Introduction

Five years after the Institute of Public Health Surveillance (InVS) was created, the year 2003 confronted it with important health alerts that were entirely new in their nature, origin, and spread. These events caused InVS to examine the procedures for transmission and analysis of health information and its use for decision-making in France.

The health alerts in 2003 were diverse. Infectious disease epidemics occupied the forefront of the stage at the beginning of the year. A serious respiratory syndrome, unknown until then and called severe acute respiratory syndrome (SARS), emerged on the international scene. There was also a legionellosis epidemic in northern France. Although the latter might seem to be a routine problem, it turned out to be especially serious and involved new modes of diffusion.

Environmental phenomena took over the leading role during the first weeks of August: a brutal heat wave caused dramatic health consequences in France.

The health alerts of 2003 also had varied origins and modes of diffusion. The SARS epidemic involved many countries across the world: it came from a source in Asia, but the fight to understand and control it mobilized North America and Europe as well, and France participated substantially in this movement even though the epidemic did not spread here.

Europe also experienced a major heat wave that shook French health institutions hardest. Their responses included estimating its impact and identifying and applying the organizational lessons learnt.

The importance of these events to InVS led us to focus our 2003 annual report on describing and analyzing them.

SARS, international alert

SARS emerged in China in 2003. This epidemic rapidly became international: more than 8000 persons fell ill and 774 died, in some 30 countries. The response to this emergence was particularly remarkable and pooled scientific capabilities through international networks coordinated by the World Health Organization (WHO). It contributed to the progress and rapid dissemination of knowledge and thus facilitated the implementation of appropriate prevention and control measures and led to the control of this pandemic within four months (from the official international alert issued by WHO on 12 March to its official end on 5 July).

In France, the response, based largely on existing plans for response to bioterrorism threats (Biotox plan) and to the risk of an influenza pandemic, enabled us to cope with the introduction of the first SARS cases and to limit secondary transmission: overall, seven probable cases were identified in France and the consequences of the epidemic remained limited.
## How it began

During the last week of February 2003, WHO received reports of two outbreaks of a respiratory syndrome, one in Hanoi (Vietnam) and the other in Hong Kong SAR (China). These outbreaks were linked to the epidemic of atypical pneumonia of unknown etiology that had been ravaging the province of Guangdong, China, since November 2002. The initial hypothesis of avian influenza was rapidly supplanted by that of an unknown infectious agent that caused a new nosological entity named severe acute respiratory syndrome (SARS).

The origin of the outbreaks in Hanoi and Hong Kong was the same: contamination, around 20 February 2003, of a group of guests at a Hong Kong hotel by a Chinese physician from Guangdong. Other contaminated hotel guests were at the origin of outbreaks in Singapore and Toronto (Canada) and accounted for isolated cases in Germany, the United States, and Ireland.

In Hanoi, the epidemic developed in early March among staff and patients at the French Hospital where the index case, from the Hong Kong hotel, had been admitted. A physician from this hospital returned to France on 22 March to become the first patient reported here. Other cases were exported from different cities in Asia to many other countries.

Beginning on 28 February, WHO mobilized GOARN, its global outbreak alert and response network. Events sped up within days, in Southeast Asia and elsewhere. On 12 March 2003, WHO issued an international alert for these epidemics, marked by a high proportion of cases among hospital personnel, a severe clinical picture, a rising mortality rate, and an increasing number of countries affected.

This was the beginning of an unprecedented international collaboration in which the swift exchange of information between countries enabled WHO to coordinate the response. At a scientific level, this cooperation led to the identification of the coronavirus responsible for SARS (SARS-CoV) and the development of a diagnostic test in the weeks following the international alert.

France immediately set up an interministerial management procedure, aimed at reducing the risk of secondary transmission of SARS nationwide. It relied on the combined mobilization of InVS, the Directorate-General of Health (DGS), biologists, especially from the Pasteur Institute, reference hospitals and clinicians in each region, emergency services (SAMU), and others.

## InVS participation at the international level

InVS conducts health surveillance of events abroad and participates in the WHO network for epidemic alert and response. From mid-February, several signals attested to the development of an epidemic of atypical respiratory disease in China, Hong Kong, and then Vietnam. A week before the WHO alert of 12 March, InVS informed the Ministry of Health of the situation and mobilized for international cooperation. It sent an epidemiologist to Hanoi with a WHO multidisciplinary team that went to help control the epidemic reported at the French Hospital. A month later, another InVS epidemiologist left for Beijing to conduct the same work, this time to support the Chinese authorities. These field missions, under the aegis of WHO, together with those of other teams in Singapore, Hong Kong, and Toronto, documented the epidemiologic characteristics of this new disease and set up early and appropriate preventive measures, including in France.
Participation in the WHO mission to Hanoi

Arriving in Hanoi on 14 March 2003, the WHO mission very rapidly set up emergency measures aimed at keeping all the patients from the second wave (which started 12 March among family and friends of the medical personnel affected) together in a single isolation center (Bach May Hospital), to organize the management of patients and suspected cases, to reinforce hospital hygiene measures, and to monitor follow-up of case contacts in the community. The first clinical and epidemiologic observations allowed rapid formulation of hypotheses about the disease’s incubation period and modes of transmission (Figures 1 and 2). These clinical and epidemiologic elements became the basis of the case definition developed in France to control the epidemic and, from 16 March onward, of the protective measures recommended for monitoring exposed persons in France:

- only taking samples, especially nasopharyngeal, in a strictly protected environment, because of the risk of infection;
- isolation of all symptomatic patients;
- wearing a mask (type N95) as the minimum level of protection during contacts (except for medical procedures) with symptomatic patients (mask to be worn by the contact and the patient).

Epidemiologic bases of SARS transmission

- On the basis of information from the first outbreaks, the incubation period of SARS was estimated at 2 to 10 days. This estimate has since been confirmed. This characteristic is important for several reasons:
  - It is essential for the definition of cases: the diagnosis of suggestive signs must be based on the identification of exposure to the pathogenic agent in a time frame compatible with the incubation period;
  - It also makes it possible to define the quarantine period necessary for contacts of probable cases before risk of disease can be ruled out.
- It rapidly became clear that contagiousness began at the same time as the clinical symptoms (for each new case, exposure to a patient with SARS in the 10 days before signs began was almost always found). It was thus hypothesized that the disease was not contagious during the incubation period (a hypothesis not challenged since); in other terms, only symptomatic patients are likely to transmit the infection.
- A direct mode of transmission, from person to person by close contact, was rapidly suspected because of the high number of cases among personnel caring for patients in the first outbreaks. Study of the contamination of 125 inhabitants of the Amoy Garden building in Hong Kong then suggested an environmental type of transmission (from aerosols containing the virus). This information was of major importance because the mode of transmission determines the measures necessary to prevent contacts likely in their turn to transmit the infection (for example, protective measures for healthcare staff).

Figure 1: SARS cases (N=63) by date of onset of symptoms and estimated incubation period, Hanoi, February-March 2003
In its 13 June update, WHO reevaluated the level of SARS, and overall, this new cluster includes 105 cases. Retrospective investigation of this orthopedics department determined that 8 cases of respiratory diseases were probably SARS cases. Two of these 5 patients were hospitalized in the orthopedics department of North York General Hospital in Toronto.

The second cluster was identified on 20 May, after diagnosis of 5 patients from a rehabilitation hospital in Toronto with febrile syndromes. Two of these 5 patients were hospitalized in the orthopedics department of North York General Hospital in Toronto.

Figure 2. Probable SARS cases (N=57) by date of onset of symptoms and exposure at the French Hospital, Hanoi, February-March 2003

- Participation in the WHO mission to China

The mission to China, from 23 April to 17 May, took place under difficult conditions, in view of the political and media context of the crisis, the complexity of the Chinese healthcare system, and the differences in language (databases in Chinese). Nonetheless, collaboration began, as did the epidemiologic analysis of the data available for Beijing. The trip also permitted the exchange of information about SARS and the situation in Beijing with the embassy staff, including scientific and medical personnel, and helped to assess needs for bilateral aid, both for the emergency and over a longer term. Finally, it underlined the determinant and very positive role played by WHO in this crisis that shook China in 2003.

- International surveillance

At the same time, InVS collected, analyzed, synthesized, and disseminated on a daily basis the information available about the characteristics and progress of the epidemic and about this new disease. This monitoring was conducted from sources of information mostly accessible by internet, in particular, the websites of WHO and of the ministries of health of the affected countries.
Each day, InVS collected, sorted, validated, analyzed, and distributed information to multiple national stakeholders affected by the epidemic. Nearly 50 daily updates were distributed between 10 March and the end of June.

International health surveillance contributed to the early alert of the French system and to the dissemination of scientific knowledge that allowed control measures to be adapted appropriately throughout the epidemic.

– International SARS epidemic: final findings
By 31 December, 2003, WHO had received reports of 8096 probable SARS cases from 29 countries; 774 (9.6%) of these patients had died and 7322 (90.4%) were considered cured. Lethality increased with age and reached 50% among those older than 65 years. SARS took a heavy toll on healthcare staff, who accounted for 21% of the probable cases.

Three epidemiologic situations can be distinguished in the affected regions (Figure 3).

• Mainland China
The epidemic probably originated in China. In the province of Guangdong, primary transmission from a still unidentified reservoir is thought to have led to the introduction of the virus into the human population. By 31 December 2003, China had reported 5327 probable cases to WHO—65.8% of the cases worldwide. It is feared, however, that the extent of the epidemic in China has been underestimated. These concerns arise from the Chinese authorities’ absence of transparency until quite recently, as well as from the weight and complexity of the surveillance system they established.

• Outbreaks in Hanoi, Hong Kong, Singapore, Taiwan, and Toronto
In these areas, imported index cases (one or more) spread the disease in the hospitals to which they were admitted, thereby causing secondary epidemics. Those initially affected were mainly healthcare personnel and their families and friends. In Hanoi, the epidemic included 63 cases and lasted approximately one month before finally being controlled. Other outbreaks subsided, except in Taiwan, where the epidemic developed last. The number of probable cases reported to WHO as of 31 December 2003 was 1755 in Hong Kong, 238 in Singapore, 346 in Taiwan, and 251 in Canada (including 247 in Toronto).

• Other countries reporting imported cases, with no secondary transmission
Imported cases were identified in 24 countries, including France. Reports from South Africa and Australia show that no continent was spared. These countries reported from one to several dozen cases.

Figure 3. Probable SARS cases reported to WHO by 31 December 2003
International response

On 12 March 2003, WHO issued an international epidemic alert for the first time in its history. This alert was accompanied by recommendations for the movement of people and goods. Because of the risk of contamination on international airplane flights, WHO recommended that the countries affected conduct rigorous health checks of people leaving their territory, and most countries set up procedures for medical checks of passengers arriving from the affected areas. The airlines were responsible for ensuring that travelers arriving from these areas could be traced.

WHO organized under its aegis a network of 13 international laboratories engaged in research on the etiology of the new disease and in the development of diagnostic tests; it also coordinated epidemiologic studies. Reinforcement of hospital hygiene and sometimes drastic quarantine measures made it possible to control the principal SARS outbreaks throughout the world and to stop the progression of the pandemic. Nonetheless, many unknowns remain about the virus’s modes of transmission and its reservoirs.

Perspectives and recommendations

SARS, the first pandemic of the 21st century, emerged in one of the most populous regions of the planet. The disease spread within a few weeks—with unprecedented rapidity—because of the population density and because of air travel. The principal outbreaks (Hong Kong, Singapore, Taiwan) occurred in the major economic centers and communication nodes of Asia. The SARS epidemic illustrates a new type of health risk in a globalized world and underlines the importance of international collaboration. In this new world context, France must reinforce its participation in the alert network coordinated by WHO. The ongoing revision of international health regulations, to which InVS contributes, should eventually provide a legal framework for the exchange of health information between countries. In the face of these new stakes, Europe is building an operational European system of disease control (European Centers for Disease Control and Prevention), in which France participates.

Case management in France

Organization of SARS surveillance and management in France

Using its emergency plans for an influenza pandemic or a bioterrorism attack (Biotox) as a basis, France quickly established an operational response.

To meet its objective of reducing the risk of secondary transmission in France from one or more possible cases, this response applied the following priority measures:

- early detection of cases, through the provision of information to all healthcare professionals and to the public, as well as specific information for passengers arriving from affected areas;
- medical management of possible cases, including strict isolation and transfer to the infectious disease department of the relevant Biotox reference hospital (11 hospitals across the country) and protective measures for healthcare personnel;
- identification and surveillance of the contacts of the patients determined to be probable cases, including the quarantine of these contacts for 10 days, at their homes. All healthcare professionals nationwide received the official definitions of possible and probable SARS cases.

Operationally, the healthcare response was organized around the following plan:

- national and international health surveillance by InVS;
- early detection of possible cases by the emergency medical service (SAMU) centers for transfer in secure ambulances;
- preferential hospitalization of possible cases in Biotox plan reference hospitals or in the infectious disease departments of university hospital centers (UHCs);
- investigation and epidemiologic follow-up of contacts of probable cases by InVS, district health and welfare bureaus (DDASS), and the regional epidemiology units (CIRE);
- medical follow-up of contacts initially conducted by general practitioners belonging to the regional networks for influenza observation (GROG).
Epidemiologic surveillance according to a simplified plan centralized at InVS (Figure 4).

The urgency of the situation of this severe disease, the modes of transmission of which remain hypothetical, made it essential for a rapid and direct system of information communication and management to be centralized at InVS. Physicians in the public and private sectors were required to report any suspected case promptly by telephone to InVS. The telephone number for the hotline, available 24 hours daily at InVS (01 41 79 67 15), was distributed to all concerned. An InVS epidemiologist and the patient’s physician assessed each possible case reported to classify it according to the criteria chosen: probable, excluded, or under investigation. All probable cases and any cases that raised a particular problem or otherwise required discussion were reported to the DGS. Once a probable case was identified, this person’s contacts were quarantined (isolated in their homes), for 10 days following the last at-risk contact; InVS managed their daily epidemiologic follow-up, in liaison with the DDASS and the applicable regional epidemiology unit.

**Definition of SARS cases** (DGS protocol dated 22 May 2003)

- **Possible case:** any person with all of the following signs: fever > 38°C and one or several lower respiratory signs (coughing, dyspnea, respiratory discomfort, abnormal sounds on auscultation, radiologic abnormalities if the chest x-ray has already been taken, or oxygen desaturation if oximetric measurements were taken) and exposure within the 10 days preceding the onset of signs by either hospitalization in an area considered by WHO to have active local SARS transmission or by close contact with a probable case.

- **Probable case:** all possible cases with signs of respiratory disease on radiography or pulmonary scanner, in the absence of another diagnosis.

- **Excluded case:** all possible cases for which another diagnosis explains the symptoms or for which the following four criteria are met: good clinical condition, negative findings on chest radiography or pulmonary scanner, no reduction in lymphocytes (white cell subpopulation), no contact with a probable case.

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**Figure 4. Simplified diagram of the SARS surveillance system in France, 2003**
Summary of the SARS epidemic in France in 2003

From the initial alert through 5 July 2003, the surveillance system centralized at InVS identified 437 possible cases, all of which were investigated; there were finally seven probable cases (1.6%), four of which were confirmed (1%). One patient died (lethality = 14%).

The seven cases classified as probable and reported to WHO and the European Union were all imported from Asia, in two distinct groups (Table 1):

- in the first group (group A), four persons were exposed to one index case—a French physician at the French Hospital in Hanoi, returning to France; three were exposed during the doctor’s journey on AF flight 171 from Hanoi to Bangkok and Paris during the night of 22-23 March 2003;
- in the second group (group B), two people were exposed in Nanjing (China) in April during a business trip. Of these seven probable cases, four were confirmed by the diagnostic tests available during the epidemic (serology and/or PCR).

Table 1: SARS epidemic in France - number of probable cases and classification, March-July 2003

<table>
<thead>
<tr>
<th>Group</th>
<th>N° Cases</th>
<th>Onset of signs</th>
<th>Exposure</th>
<th>Outcome</th>
<th>Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>1 index case, group A</td>
<td>20/03/03</td>
<td>Hanoi</td>
<td>Death</td>
<td>Confirmed</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>26/03/03</td>
<td>Hanoi-Paris airplane flight</td>
<td>Favorable</td>
<td>Confirmed</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>27/03/03</td>
<td>Hanoi-Paris airplane flight</td>
<td>Favorable</td>
<td>Confirmed</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>29/03/03</td>
<td>Hanoi-Paris airplane flight</td>
<td>Favorable</td>
<td>Probable, not confirmed</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>01/04/03</td>
<td>Hanoi</td>
<td>Favorable</td>
<td>Confirmed</td>
</tr>
<tr>
<td>B</td>
<td>6</td>
<td>30/04/03</td>
<td>Nanjing (China)</td>
<td>Favorable</td>
<td>Probable, not confirmed</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>03/05/03</td>
<td>Nanjing (China)</td>
<td>Favorable</td>
<td>Probable, not confirmed</td>
</tr>
</tbody>
</table>

InVS and then the appropriate regional epidemiology unit followed four cohorts of contacts of these probable cases, 77 persons in all, daily for ten days:

- one cohort of 24 subjects, all hospital staff returning to France from work at the French Hospital in Hanoi (March 2003);
- the 7 passengers who traveled on AF flight 171 on 22-23 March, in the two rows in front of and behind the seat of the group A index case;
- 32 contacts of the 2 probable cases from Nanjing in April-May 2003;
- and the 14 contacts of a final probable case, later excluded.

No cases of secondary transmission were identified in France, among either the close contacts of probable cases or their healthcare providers.

Of the 430 cases excluded, 175 (40%) were ruled out within 24 hours, as soon as the epidemiologists confirmed that they had not been exposed. These rapid exclusions were most numerous during the first week following the alert; as general practitioners and SAMU supervisors gained experience, they were able to evaluate exposure better before classifying and reporting possible cases. Because of a strong suspicion of exposure, 86 possible cases (20%) remained under observation for 24 to 72 hours before the SARS diagnosis could be excluded. Finally, 24 possible cases (5%), for whom exposure to a probable SARS case was strongly suspected or definite, remained in isolation for more than 72 hours before a differential diagnosis was established. Data were missing for 145 possible cases.
– Results of specific investigations
Aside from surveillance, specific studies were also conducted. These included a survey to investigate the circumstances of the introduction of SARS into France and another to assess the possibility of asymptomatic transmission of the SARS coronavirus to persons who had contact with confirmed cases.

• Survey to investigate the introduction of SARS in France in March 2003
This survey demonstrated the transmission of the SARS-CoV during a long-haul airplane flight based on data collected from five probable cases and passengers exposed to the group A index case in the cohort of AF flight 171 from Hanoi to Paris on 22-23 March 2003. Exposure to the index case for two of the three confirmed cases occurred while he was symptomatic, during this flight (Table 1):
– one was part of the group of seven passengers sitting near the index case (two rows in front of and behind him);
– the other was seated several rows back and had no documented close contact with the index case.

• Seroepidemiologic study among subjects exposed to a probable SARS case
This study of the subjects exposed to the first probable SARS case in France (group A index case) was intended to assess the possibility of asymptomatic transmission of the SARS coronavirus to contacts of a confirmed case.

The results of this survey, conducted and coordinated by InVS and the influenza CNR-Nord at the Pasteur Institute, are not yet available. Because this study required a rapid ethical opinion from the French Ethics Committee (CCPRPB), a special emergency meeting took place to reduce the application deadlines. This procedure will henceforward be applied for other studies conducted on an emergency basis by InVS as part of its epidemiologic surveillance activities.

– Workload
SARS surveillance mobilized 19 persons within InVS, including 15 epidemiologists in the department of infectious diseases (DMI) and two in the international and tropical department. In the first weeks, the team met daily, and then twice a week to discuss the cases, their classification, and problems related to their management. Night and weekend on-call duty was also reinforced. Two regional epidemiology units were mobilized to follow up the contacts of probable cases. One coordinating team (three persons) managed liaison with the DGS, the Pasteur Institute (the influenza reference center in the Nord), general practitioners, district health and welfare bureaus, the regional epidemiology units, occupational physicians for airlines, and other companies with commercial ties to the affected areas. InVS participated actively in three sessions of the High Council of Public Health of France (CSPHF). International telephone conferences took place with WHO, the European Commission, and the other
member states.

Qualitative aspects of the epidemiologic management of SARS in France
The team of epidemiologists responsible for SARS management in France also made qualitative assessments that went beyond the framework of this surveillance. Because the follow-up of possible cases until classification can be relatively long, the epidemiologists needed to consider the operational constraints of the clinicians in hospitals, as well as the constraints of access to laboratory diagnoses (confirmation of SARS diagnosis or differential diagnosis of another respiratory disease). Moreover patients or their families sometimes objected to the consequences of classification, and the experience of isolation or quarantine was particularly difficult for some. The epidemiologists were confronted with these problems on several occasions, as well as with incidents involving the lifting of the patient’s anonymity or failure to respect the confidentiality of medical information.

Lessons from the 2003 SARS epidemic

The system set up in France identified seven probable SARS cases, 1.6% of the possible cases reported. While a cost-benefit ratio for the measures implemented could be calculated from this result, the essential point is that no cases of secondary transmission occurred.

Overall, the effectiveness of the response to SARS demonstrated the advantages of multidisciplinary advance planning and preparation. The updated version of the "SARS response plan" drafted in December 2003 by the DGS and available on its website has been distributed to our European partners. This plan, conceived as a prototype, can be adapted to other infectious epidemic phenomena.

Similarly, the SARS experience has helped to identify some useful improvements for this management system. The application of these improvements goes beyond the framework of SARS and should improve our response to all other emerging infections.

Anticipation of the risk is essential, through epidemiologic surveillance that includes monitoring of infections outside France or Europe.

This surveillance must be complemented by a reactive alert system that can detect emerging infections in France. Such a system should involve participation of physicians from hospital infectious disease departments and the epidemiologic expertise of InVS. It is currently being developed.

- It is also essential to strengthen the capacities for and quality of patient management in these departments, by decentralizing the management of these patients to university hospitals not included in the Biotox plan. In the event of a larger-scale epidemic, hospital capacity would require enlargement, in terms of both the number of patients expected and the management of isolation as well as, more generally, nosocomial transmission risks.

- SARS has clearly shown that a rapid etiological diagnosis of respiratory diseases is needed. One of the major research issues is thus the development of techniques permitting the diagnosis of SARS-CoV and some differential diagnoses, with sufficient specificity. At the end of 2003, after the epidemic, the reference laboratories authorized to conduct research on the SARS coronavirus were decentralized. This decentralization must nonetheless be accompanied by strict precautionary measures to avoid any risk of infection in the laboratory.

- Different research topics must be developed, for SARS and for other emerging infections. Epidemiologic research will help elucidate the reservoirs and modes of transmission of these emerging infections, and modeling studies
can specify how these infections are imported and disseminated.

- Finally, SARS illustrated the need to take into account and anticipate the social characteristics of such an epidemic (for example, representations, emergency communication, rumors, and the consequences of panic). The implementation of drastic isolation measures raised numerous ethical questions, especially about the possible effect of these measures on private and work life and about respect for confidentiality.

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Alerte et conduite à tenir en cas de résurgence du Sars (http://www.invs.sante.fr)

Health consequences of the heat wave, national alert

The heat wave that scorched France in the first weeks of August 2003 was exceptional in its duration, in the increases in maximum as well as minimum temperatures, and in the ozone pollution levels that accompanied these temperature peaks. Even though the summer of 2003 had already been the hottest in France for 53 years, the August heat wave occurred so abruptly that it has been described as a "heatquake".

It induced a wave of excess short-term mortality estimated at approximately 15 000 deaths, especially among those older than 75 years. This dramatic toll, which places this heat wave among the gravest health catastrophes France has ever known, cast doubt on the capacity of our public healthcare system to anticipate this type of crisis. The work begun during the heat wave, at the request of the Ministry of Health, led to the development of a national heat wave plan.

InVS also conducted several case-control studies to identify the risk factors for mortality among the elderly; these factors can be used to define profiles of the most vulnerable and thus facilitate their identification and prevent health consequences to them in another heat wave. Moreover, InVS and the French weather bureau (Météo France) together developed a biometeorological alert system that was operational for the summer of 2004.