking account of the severity of the virus and its lethality does not justify measures which do not appear to match reality.

To keep its legitimacy, which is essential with a view to future pandemics and forthcoming international negotiations, the WHO must reintroduce a severity criterion in its definition of the pandemic and give any necessary explanation on the role of experts in its various committees and the absence of conflicts of interest between them. Although complex, the issue must be addressed. Secrecy over the composition of the International Health Regulations Emergency Committee is no longer acceptable.

The IOE deserves to be better known.

The International Office of Epizootics, also called the World organisation for animal health, is tasked with ensuring transparency on the animal health situation of the member countries and elaborating health standards applicable to trade in animals and their products.

This international structure, grouping 176 States, is presently monitoring a hundred or so diseases.

According to its studies, it is highly probable that the A(H1N1) virus was transmitted from man to the pig. That's why the IOE is battling against use of the term 'swine flu'. At a very early stage it considered that the analysis of its genes, on the basis of the size of neuraminidase, suggested that this virus was less dangerous than what human health specialists were stating, yet they were nevertheless heeded by governments.

B – AT EUROPEAN LEVEL, COMPETENCES ARE SHARED BETWEEN THE EUROPEAN UNION AND ITS MEMBER STATES

The ECDC was recently created without following any pre-established plans.

The European Centre for Disease Prevention and Control (ECDC) is a European institution that was rapidly set in place after the SARS scares. It cooperates closely with the national health surveillance agencies. Its budget, like its personnel, are in no way comparable to those of the American Centers for Disease Control (CDCs).

Its debates concern the difficulty of assessing the gravity of a pandemic. Present surveillance methods have indeed reached their limits: data is often non-existent and diagnosis methods vary from one country to another; the methods of counting deaths vary; acute respiratory diseases are monitored only in 11 of the European Union States.

The ECDC feels that only serological studies and the observation of cohorts would provide data exploitable at the European level and would allow relevant international comparisons to be made.

The EMEA plays an important yet not exclusive role in authorising new medicinal drugs and new vaccines.

The European Medicines Agency (EMEA) has set in place a centralised mandatory procedure to control many biotechnology-based products, which concerns 95% of the new molecules used in the European Union.

But its role is not exclusive. The Member States keep some competences. They can in particular authorise medicines used only at national level.

As regards model vaccines, authorisation can be granted before the clinical tests, as these vaccines have already been authorised with a different viral strain.

The Member States are keeping major prerogatives.

They are keeping control over their vaccination policy, choice of the vaccine among the many vaccines authorised at European level, the number of doses to be administered, organisation of the vaccination campaign (at GPs' or at special vaccination centres), definition of priority categories, and the number of persons to be vaccinated.

It is they which decide on the conditions under which antivirals will be used, negotiate vaccine orders with laboratories and decide whether vaccination will be free or not. Last, they keep control over their communication.

C – AT NATIONAL LEVEL, POLICIES REMAIN VERY DIFFERENT

In England, Tamiflu was widely distributed and the population could phone call centres empowered to write prescriptions. Vaccination was not carried out at special centres. The contracts signed with pharmaceutical laboratories remained confidential but could be cancelled or renegotiated, and this happened. They allowed for vaccines to be bought for 100% of the population from the moment the WHO would declare a level 6 pandemic.

In Germany, the Länder applied different policies, but the population was generally hesitant about getting vaccinated.

In Sweden, confidence in the public health system had considerable consequences on the vaccination rate. More than 60% of the population followed the health authorities' recommendations, in the framework of a highly decentralised system. The pandemic plan was debated in Parliament. Vaccination began earlier than elsewhere.

In Canada, the choices of the public authorities were very close to those made in France, but the results were very different, since a third of the population got vaccinated. The vaccination rate even exceeded 50% in Quebec. It is also the country where the virulence of the A(H1N1) virus was particularly severe. The pandemic was managed there in a participative manner.

In the United States, vaccines did not contain an additive because the population did not want one. The vaccination policy varied depending on States. From September 2009 on, it was accepted that a single dose of vaccine would be sufficient. Communication was very active, backed up by the new social networks which were regularly analysed.

In China, which has just set up health surveillance structures comparable to those that exist in many countries, 100 million people were vaccinated with a national vaccine, priority categories being defined. World-level research is being conducted on several viruses.

III. WHAT PUBLIC MANAGEMENT OF PANDEMICS?

A – PANDEMIC PLANS ARE USEFUL BUT MUST EVOLVE TO BE BETTER ADAPTED AND UNDERSTOOD

Such plans are useful instruments providing guidance in times of crisis. Indeed, during a crisis it is too late to devise coherent projects involving a multitude of players and providing for various levels of reaction in keeping with the gravity of the situation. They are useful in anticipating complex situations such as those which would result from a very high number of sufferers having to stay at home to avoid even greater contagion, or from severe cases that cannot be treated and which could lead to many deaths, as during the Spanish flu outbreak in 1919.

But they must evolve, because they have been seen as either too authoritarian or as catalogues of measures utilisable in circumstances that were not specified. As take-up by the population is necessary for all measures which are not mandatory, such as vaccination, it would be preferable to debate these plans, especially if exceptional measures or ones affecting public freedoms were envisaged.

B – NEW INSTRUMENTS MUST BE SET IN PLACE TO BETTER ASSESS THE BREVITY OF THE SITUATION

The present methods are insufficient.

– The number of persons infected by the A(H1N1 virus was five times higher the official measures, which were nevertheless improved by the coordination of the 'GROG' and 'Sentinelles' flu surveillance networks;

– The measure of mortality is not satisfactory: the method consists, as for seasonal flu, in taking account of excess mortality and is not adapted; the classification of deaths is not sufficiently strict.

New instruments are necessary.

In this context, it is necessary to think about defining categories of priority persons in the event of vaccination: persons more exposed to the risk are not only those belonging to health professions or a fragile category according to medical criteria, but also those permanently in contact with the public and who can either be more easily infected or become carriers of the virus.

The identification of at-risk categories would be facilitated by a common study with patients' associations, and by a new approach by the CNIL (French National Commission of Data Processing and Freedoms) concerning the cross-comparison of certain data files.

The crisis must be managed differently by: clarifying the relations between the ministry of health and the ministry of the interior; basing ourselves on professional organisations and patients' associations; communicating differently and in a more innovatory manner; drawing inspiration from the preventive principle rather than the precautionary principle; ensuring transparency of experts' reports; and seeing to the follow-up of the biological and health risk.

A debate must be held on crisis communication methods and the taking into account of social networks.

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From left to right: Mr Jean-Pierre Door, deputy, Mrs Roselyne Bachelot-Narquin, Minister for Health and Sports, and Mrs Marie-Christine Blandin, senator