Surveillance of infectious diseases: a major preoccupation

InVS plays a pivotal role in the surveillance of infectious diseases (e.g., HIV and HCV infections, STDs, nosocomial infections, and invasive meningococcal diseases). In addition to its missions of surveillance and alert, it contributes to the expertise necessary in this field within the Ministry of Health, the High Council of Public Health (specifically, its advisory committees on vaccinations and on nosocomial infections), and the other health and safety agencies (the French Food Safety Agency and the French Health Products Safety Agency). InVS also leads and provides coordination for the national reference centres (CNRs) and is the French partner for European surveillance within the European surveillance network coordinated by the ECDC.

Ten years of HIV/AIDS and STD surveillance

In 2007, InVS published an important retrospective report about a decade of surveillance of HIV/AIDS and other sexually transmitted diseases (STD). Covering the period 1996-2005, it retraces the course of the disease in its different aspects.

The incidence of HIV infection accelerated from the early 1980s through 1995, when it reached nearly 6000 new AIDS cases. That year, however, saw the introduction of the first antiretroviral (ARV) combination treatments that made it possible to delay the onset of AIDS in people with HIV infection. These combinations, to which antiproteases, yet another ARV class, were added shortly thereafter, led to a very significant reduction in the number of new cases (4000 in 1996 and 1200 in 2005).

The number of people with HIV infection in 2005 was assessed at 135 000 (with a plausibility interval ranging between 100 000 and 170 000), and approximately 27 000 had developed AIDS. In 2005, more than 6000 persons discovered they were HIV-positive; this number has been stable since 2003.

Despite the decline of the disease, there remain difficulties in access to screening. In 2005, more than one-tenth of newly discovered cases of HIV infection were not diagnosed until the patient had AIDS (and could therefore not benefit from the advances in ARV treatment).

Sexual transmission remained predominant, but some interesting trends developed during the decade between 1996 and 2005:

• an increase in at-risk sexual practices among men having sex with men: The "Presse gay" surveys by InVS in 1997, 2000, and 2004 demonstrate this trend, even though this population is theoretically better informed of the risks and modes of protection. Between 1997 and 2004, the proportion of unprotected anal penetration went from 26% to 49% among seropositive homosexuals and from 15% to 27% in seronegative homosexuals. Since 2000, this risk-taking has been associated with the emergence of some STDs (e.g., syphilis and venereal lymphogranulomatosis of the rectum) and since 2003 by an increase in the number of new cases of HIV infection in this population. Nearly half of newly seropositive men having sex with men were infected in the 6 months preceding the discovery;

• a reduction in the number of injecting drug users (IDUs) infected by HIV: This decline took place nearly continuously over the 1996-2005 period and is explained especially by their adhesion to policies of risk reduction. IDUs now account for a very low proportion of newly discovered HIV infections. On the other hand, the prevalence of HCV remains high among drug users as a whole;

• an increase in the number of people from sub-Saharan Africa infected by HIV: Between 1996 and 2005, the proportion of foreigners among the cases of AIDS reported in France grew markedly, a change explained in part by the decline in the number of French patients. In absolute values, nonetheless, the number of AIDS cases in people from sub-Saharan Africa increased strongly from 1998 through 2002, and their screening was often late. A trend visible since 2003 shows a diminution of the number of AIDS cases and newly discovered seropositivity, due to recent improvement in screening. But the risk of treatment failure remains higher in this population, which is strongly affected by the precarity that complicates treatment follow-up;

• slow feminization of the epidemic: The proportion of women among the new AIDS cases has increased regularly. From 1986 through 2005, it rose from 21% to 33%. This trend is associated in part with the distribution of the virus in the heterosexual population, especially among women of foreign nationality and still more especially those originally from sub-Saharan Africa.

The trends observed in France over this period are found in other western European countries.

These 10 years have also been marked by increased epidemiologic surveillance and by reinforced prevention, both of which explain these results in part.
Nosocomial infections

In 2007 InVS presented the results of the national survey of nosocomial infection prevalence conducted in 2006 with the nosocomial infection control coordination centres (CCLIN). This survey was established as part of the 2005-2008 national programme against nosocomial infections. Its objective was to describe these infections in healthcare facilities on a given day. The study covered 2337 establishments (83.3% of the total in France and 93.6% of all hospital beds) and 358 353 patients. It is thus the largest survey of this type so far conducted.

The day of the survey, 17 817 patients had one or more active nosocomial infections, for a prevalence of infected patients (PIP) of 4.97%, and 19 294 nosocomial infections were enumerated, for a nosocomial infection prevalence of 5.38%. The PIP nonetheless varied according to the size of the facility, its type (from 1.84% in psychiatric hospitals to 9.34% in cancer centres), and according to department (from 0.89% in obstetrics to 22.4% in intensive care). PIP also differed according to sex, age, and immune status. It was higher in patients who had a fatal disease that caused them to die within 5 years, in those...
with a surgical intervention within the past 30 days that caused them to die within one year, and in those with a vascular or urinary catheter or intubation/tracheotomy tube.

The variations observed in regional prevalences (figure) are due mainly to the variation in the types of facilities, departments, and patients included in each region.

Three sites account for nearly 60% of all documented infectious sites: urinary tract infections (30.3%), lung diseases (14.7%), and surgical site infections (14.2%).

At least one microorganism was identified in 13,504 of the nosocomial infections (70%), and 3 microorganisms accounted for more than half (53.5%) of the 15,800 organisms isolated: *Escherichia coli* (24.7%), *Staphylococcus aureus* (18.9%, 52% of which were resistant to methicillin (MRSA), and *Pseudomonas aeruginosa* (10.0%).

Compared with the 2001 national prevalence survey, the prevalence of infected patients fell slightly, from 4.61% in 2001 to 4.25% in 2006. This decline was seen in all categories of facilities, except army hospitals and hospitals with fewer than 300 beds. It increased in intensive care departments, remained stable in medical and surgical departments, and fell in all others. The reduction in MRSA infections was greater, with the PIP falling from 0.49% in 2001 to 0.29% in 2006. The prevalences observed in this French study are within the lower limits of prevalence measured during similar European surveys since 2000.

These decreasing trends are encouraging, but we must nonetheless recall that in 2006 nosocomial infections still involved one in 20 hospitalized patients. This justifies the pursuit of efforts to reduce them.

### An epidemic of *Clostridium difficile* infection

*Clostridium difficile* infections (CDI) are responsible for post-antibiotic diarrhoea and pseudomembranous colitis. In 2006, an epidemic of CDI, associated with a particular strain known as 027, plagued several healthcare facilities in Nord-Pas-de-Calais. From January 2006 through March 2007, 41 facilities reported 515 cases of CDI; 31 facilities had case clusters. Of 410 strains transmitted to the CNR, 65% were type 027. This regional epidemic led InVS and the CCLIN to reinforce CDI surveillance in France in 2006 and to set up, with the CNR for anaerobic bacteria and botulism, a *C. difficile* laboratory working in a network with 5 other regional laboratories.

The alert in Nord-Pas-de-Calais ended officially in March 2007. Nonetheless, the surveillance, control, and prevention of CDIs continue to mobilize healthcare facilities in this region and elsewhere in France. The total number of CDI reports nationwide increased in 2007 (258 compared with 193 in 2006), even though the total number of cases reported remained stable (640 compared with 645). The number of reports from the combined Paris-North region diminished slightly in 2007 (126 vs. 137 in 2006), but it increased elsewhere in France (132 vs. 56). The 027 strain continued to circulate in the Nord-Pas-de-Calais region but at a lower level. It remained responsible for sporadic CDI cases, but these were rapidly detected and controlled; they did not cause epidemics such as those observed in 2006. Its distribution outside this region remained limited in 2007: it was found, on a one-off basis, in several establishments in Picardy, Rhône-Alpes, and Lorraine.

This trend demonstrates the increasing compliance of healthcare facilities with the guidelines for CDI reporting and control issued in 2006 by the nosocomial infection and treatment-related infection advisory committee. Particular vigilance must nonetheless be maintained. A study will therefore begin in 2008, under the aegis of InVS, the CNR, and RAISIN (network for alert, investigation, and surveillance of nosocomial infections) to measure the incidence of CDI in France and to ascertain the geographic distribution of the different strains of *C. difficile* responsible for infections.
An epidemic of glycopeptide-resistant enterococci in Lorraine

In January 2007, a hospital in Lorraine reported an epidemic of infections and colonizations by glycopeptide-resistant enterococci (GRE). In April, an increase in the reports of GRE infection and colonization from other health facilities in Lorraine suggested a regional extension of the epidemic. The CIRE and local nosocomial infection control committee began a prevalence study in June 2007.

A rectal swab was requested of all patients present on the day of the study in the departments at risk (hemodialysis, cancer and blood diseases, surgery, intensive care, and geriatrics) of 26 facilities that had accepted infected or colonized patients from the first facility as transfers.

Of the 2718 patients included, 48 (1.8%) carried GRE, including 31 (65%) unknown before this survey. The prevalence ranged from 0 to 11.5% according to facility. The survey allowed 10 facilities to identify one or more (up to 13) new GRE carriers, all with the same epidemic clone.

This survey provided guidance for the control measures recommended by the CCLIN and implemented by the healthcare facilities concerned. The regional prevalence of GRE, higher than the results of a national survey in 2006 (0.3%), confirms the diffusion of GRE in Lorraine and underlines the interest of a regional policy for the control of these emerging multidrug-resistant bacteria.

Meningococcal infections and vaccination in Seine-Maritime

Since 2003, the Seine-Maritime district has been home to a large number of patients with invasive meningococcal disease (IMD). The incidence ranges from 2.5 to 4 cases per 100,000 inhabitants, that is, 2-3 times greater than the national incidence. Geographic analysis of the cases shows a hyperendemic area (with an incidence since 2003 varying from 12 to 17 cases per 100,000 inhabitants). The area includes 75 municipalities around the city of Dieppe, with a total population of 84,000 inhabitants.

In view of the persistence of this hyperendemic and on the advice of public health bodies, the health authorities decided in mid-2006 to implement a vaccination campaign for the children aged 1 to 19 years living in Seine-Maritime. The vaccine used is MenBvac®, developed by the Norwegian Public Health Institute, which has demonstrated its efficacy in vitro against the Normandy strain B:14:P1.7.16. But this vaccine nonetheless presents several constraints:

- it has not been approved for marketing and is therefore used according to a particular authorization procedure with vaccination campaigns organized under the supervision of the State;
- the regimen recommended by the manufacturer consists in 4 injections (3 injections 6 weeks apart and a booster 12 months later);
- the manufacturer’s production capacity is limited, and the campaign is thus taking place in several phases; the vaccinations are performed as the vaccine doses are delivered.

This has required the definition of priority populations, specifically those of the 6 cantons of Dieppe and its immediate environs, where more than 50% of the confirmed B:14:P1.7.16 cases were identified. The epidemiologic investigations by the Upper Normandy CIRE and InVS led to the selection as the highest priority group among the 21,500 young people in the area the population of preschool children (1-5 years).

The announcement in July 2007 of the arrival of a new batch of vaccines nonetheless led the CIRE and InVS to develop a new priority definition, now focused on the 10-14 and 15-19 year-old age groups. The recommendation therefore is to complete the vaccination of the children 1-5 years old in the 3 cantons remaining (this age group was vaccinated in the first 3 cantons in summer 2006 with the first doses), then to vaccinate, in order, the high school students (15-19), middle school students (11-14), and finally, the primary school children (6-10). The vaccination campaign started again in December 2007.

The epidemiologic follow-up established by the CIRE and InVS for the Dieppe area should make it possible to assess the efficacy of the MenBvac® vaccination campaign. Analysis of Seine-Maritime as a whole will allow us to measure the impact of these vaccinations on the circulation of this strain and, where appropriate, identify other priority sectors where vaccinations should be continued.
Course of the incidence of invasive meningococcal disease in Seine-Maritime, 2003-2007

A vaccination campaign in Barcelonnette

In a 10-day period in January 2007, 4 cases of massive IMD (3 serogroup C) were reported among children and adolescents of the Barcelonnette valley (Alpes-de-Haute-Provence). The incidence of 107 cases per 100,000 inhabitants exceeded the epidemic threshold, and a vaccination campaign began in Barcelonnette and 7 neighbouring villages, targeting those younger than 21 years. But in February, 3 new cases occurred, 2 in patients aged 23 and 26 years. This led to a second campaign expanded to include 21-29 year-olds and to 5 new villages.

The South CIRE then assessed vaccination coverage at the end of these 2 campaigns. The target population of 3165 people was determined from the files of the health insurance funds for the residents of the municipalities concerned and from school and daycare centre lists for nonresidents. The number of people vaccinated was obtained through vaccination registries. The overall vaccination coverage reached 67%: 75.5% for the first campaign (younger than 21 years) and 48.8% for the second (expanded to 21-29 year-olds). Coverage varied greatly according to age group: 81% of those aged 1-5 years, 77% of those 6-16 years, and only 47% of those 21-29 years. Moreover, the epidemic took place during the high season for skiing. Only 63 nonresident seasonal workers aged 21-29 years were vaccinated, and it was not possible to determine the rate of vaccination coverage rate for this population.

Thus, the results of the first campaign were appreciably better, because of the invitation by individualized mail and the organization of sessions at school. The second was performed under very short deadlines and with a target difficult to reach — seasonal workers in tourism-related jobs.

Vaccination coverage of children and adolescents

In 2007, InVS, in collaboration with the Ministries of Health and Education, published the results of several surveys of vaccination coverage of children and adolescents in France. They are part of a triennial cycle of surveys in schools, first established in 2000 and intended to monitor the health status of children through a variety of indicators, including vaccination coverage rates. The published article reports the results of surveys conducted in 2001-2002 in the 5th grade classes (10-11 year-olds), in 2002-2003 in kindergartens (5-6 year-olds), and in 2003-2004 among 9th graders (14-15 year-olds). The samples were set up by 2-stage sampling: first public and private schools were chosen, and then students randomly selected.

The results showed that vaccination coverage is generally high up to adolescence, especially for the diphtheria, tetanus, and polio vaccine (DTPolio) (80% to 96%). For whooping cough,
coverage before the age of 6 is satisfactory. The second booster, however, is erroneously offered at 6 years, at the same time as the second DTaP booster (35% of the 10-year-olds received a fifth dose before 10 years). Thus, not enough teenagers had had 5 doses of vaccine at adolescence (57.4% at 15 years in 2003-2004), and only 17.4% of them had received the fifth dose after the age of 11 years. BCG vaccination coverage against tuberculosis is excellent (99%, regardless of age). For the measles-mumps-rubella (MMR) vaccination, coverage at 6 years for the first dose seems satisfactory (95%), but that for the second dose is still very insufficient (24%-61%). Vaccination against hepatitis B remains much more of a problem, with very low coverage (33%-42%).

Impact of vaccination against rotavirus

In 2007, InVS, in partnership with the University of Lille department of infectious diseases and travelers, the Lille laboratory of economic and social research (CNRS), and INSERM, published the results of a study of the impact and cost-efficiency ratio of vaccination against rotavirus in France.

Rotavirus is the principal cause of acute severe diarrhoea in children, and a vaccine against it was added in 1998 to the vaccination schedule of infants in the United States. Acute intestinal intussusception turned out to be associated with this vaccine, however, and it was withdrawn from the market in 1999. In 2006, 2 new vaccines (one monovalent and one pentavalent) — that do not appear to present this adverse effect — were approved in Europe.

A medicoeconomic study was conducted to provide decision aid about the possible inclusion of this vaccination in the vaccination schedule. It followed 2 virtual cohorts of children from birth to 3 years, one vaccinated and the other not. The onset of rotavirus infection in these 2 cohorts was modeled in a decision tree. The study made it possible to measure the impact of vaccination from several points of view: the number of cases and of hospital admissions avoided, number of years of life gained, direct medical costs, cost of avoided hospitalization, cost per year of life gained, and cost per year of quality-adjusted life gained.

It showed, in particular, that vaccination could prevent 89 000 cases of acute diarrhoea each year in children younger than 3 years (of the 182 000 episodes for which rotavirus is responsible), 10 500 hospitalizations (of 18 000) and 8 deaths (of 13). At €150 for a complete vaccination series (2 or 3 doses, depending on the vaccine), the vaccine programme would represent an additional cost of €68 million. The cost-efficiency of vaccination was estimated at €299 000 per year of life gained, €138 000 per year of quality-adjusted life gained, and €6500 per hospitalization avoided. The sensitivity analysis — which takes into account the uncertainty surrounding some of the model indicators — varied the cost-efficiency ratio from €64 000 to €212 000 a year of quality-adjusted life.

The onset of a vaccination programme of these new vaccines would have an important impact on the severe morbidity associated with rotavirus, but it would not be “cost-effective” relative to the thresholds generally accepted unless the price of the vaccine falls considerably.

Taking this study — among other elements — into account, the High Council of Public Health decided to delay the recommendation of routine antirotavirus vaccination for infants younger than 6 months and then reassess the situation in 2 years, after implementation of a set of measures intended to improve management of these infections.

Surveillance of acute respiratory infections

Influenza, and more generally winter epidemics of acute respiratory infections (ARI) have a major health impact each year, especially among elderly groups. ARI are thus the leading cause of infectious mortality in institutions for the elderly and specifically in nursing homes (EHPAD). In 2003-2004, InVS drafted a guide for the investigation of ARI case clusters, for use by district health and welfare bureaus. This guide has since been integrated into the recommendations of the High Council for Public Health in France, distributed in the November 2006 circular about management of acute lower respiratory infections in the elderly. In 2007, InVS published an issue of its weekly epidemiologic bulletin entirely devoted to flu surveillance and ARI outbreaks. It presented the results of a study of ARI outbreaks in residences for the elderly in France in 2006-2007.

This study focused on the ARI outbreaks between August 2006 and July 2007, reported by the facilities to their local DDASS, CCLIN, or CIRE, which subsequently reported them to InVS. Since January 2007, an Internet application has made it possible for the DDASS, CIRE, and InVS to exchange epidemiologic information about these episodes in real time.

During this period, 64 outbreaks of ARI in residences for the elderly were reported to InVS: 41 in nursing homes, 10 in independent or assisted living facilities, 9 in long-term hospitals, and 4 in other hospital departments. The epidemiologic investigations of these case clusters identified an influenza
virus in more than 30% of the episodes. The mean attack rates were 22% for residents and 7% for staff. The mean lethality rate for residents was 4%. Mean influenza vaccination coverage in these episodes was 91% for residents and 38% for staff. Staff members became ill in 51% of the episodes. In at least 4 of the 64 outbreaks reported, staff members became ill before the residents. The mean duration of the episodes was 13 days. Control measures were put into place an average of 7 days after the episode began and in 36% of the cases, after the episode was reported. In the episodes where control measures were instituted late, the mean duration of the epidemic was longer and residents had a higher risk of becoming ill.

The results of this study show that flu vaccination coverage in the staff at residences for the elderly is insufficient, even though staff frequently become ill and can contribute to the introduction and dissemination of the epidemic. Similarly, while control measures (such as wearing masks) are recommended once the first ARI case is identified, it appears that their implementation takes time. Finally, the advice and expertise provided during reporting help in the management of these episodes and thus reinforce their epidemiologic interest.

From the general to the particular

In addition to this nationwide study, InVS also intervened in 2007 in more local episodes. In Vendée, for example, the Pays-de-la-Loire CIRE conducted an epidemiologic survey of 26 ARI case clusters in one retirement home, including 2 deaths.

InVS also intervened in a nursing home in Tarn. The cohort study conducted on this occasion by the Midi-Pyrénées CIRE, together with rapid influenza tests, produced a descriptive analysis of the epidemic and identified factors associated with its onset. The study showed the impact of inadequate vaccination coverage — only 65% in residents and 0% in staff. Attack rates during the episode were 48% in the residents and 26% in the staff. The study also confirmed the importance of early alerts.

Case clusters of acute respiratory infections in the Landes

On 24 May 2007, the Landes district health and welfare bureau reported to the Aquitaine CIRE a suspected epidemic of atypical lung disease in children at 3 schools in Saint-Martin-de-Seignanx, in the southern end of the district. A cross-sectional survey collected retrospective and prospective data once the epidemic was reported. A case was defined as confirmed if the PCR (polymerase chain reaction) test was positive, probable if it was identified by radiology, and possible if there was a clinical picture of lung disease associated with a recent contact with a previously identified case.

The epidemiologic survey identified 99 cases of lung disease in all — 4 confirmed, 93 probable and 2 possible — with a median age of 6.1 years (range: 1.2 to 45.1 years). None of the cases required hospitalization.

In addition to the main cluster (84 children in 2 elementary schools and one nursery school in the municipality), 2 secondary clusters (4 and 5 cases) were identified in schools in neighbouring municipalities. In the principal epidemic outbreak, the attack rate was 9.9% in those younger than 5 years and 18.9% in children 5-9.

The investigations confirmed the epidemic character of the episode and identified the etiological agent responsible (Mycoplasma pneumonia). The early reporting thus made it possible to optimize medical management.