Editorial

Gilles DUHAMEL
Chairman of the InVS board

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Here for the third consecutive year is InVS's annual report, submitted in compliance with the Law of 1 July 1998.

The scientific results summarized here illustrate the diversity of the subjects we treat and the urgency of the need to continue to construct and adapt our surveillance systems.

2002 was marked by reinforced cooperation between the various agencies of the French health security system, as many studies demonstrated: with AFSSA (French food safety agency) for risks associated with zoonoses (Q fever epidemic in the Chamonix Valley) and food products (salmonellosis and listeriosis, in particular); with AFSSE (French agency for environmental safety and health) and AFSSA for dioxins; with AFSSA and AFSSAPS (French drug agency) for risks related to aluminium. These surveillance projects – designed and followed jointly – provide the best guarantee of consistency between the agencies. Joint referrals by the government to different agencies also promote this coordination.

Our information systems also improved: 2002 was devoted mainly to the design and development of a new system of mandatory disease reporting, one that takes into account simultaneously the need for exhaustiveness, validity, and, especially, confidentiality. We designed and constructed what is probably one of the most secure systems in the world; 2003 will tell us if its implementation meets our objectives for improving surveillance, especially of HIV and HBV.

The continuing growth of our surveillance programs must be accompanied by carefully thought through and reasoned out choices. It is impossible to monitor everything and everywhere and also respond rapidly to unpredictable (in type and number) alerts that are usually urgent.

An obvious example in early 2003 was severe acute respiratory syndrome (SARS), but in 2002 the resurgence of syphilis in Paris, the diphtheria alert, and epidemics of fascioliasis, legionellosis, and listeriosis all tested InVS's ability to adapt and intervene.

Better response to all of these issues entails:

– developing surveillance policies targeted at the most exposed or most vulnerable groups: immigrants, the poor and disadvantaged, exposed workers who are monitored poorly if at all.

– strengthening the role of the social sciences so that we can better consider behavior in our epidemiologic analyses.

Information alone is not enough. We must also be able to transmit clear and accurate messages to the government, to physicians and other professionals, but also to the public – messages that are scientifically based yet describe in understandable terms the reality of the risks and the need for action or intervention.

We have endeavored to accomplish this objective through different activities: reinforcement of the Weekly Epidemiologic Bulletin, internet posting of available information (during the SARS epidemic, InVS posted a daily information bulletin).

We have worked in as close proximity as possible to the populations concerned to develop health surveillance in the regions. The staffing for the 16 regional epidemiology units (CIRE) increased in 2002 by 26 persons, strengthening them markedly.

Only the substantial support we received from our sponsoring ministry to increase funding for regional activity made this development possible.

Nonetheless, the recruitment of staff with the needed skills and knowledge presents some difficulties: France has only a limited number of trained and available professionals in this field, and the personnel statutes for agencies here have not helped this situation. 2002 did, however, mark the culmination of a joint project for all these agencies to obtain appropriate civil service status for their personnel.

The organizational chart now includes two new departments, created this year: the department of training and documentation (DFD) and the international department (DIT). These two departments incarnate essential developments in our mission of health monitoring:

- The need for training continues to grow in France, in Europe, and in many countries that ask InVS to provide them with training programs in epidemiology and health surveillance. Accordingly, we have created a new program of orientation and training, PROFET (Field Epidemiology Training Program), which applies in France the EPIET (European Program for Intervention Epidemiology Training) strategy tested and validated in Europe: the integration of formal instruction and field placement in epidemiologic training. It should enable us to respond to the personnel and training needs of our own departments and the regional teams, as well as those of other health and safety agencies.

- Our participation in international health surveillance reached full speed very rapidly, through European commitments, of course, but also through our work with WHO. InVS, for example, was able to respond to WHO's call to assess and control the Madagascar influenza epidemic in 2002; this partnership showed its range in 2003 in the SARS epidemic, which illustrated, as never before, the importance and urgency of international coordination.

Today we cannot think of health surveillance as monitoring only within our borders, shut off from the world: the circulation of goods and people, accelerated through the globalization of trade, human migration, politics, economics, and tourism, has made them potential vectors of infectious agents that can be controlled only by globalizing health surveillance at the same time.

These networks for the exchange of information can develop effectively only if we build them in a spirit of solidarity. It is in this spirit that InVS is a participant.

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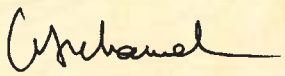
Chairman of the InVS board



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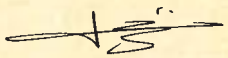


Summary

Health surveillance highlights in 2002

Health status surveillance

Alerts and responses to public health threats and emergencies

Setting up surveillance tools

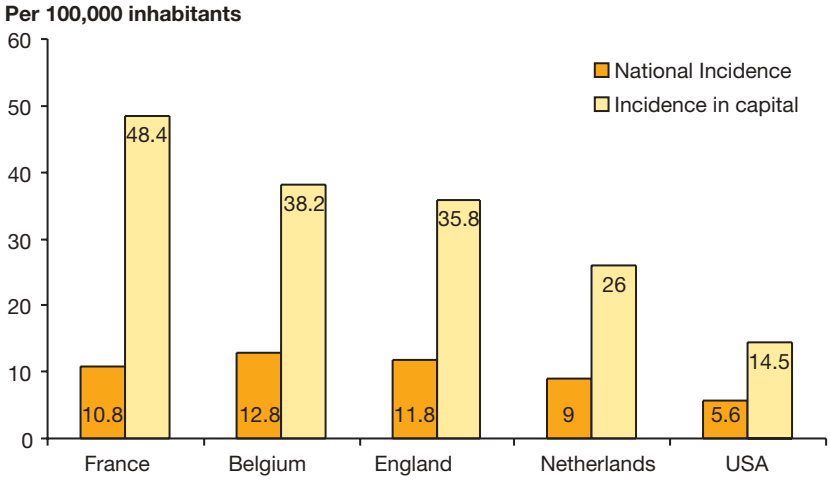
European activities coordinated by InVS

Tuberculosis surveillance: increased incidence among immigrant populations in 2001

Tuberculosis is subject to mandatory reporting in France. Analysis of the cases reported in 2001 shows a worrisome epidemiologic situation in Ile-de-France and among those born abroad, especially in sub-Saharan Africa.

Mandatory reporting data indicate that the mean incidence of tuberculosis in France has declined from approximately 60 to 11 cases per 100,000 inhabitants between 1972 and 1997. The figures for 2001 show that this incidence has remained stable and low (10.8 cases per 100,000 inhabitants, for a total of 6296 cases reported in metropolitan France) for the past five years. Nonetheless, analysis reveals strong regional, social, and demographic disparities.The epidemiologic situation for tuberculosis is especially troubling in Ile-de-France (27.2 cases per 100,000 inhabitants) and most particularly in Paris, where the incidence has reached 48.4 cases per 100,000 inhabitants (1029 reported cases): this distribution of cases concentrated in the capital is also found in other European countries and in the United States (figure 1), to varying degrees. In New York, reinforcement of the local program against tuberculosis reduced the incidence of this disease from 36.0 to 14.5 per 100,000 inhabitants between 1989 and 2001.

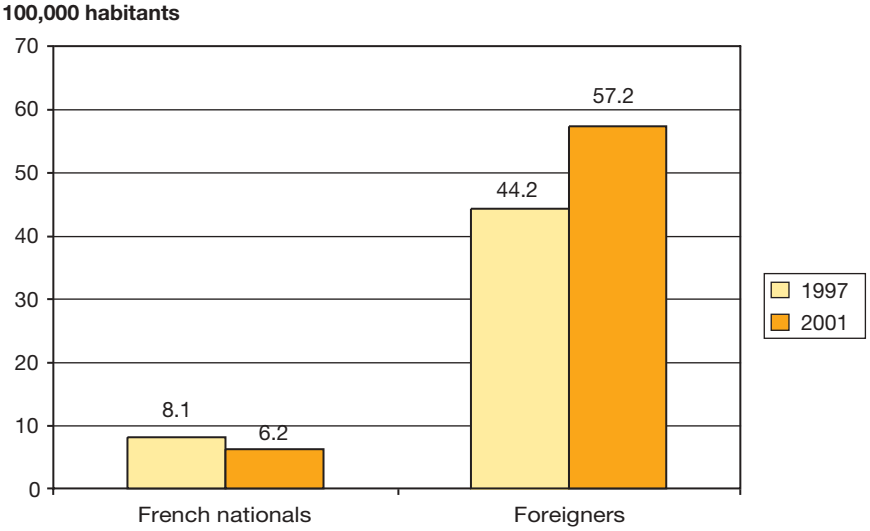
Figure 1: Tuberculosis incidence rate in France, in Paris, and in other industrialized countries and their capitals – 2001
(sources: EuroTB and CDC)



Moreover, the 2001 data show that although the incidence of tuberculosis has diminished among French citizens since 1997, it has increased progressively by 7% per year among foreign citizens living in France (figure 2), especially those from sub-Saharan Africa. As in other western countries, the highest risk of tuberculosis disease is incurred by immigrants from countries where its prevalence is high. In metropolitan France, foreigners have a risk of tuberculosis nine times higher than French citizens, and this risk multiplies by 16 for those aged 24-39 years.

Tuberculosis disease: cases expressed by clinical or radiologic symptoms for which anti-tuberculosis treatment is administered and which must be reported to the government. The disease is distinguished from cases of tuberculosis infection, which is expressed only immunologically ("primary infection without patent site" or "simple visual inspection of tuberculin tests") and is not subject to mandatory reporting, except (since 2003) for latent tubercular infection in children younger than 15 years (so that the source can be traced back).

Figure 2: Tuberculosis incidence rate in metropolitan France, by nationality – 1997-2001



These disquieting observations make it imperative to reinforce the fight against tuberculosis by case finding (active search for tuberculosis diseases), targeted especially at the populations at highest risk: immigrants from countries with a high prevalence of this disease and persons recently infected. Follow-up of treatment compliance must also be improved. Finally, improving tuberculosis control requires a multidisciplinary approach that uses healthcare personnel and social workers.

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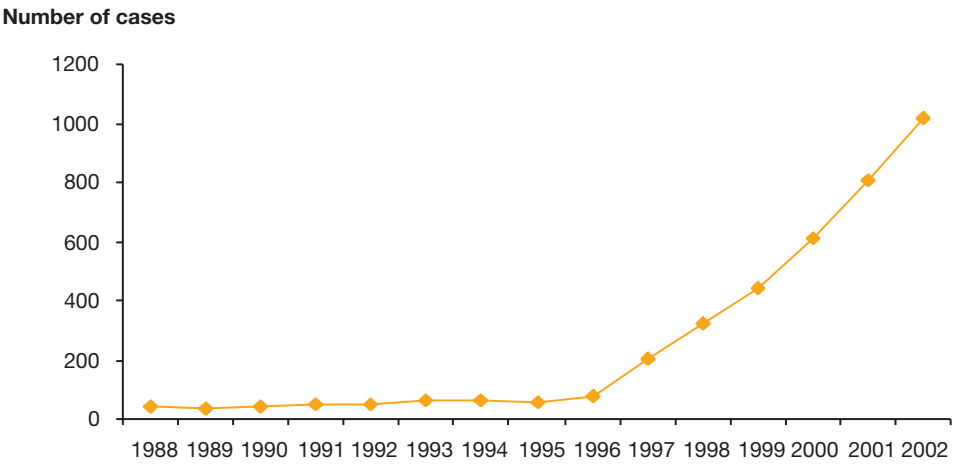
Cailhol J, Che D, Campese C, Decludt B. Les cas de tuberculose déclarés en France en 2001. In : Tuberculose en France : la situation aujourd'hui. *BEH* N° 10-11/2003 (numéro thématique) : 54-7

Legionellosis: progress in surveillance

Since the reinforcement of surveillance in 1997, the number of reported cases of legionellosis has increased continuously, at a mean rate of approximately 32% each year (figure 3): the figure has grown fivefold in six years and epidemic alerts are increasingly frequent. This rise results in part from the efforts undertaken to detect, diagnose, treat, and monitor this potentially serious disease. A nearly linear increase in the reported rate results from earlier reporting by physicians to district health and welfare bureaus (DDASS), collaboration between the legionella CNR, the local DDASS and InVS, and media coverage of recent epidemics. Nonetheless, the 2002 data indicate the continuing need for improvement in clinician involvement, in the system's ability to react, and in the quality of the information collected.

Figure 3: Number of reported legionellosis cases over time - France, 1988-2002



Based on the number of reported cases (n=1021), the incidence of legionellosis in metropolitan France was estimated at 1.7 cases per 100,000 inhabitants for 2002. Case characteristics were similar to those in earlier years: incidence was highest among men and those older than 80 years, with promoting factors (cancer, blood disorders, corticoid or immunosuppressive treatment, diabetes) present in most cases. The disease course is better documented now and is known for 82% of cases (69% in 2001). The mortality rate was 13% (20% in 2001). Mandatory reporting data since 2001 indicate a diminution in the proportion of nosocomial legionellosis (10% in 2002, 13% in 2001, and 20% in 2000), but the absolute number of cases remains stable (table 1). Although it is too early to reach a conclusion, this new trend may reflect the initial impact of the measures taken in healthcare institutions to control these risks. On the other hand, cases reported among residents of retirement homes indicate the need to reinforce surveillance in these facilities, which house a population at risk. Moreover, cooling towers were again the source of two important epidemics in 2002: risk control and prevention in these systems at risk must clearly be strengthened.

Table 1: Exposure to risk factors among reported legionellosis cases (% of cases) – France, 2000-2002

	2000	2001	2002
Hospital - clinic (% of confirmed nosocomial cases)	20% (60%)	13% (35%)	10% (41%)
Hotels - campgrounds	9%	11%	12%
Spas	1%	1%	1%
Other health facilities	1%	1%	<1%
"Travel"*	3%	4%	2%
Temporary residence	-	3%	3%
Retirement home	-	2%	3%
Workplace	-	4%	3%
Other	15%	3%	8%
TOTAL	**48%**	**42%**	**43%**

* without specification of place or type of accommodation

Real progress has been made in legionellosis surveillance and has reinforced its prevention. Nonetheless, numerous questions about this disease remain; we know that more than half the cases identified are isolated ones, with no identified source, and that complete eradication of the bacteria from water systems seems impossible.

Legionellosis or Legionnaire's disease

This infection was identified in 1976 following an epidemic that occurred among participants in a convention of US veterans belonging to the American Legion, whence its initial name of Legionnaire's disease. It is caused by bacteria of the Legionella family, which grows in fresh water, at an optimal temperature of 35 to 40°C. It is thus found in all aquatic environments – natural and artificial – that meet these conditions: showers, faucets, air conditioning and cooling systems, fountains, spas, medical aerosols, etc. These bacteria can lead to a benign infection, known as Pontiac fever, which resembles influenza. Legionellosis, however, is a potentially fatal pulmonary infection – with a mortality rate of approximately 15% – in fragile subjects, including the elderly or immunocompromised. This explains the fatalities in hospital-acquired cases.

It has been subject to mandatory reporting in France since 1987 and is closely monitored. InVS stresses the need to inform healthcare professionals in order to improve diagnosis, the reporting rate, and the transmission of strains to the legionella CNR (central microbiology laboratory of Edouard Herriot Hospital, Lyon). Only this transmission allows us to compare human and environmental strains to confirm, where appropriate, the source of contamination.

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Upsurge in syphilis: evaluation of the campaign to promote screening in Paris

The obligation to report venereal diseases ended in July 2000, but voluntary reports of syphilis cases to InVS since the end of that year bear witness to an alarming upsurge in this sexually transmissible disease (STD) in Paris. This upsurge in syphilis has been observed in other European countries and in North America. InVS data and recommendations led the DGS, the Paris DDASS, and the Paris city government to launch an informational campaign to promote syphilis screening in the capital. From 15 May to 30 September 2002, this campaign, entitled Syphilis Alert, offered free, anonymous screening for syphilis among all those potentially at risk, in the 11 clinics providing free, anonymous HIV screening (known as CDAGs). InVS assessed its impact as it occurred, in real time.

To study the effects of the Syphilis Alert campaign, InVS relied on several data sources:

– syphilis screening activity in the CDAGs (from May to September 2002) and in the public and private medical laboratories that volunteered to report their activity (2001-2002);

– the number of syphilis cases identified in the Parisian surveillance network: STD health centers (known as DAVs) and CDAGs, hospital outpatient clinics, and a private practitioner network established by InVS in 2000;

– monthly sales in Paris pharmacies of Extencilline®, an antibiotic used almost exclusively to treat syphilis; these figures, obtained from a specialized agency, are available from January 2001 onwards.

The four themes of the Syphilis Alert campaign in Paris

- Mobilization, information, and training of healthcare personnel, many of whom have never seen this disease.
- Mobilization of associations and advocacy groups to conduct and relay these informational and screening-promotion activities among the homosexual population primarily affected by the syphilis epidemic.
- Establishment of free, anonymous screening for syphilis for all persons potentially at risk, in all 11 Paris CDAGs (previously, syphilis testing was available, and not anonymously, only at the 9 DAVs – which also offer free anonymous HIV screening).
- Mobilization of InVS to assess this campaign as it occurred, in real time.

Very positive impact

The number of persons seeking testing in the CDAGs increased as early as the first two months of this campaign, and more than 90% – those with any risk factor for syphilis – thus received a free blood test. Similarly, the number of blood tests performed in other laboratories increased over the same period in 2001, peaking in July 2002, during the weeks that followed the beginning of the campaign, and then again in October 2002 (figure 4). The increased recourse to screening of the population at risk shows that the campaign reached its target. It also had a real impact on the diagnosis and treatment of persons with syphilis: the number of cases diagnosed in the Parisian surveillance network increased from the second quarter of 2002, and sales of Extencilline® in Paris pharmacies shot up abruptly between May and June 2002 (figures 5 and 6).

Figure 4: Number of blood tests (TPHA-VDRL) performed monthly in 40 clinical laboratories that volunteered to provide data
Paris, 2001 - 2002

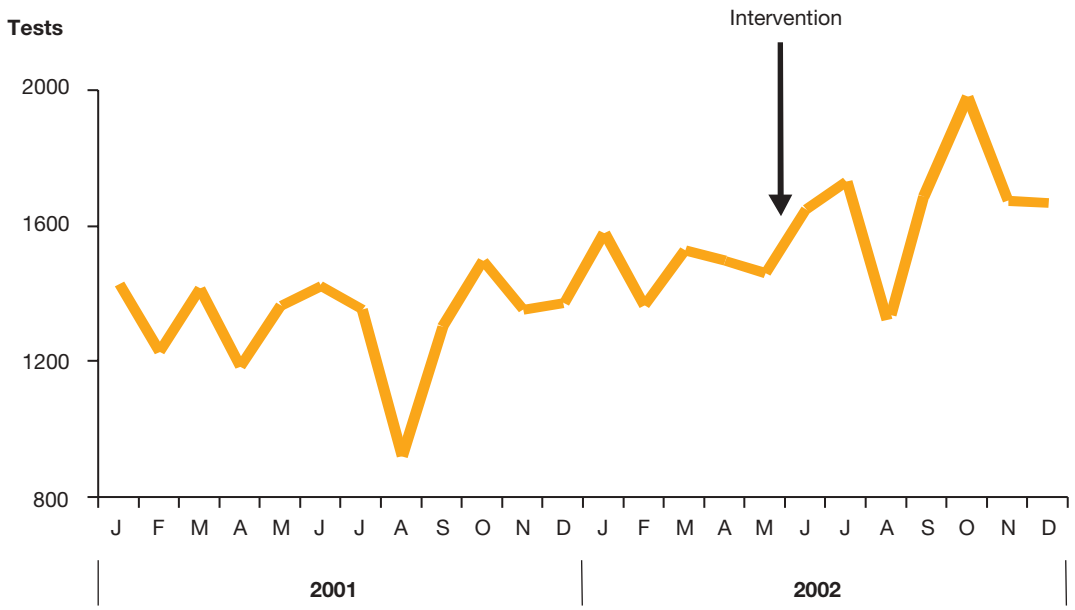


Figure 5: Number of syphilis cases diagnosed per quarter - Paris, 2000 - 2002

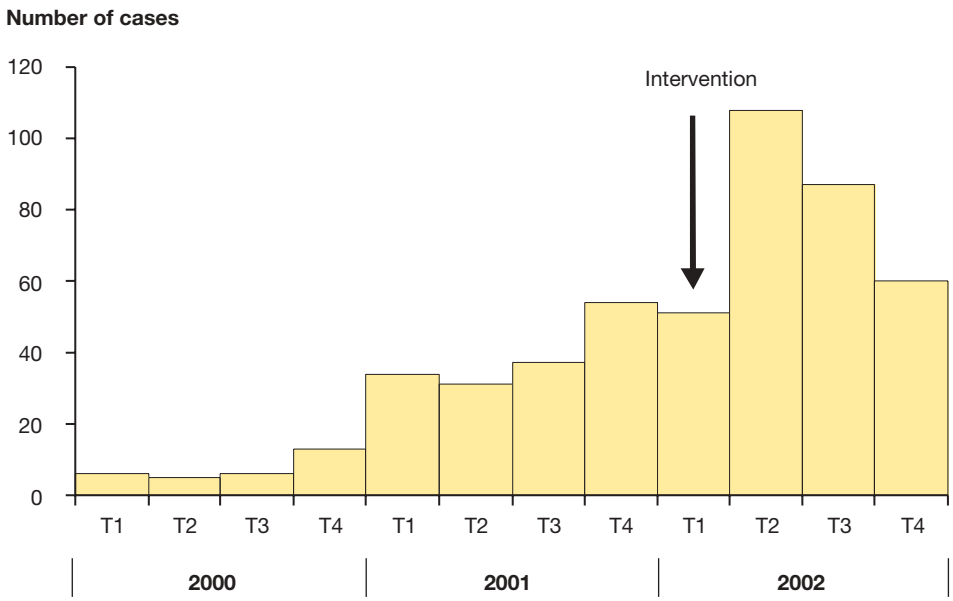


Figure 6: Monthly Extencilline® sales in Parisian pharmacies - Paris, 2001-2002 (data from Gers)

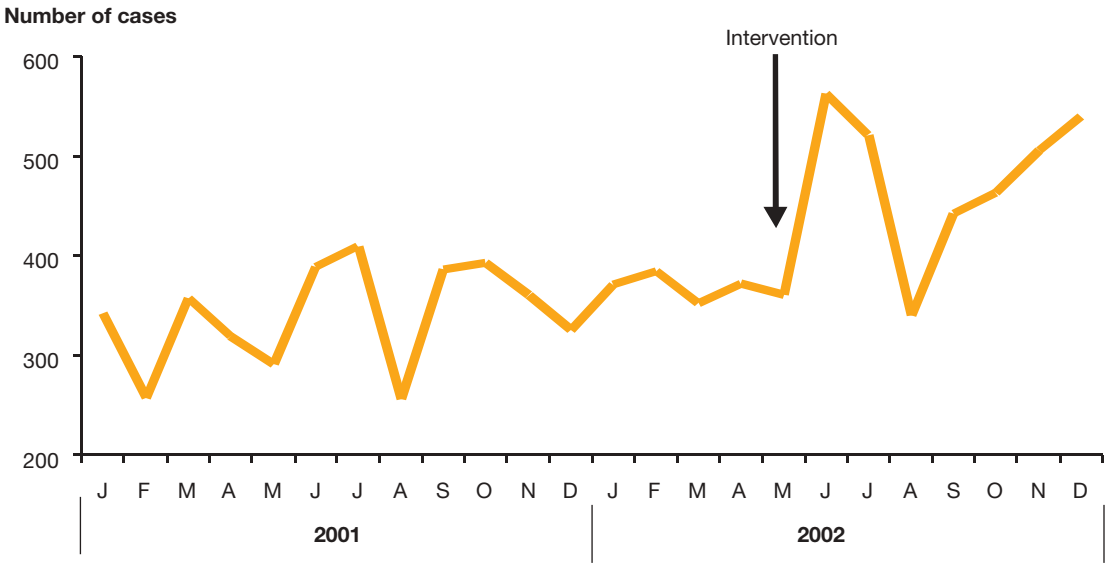
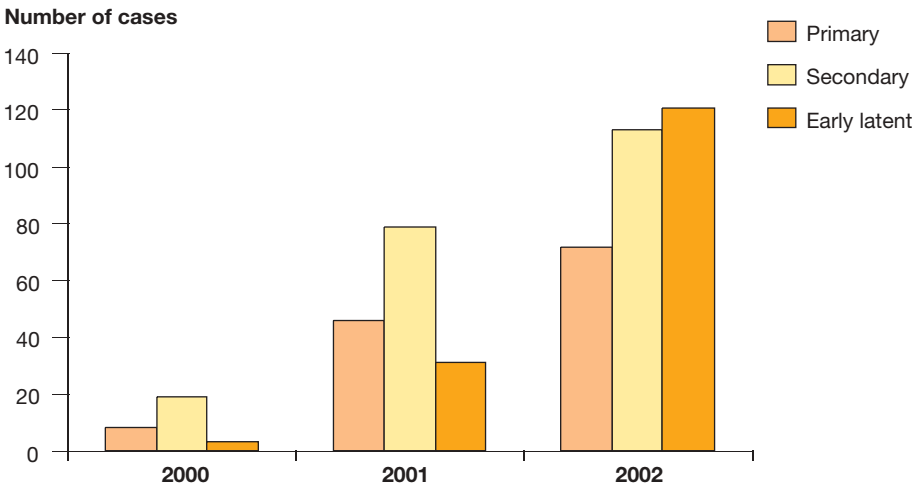


Figure 7: Number of syphilis cases by stage and per year - Paris, 2001 - 2002



Moreover, the number of early syphilis cases diagnosed and treated among clients with no symptoms (latent syphilis) tripled between 2001 and 2002, a result that attests to the positive reception of the campaign's message: "Syphilis simulates other diseases. Treatment is simple and avoids complications." This campaign also affected HIV screening and enabled the detection of previously unknown HIV infection.

An active epidemic

The data collected by InVS also show a strong rise in the number of syphilis cases, especially primary syphilis (figure 7). This indicator of recent infection suggests that the epidemic is active and syphilis transmission persists.

The epidemic affects mainly men having sex with men: based on those seeking screening at the CDAGs, the prevalence of this STD is 9 times higher than among heterosexuals with multiple partners. Promotion of syphilis screening must therefore continue and improve, especially since the campaign's effect appeared to falter near the end, with the proportion of bi- and homosexuals consulting at the CDAGs diminishing with time. InVS data also indicate that the resurgence of syphilis is affecting other large French cities outside Paris.

Following the InVS evaluation, the DGS decided to continue the promotion of screening among men having sex with men in the Parisian CDAGs, first through the end of 2002, then until May 2003, and to extend this campaign to other cities. Priority will go to those that have already reported syphilis cases to InVS and to the metropolitan areas and districts in which new cases are reported, after a census coordinated by the chief medical officers of each DDASS public health service. The organization of this campaign is similar to the system used in Paris. InVS is also setting up a syphilis surveillance network in the largest French cities.

To know more about contagious syphilis

This STD is due to a bacterium: *Treponema pallidum*, visible on microscopic examination of the lesions or by simple blood test (TPHA/VDRL serology). This disease has different clinical and developmental stages.

Primary syphilis: 3 weeks on average (9-90 days) after contamination, a chancre appears – a small ulceration 3-5 mm in diameter, painless – at the bacterium's portal of entry, most often on the genital organs, but sometimes on anal or buccal mucous membranes.

Secondary syphilis: this stage, which occurs between 2 and 6 months after contamination, is expressed by cutaneous or mucosal rash, accompanied by an influenza-like syndrome and enlarged lymph nodes. These lesions are extremely contagious, through simple contact with affected skin or mucosa, especially genital organs.

Early latent syphilis: this stage is characterized by the absence of symptoms although the person remains contagious.

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Couturier E, Michel A, Basse-Guérineau AL *et al*. Evaluation de l'action d'incitation au dépistage de la syphilis à Paris. InVS, 14 novembre 2002.
Couturier E, Michel A, Basse-Guérineau AL *et al*. Evaluation de l'action d'incitation au dépistage de la syphilis à Paris. *In* : SIDA, VIH et IST. Etat des lieux des données en 2002. Programme et communication de la journée d'information publique Sida, VIH et IST du 20 novembre 2002. Rapport InVS 2002 : 3-4

Treatment after HIV exposure: evaluation after three years

Since July 1999, InVS has coordinated a nationwide assessment of the therapeutic management of persons recently exposed to HIV (occupational exposures for healthcare personnel, and non-occupational). The French drug agency (now AFSSAPS) mandated this assessment in its approval of the "off-label" use of antiretroviral drugs called for by the 1998 recommendations that extended the indications for post-exposure antiretroviral treatment (prophylactic treatment) to non-occupational exposures (sexual relations, needle-sharing by injecting drug users, etc.). This study, cumbersome for the participating hospitals and the InVS, was justified by the scarcity of tolerance data for this prevention strategy and the rarity of countries where this off-label use is recommended for non-occupational exposure.

Approximately 100 hospitals participated in this evaluation of HIV post-exposure management, which was generally organized as follows: HIV specialists (in departments of infectious diseases or internal medicine, etc.) first saw most of the persons seeking treatment for initial management and laboratory follow-up for 3 or 6 months; emergency room physicians handled initial management evenings, nights, and weekends, and occupational physicians managed the laboratory follow-up of healthcare staff. The number of physicians involved explains the difficulty in collecting and transmitting these data, especially for clinical and laboratory follow-up.

Initial post-exposure management

Individual risk of HIV transmission is assessed to determine whether or not a prophylactic antiretroviral treatment should be prescribed. This assessment is based on two essential factors: the HIV status of the contact and the extent of the exposure, according to the following classification:

significant exposure: deep or moderately deep injections after intravenous or intra-arterial contact, receptive anal intercourse, receptive vaginal intercourse with ejaculation, anal or vaginal insertion with genital infection or bleeding, immediate needle-sharing between drug users;

medium exposure: superficial injection after intravenous or intra-arterial contact, deep or moderately deep injection after intramuscular or subcutaneous contact or with a suture needle, receptive vaginal intercourse without ejaculation, anal or vaginal insertion without genital infection or bleeding, deep injection with an abandoned syringe, delayed needle-sharing between drug users;

minimal exposure: superficial injection after intramuscular or subcutaneous contact or with a suture needle, projection of blood or another body fluid on the skin or mucosa, biting, oral sex, superficial or moderately deep injections with an abandoned syringe.

From July 1999 through December 2002, the participating hospitals reported 12,180 exposures through contact with a person whose HIV status was positive or unknown; these contacts were primarily sexual (50.8%) or occupational (for healthcare personnel) (34.3%). Intravenous drug users sought such treatment rarely (figure 8), principally because they were unaware of its availability, as a supplementary survey showed.

Two thirds of the sexual exposures were associated with heterosexual intercourse, and rape represented 18% of the sexual exposures reported. Condoms were not used in 25% of the relations with a regular partner and in 45% of those with an occasional partner (rapes excluded). The time from sexual exposure to consultation appeared too long (median: 17 hours) to expect maximal efficacy from any of the antiretrovirals prescribed. While the sexual exposures were judged to be principally of significant or medium importance, the occupational and "other" (injection with abandoned syringe, blood contact or biting during a fight, etc.) exposures were in the main minimal.

Antiretroviral treatment (most often a triple cocktail) was prescribed for 61% of the exposures reported. The percentage of exposed persons receiving prophylaxis varied according to the type of exposure (83% after sexual exposure, 80% after needle-sharing, 46% after "other" exposure and 35% after occupational exposure), the extent of the exposure, and the serologic status of the source (figure 9). These prescribing practices reflect the 1998 recommendations, which suggested prescription mainly after sexual or "other" exposures, specifically in two circumstances: after exposure of only minimal importance to an HIV+ source and after exposure, regardless of its extent, to a source of unknown HIV status.

Figure 8: Distribution of reported exposures to a source person of positive or unknown HIV status according to type of exposure – July 1999 - December 2002

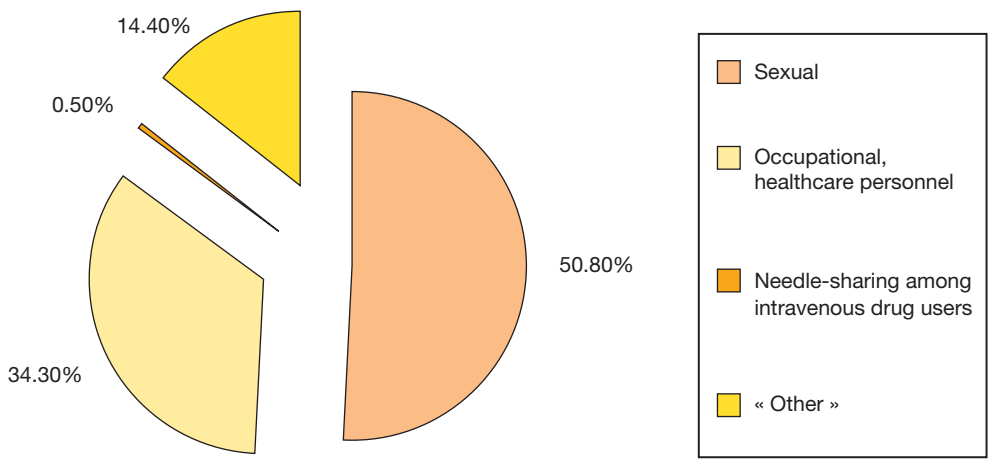
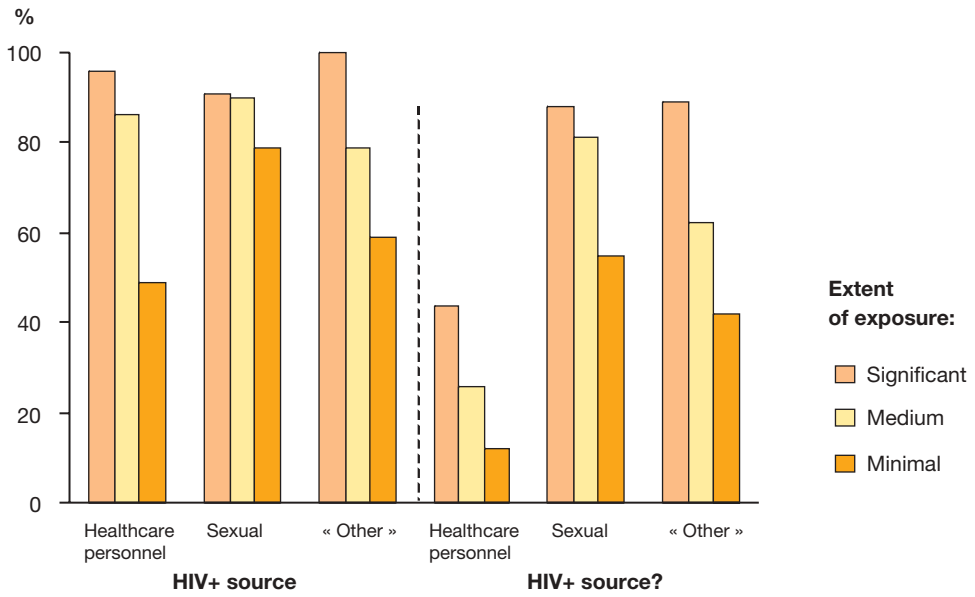


Figure 9: Percentage of persons who received prophylaxis as a function of the type and extent of the exposure and the HIV status of the source – July 1999-December 2002



Nonetheless, the clinical follow-up data show that 10% of the patients receiving prophylaxis reported side effects that interrupted their daily living activities. In 8% of the cases, treatment was stopped completely and prematurely. For comparable risks of transmission, healthcare professionals received this prophylaxis less often than exposed subjects who did not work in the health field, perhaps precisely because they were aware of these side effects.

The data available about the laboratory follow-up at 3 or 6 months (3 seroconversions reported) do not indicate the failure of prophylaxis but they do not permit us to conclude that it works either.

The 1998 French recommendations have been revised in light of this assessment, especially concerning the toxic effects of post-exposure prophylaxis and literature reports of serious side effects: the benefit/risk ratio of this emergency treatment indicates that it should be reserved for situations of high HIV transmission risk. InVS participated in the preliminary consideration of these revised recommendations under the aegis of a working group coordinated by the French drug agency. Nonetheless, the new recommendations will finally modify HIV post-exposure management only slightly, especially for sexual exposures, probably because of the reluctance of the associations involved in the decision process. In any case, the surveillance system established enabled us to monitor this strategy of antiretroviral prophylaxis and met our initial objectives (to describe the persons seeking treatment and physicians' prescribing practices) but should be modified, because of its logistic difficulties, to focus on monitoring tolerance data.

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Risk behaviors in drug users and the epidemiology of HIV and HCV: the Coquelicot project pilot phase

In view of the absence of data since 1998 on the risk behaviors of drug users, InVS proposed an original study, called the Coquelicot project, to be conducted with methodological support from the national institute of demographic studies (INED) and financial support from the national agency for AIDS research (ANRS). This cross-sectional multisite study combines three complementary approaches: 1) behavioral epidemiology – a study of the risk practices for transmission of HIV and HCV among drug users (associated with drug use and sexual behavior); 2) seroepidemiology – testing to determine the prevalence of HIV and HCV infections objectively (by laboratory testing of finger-prick blood samples); and 3) social anthropology – a survey to explore the psychosocial determinants of this risk-taking. The pilot phase of this project took place in Marseille from September 2001 through June 2002.

The pilot study in Marseille concerned a sample of 166 drug users, recruited from 15 specialized prevention, care, or shelter organizations and from 10 general practices. The participation rate of 71%, the involvement of physicians in private practice, the acceptance of outside investigators, and the 83% consent rate for finger-prick blood samples – all demonstrate the feasibility of such a study and of its extension to other urban areas.

Figures 10 and 11 present the results for self-reported and biological (blood tests on blotting paper for HCV) prevalence of HIV and HCV seropositivity. Although the sample size and the pilot nature of this study both demand a certain degree of prudence in interpreting them, these results do confirm other data and suggest that prevention activities and messages have helped to reduce the risks of HIV transmission (no seropositivity among those younger than 30 years), but had no effect on the prevalence of HCV infection. The very high level of prevalence (43%) among young drug users indicates a substantial risk of contamination that begins with drug use.

Beyond the probable reporting bias, these preliminary results also confirm the development of trends recently observed among drug users: a drop in the consumption of illegal products, replaced by alternative products and psychotropic drugs, and a substantial decrease in injection. The Coquelicot study also furnishes some data about drug users' perceptions of hepatitis C.

Figure 10: Prevalence of HIV and HCV seropositivity by type of data collection (Coquelicot study, 2002)

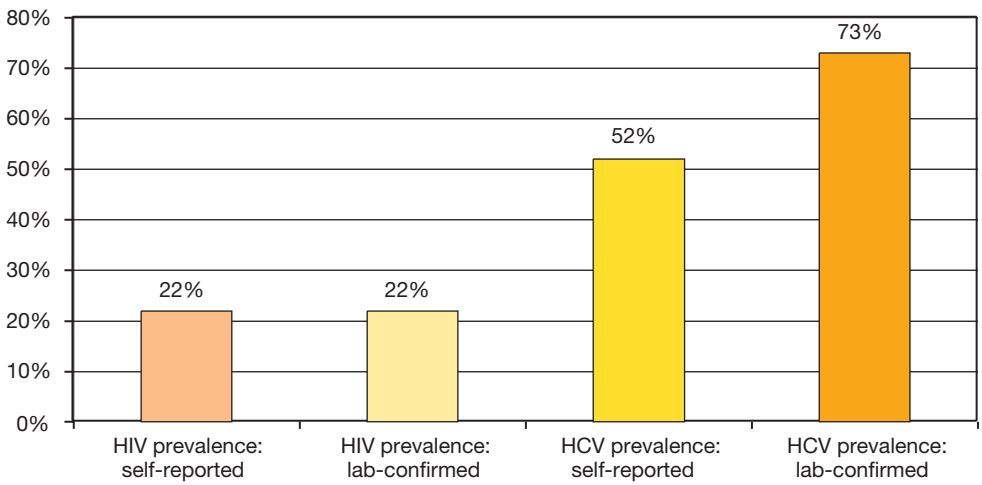
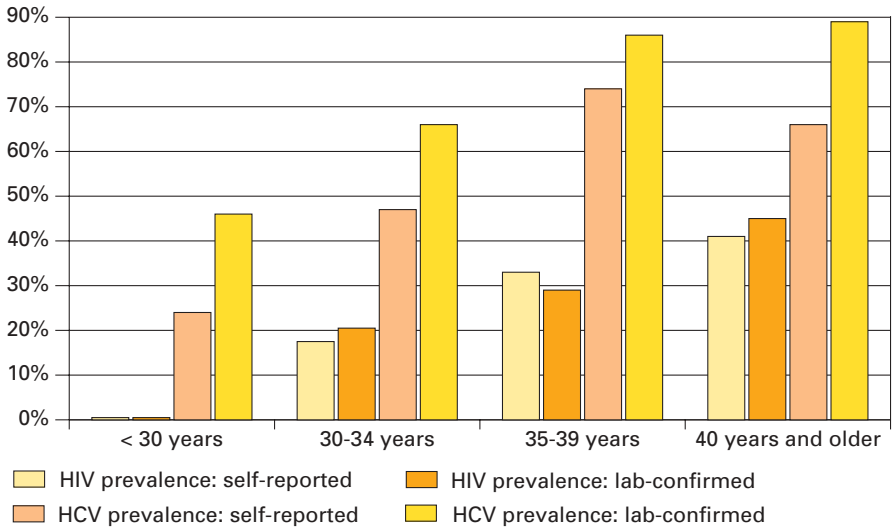


Figure 11: Prevalence of HIV and HCV seropositivity according to information source and by age group (Coquelicot study, 2002)



Other results of the Coquelicot study

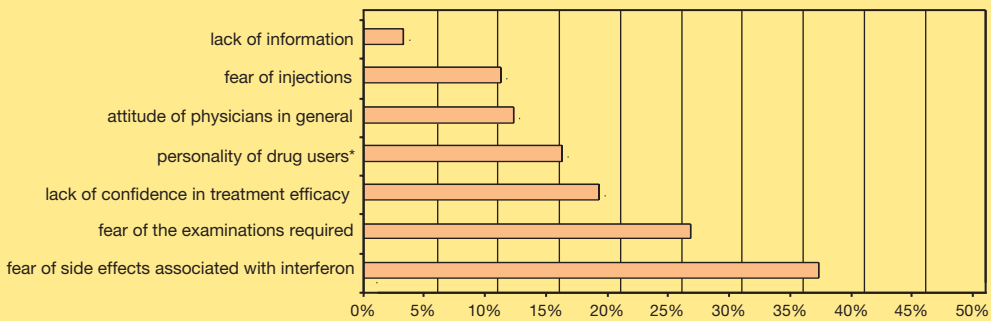
Demographic characteristics of the 166 drug users:
– 70.5% men;
– mean age 34.1 years;
– 60% spent time in prison at least once in their life (and 9% of them reported that they continued injections in prison);
– 61.2% live in what can be considered stable housing;
– 37.3% report welfare (RMI) as their only income, and 8.4% say they have no income.

Drug use:
– 15.6% report injecting and 14.5% sniffing or snorting drugs in the month before the survey;
– 80% used substitute products (methadone, subutex), 50% benzodiazepines, and 25% illegal drugs during this period;
– 70% used more than 1 drug, with a mean of 2.6 products used in the past month.

Risk practices:
– 36% of intravenous drug users said they had shared their syringes and 23% had used the recipient, filter, or cleaning water already used by someone else or let someone else use their used filter at least once in the past month. The risks of needle sharing were significantly greater among illegal drug users, sedative-hypnotic drug users, and those reporting use of more than 2 products;
– 1/3 of sniffers reported sharing their sniffing straw during the past month;
– 69% of the respondents reported sexual relations in the past 6 months; 16.5% reported unprotected relations with someone whose HIV status was different from theirs or unknown. This sexual risk-taking was significantly greater among those who reported that they were in poor or fairly poor health (RR=2.32, $p<0.05$).

Perception of hepatitis C:
– 92.3% consider it a serious disease and 77% think it can be effectively treated with medication;
– reasons given to explain why drug users who need it do not receive HCV treatment (several responses possible):

Reasons for difficulty in receiving HCV treatment, according to drug users (Coquelicot study, 2002)



*personality of the drug users: lack of willingness, motivation or desire to take care of themselves, fear or shame preventing them from taking the necessary steps or talking about the problem, indifference or negligence that prevents them from treating it as a health priority or even a problem

Following this conclusive pilot phase, the Coquelicot study will be extended in 2003 and 2004 to 6 metropolitan areas (Lille, Strasbourg, Paris, Ile-de-France, Bordeaux, Marseille), continuing under the scientific supervision of InVS and with financial support from ANRS. Initial data from the pilot study point to the need to maintain adequate accessibility to sterile injection materials and to take the reluctance of users to be tested or treated for HCV into account from the beginning in designing access to screening and treatment. This is especially necessary given the frequency of HIV-HCV co-infection and the precarious living conditions of most of these persons, factors that increase the complexity of their medical management. Accordingly, the HCV screening in CDAGs, often perceived as "long and tedious," might advantageously be replaced by testing offered in units or facilities drug users go to daily. It is thus important to envisage the conditions in which the tests would actually be used in the pilot phase as part of planning prevention programs, in order to improve the overall management of the public concerned.

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Hepatitis C: early surveillance results from Rena-HCV and the reference centers

InVS established two hepatitis C surveillance networks in 2000: one a network of clinical laboratories to monitor screening activities (Rena-HCV), the other a network of reference centers (hepatology departments) to observe the characteristics of newly referred patients. Early results for 2000 and 2001 are now available.

The Rena-HCV network of hospital and private clinical laboratories comes from the group that participated in the RENAVI national network of HIV surveillance in 1997. Of the 357 laboratories contacted, 281 agreed in principle to participate and 260 (93% of the latter) communicated their quarterly results at least once during the study period – a good participation rate. Of these 260 laboratories, 189 (73%) participated throughout the eight quarters of surveillance. They represent 4.6% of all of the laboratories performing or delegating HCV serology testing and are distributed throughout France, although coverage of regions in the south is less complete. In its first two years of surveillance this new Rena-HCV network reported nationwide results completely consistent with previous studies. It also showed that screening activity increased by approximately 10% from 2000 through 2001, at the same time as the Ministry of Health conducted screening information and promotion campaigns (figure 12). Inversely, positive findings decreased between 2000 and 2001 (table 2); this suggests that the increased screening may have included people at little risk of HCV infection.

The hepatitis C reference center network comprises 26 centers (see sidebar), all volunteers to participate in this surveillance; they saw 2063 patients for the first time in 2000 and 3906 in 2001. Analysis of these patients' characteristics shows that, in 2000-2001, approximately 10%

had an advanced form of the disease (cirrhosis or hepatocellular carcinoma) at their first consultation, while this proportion was 21% for the 1993-1995 period. These data suggest that referral and treatment now begin earlier than they did 10 years ago, a trend that must be confirmed by subsequent surveillance.
Hepatitis C was discovered fortuitously in 34-41% of the new patients and because of symptoms in 30-34% (table 3), thereby indicating that early screening can still be improved. The two most frequent risk factors for HCV were transfusion (especially among women) and injecting drug use (especially among men).

Hepatitis C reference centers
Created in 1995 (DGS/DH circular dated 5 May 1995) as part of the national program against hepatitis C, these are hepatology departments located in university hospital centers (UHC). There are 31 today, distributed throughout the country. They are part of the surveillance network developed by InVS, and their task is to monitor trends in the characteristics of new patients seen with anti-HCV seroconversion (circumstances of discovery, risk factors for infection, clinical stage at first visit, etc).

Figure 12: Changes in comprehensive Rena-HCV screening activity by quarter in 2000-2001, in relation to the timing of the Ministry of Health's screening information and promotion campaigns

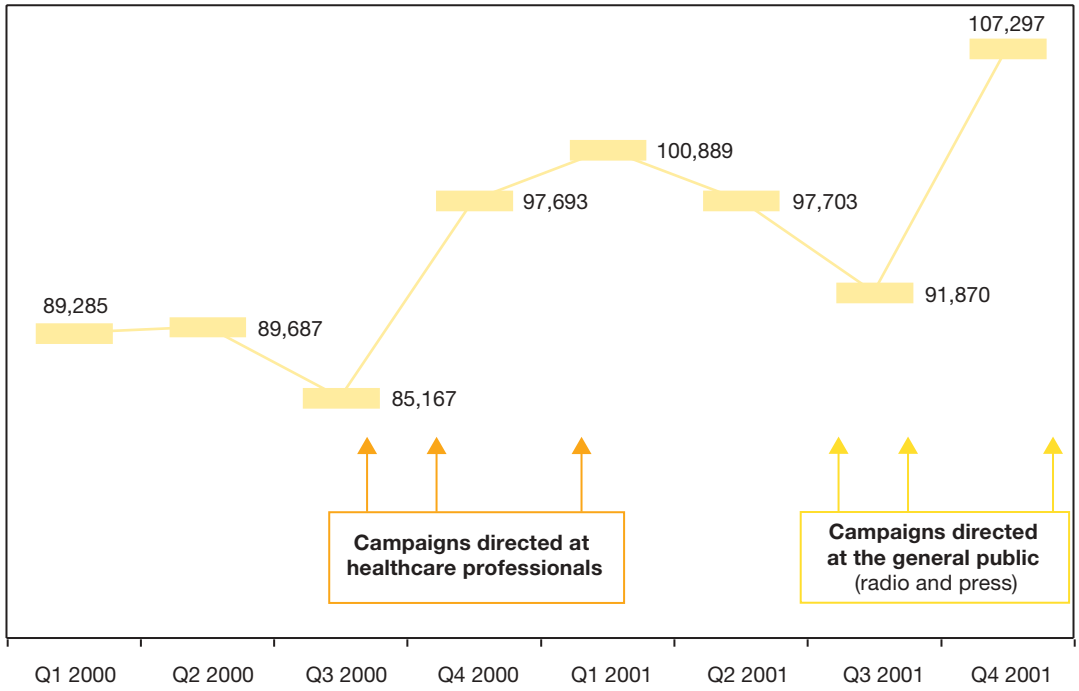

Table 2: Surveillance of Hepatitis C screening and screening activity – Rena-HCV 2000-2001

	2000	2001	Trend or p value
Overall screening activity (total number of tests performed)	361,832	397,759	+ 10%
Overall positive test rate (ratio of positive tests to total screening)	4.0% (14,814/361,832)	3.8% (15,256/397,759)	p=0.01
Screening verification activity (total number of tests performed to verify screening)	5363 (1.5%)	5165 (1.3%)	- 3.7%
Positive confirmation rate (ratio of positive tests to total screening)	1.2% (4344/361,832)	1.0% (3797/397,759)	p<0.001

Table 3: Circumstances of detection* of HCV-positive serology in new patients in the hepatitis C volunteer reference center network 2000-2001

	2000		2001	
	n	%	n	%
Fortuitous (check-up, blood donation, pre-transfusion work-up)	567	34.2	1405	41.1
Existence of a risk factor	530	32.0	849	24.8
As part of a diagnostic work-up or procedure (abnormal liver function tests, complication of cirrhosis, work-up for hepatocellular carcinoma)	364	22.0	603	17.6
Other discovery circumstances (including asthenia)	198	11.6	563	16.5

* Patients with 1 method of discovery: that is, 1659/2063 (80.4%) in 2000 and 3420/3906 (87.6%) in 2001

These two hepatitis C national surveillance networks thus appear stable and operational. The evaluation underway of the reference center network will provide a basis for discussing whether this data collection should continue and for modifying the assessment of the national program against hepatitis C. Prevalence of this disease will be surveyed again in 2003 to obtain information about the prevalence of anti-HCV antibodies in the population, to determine the proportion of infected subjects who know their status, and thus to assess progress in screening.

This study, to be conducted in collaboration with the national health insurance fund (CnamTS), will involve a sample of 15,000 persons, aged from 18 to 80 years, and invited to undergo a clinical check-up in health examination centers (a representative sample of the general French population, with no particular risk factors). It should be more representative than the first survey in 1994. Its initial results are planned for early 2004. A simultaneous study of the seroprevalence of HBV infection markers will also update the hepatitis B data for France.

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Foodborne infectious diseases: assessment of their importance in public health

Policymakers and decision makers in industrialized countries, including France, consider food safety a priority for health and economic reasons that justify the substantial funding devoted to the surveillance, prevention, and control of food poisoning. Surveillance systems enable us to follow the changing trends in these diseases and to detect epidemics, but they do not inform us of the total number of persons who become sick: the real burden of these diseases is still poorly understood. InVS, as part of a collaboration with the French food safety agency (AFSSA), conducted a study to specify and rank the importance of these infectious and toxic foodborne diseases in France, to help orient relevant public health measures.

More than 200 infectious bacterial, viral, or parasitic diseases are transmitted through food. They most often cause only gastrointestinal symptoms but can also induce severe and even fatal events, such as meningoencephalitis in listeriosis or the hemolytic uremic syndrome (HUS) that sometimes follows infection by Shiga toxin-producing *Escherichia coli* (STEC).

The study looked at 23 pathogenic agents (13 bacteria, 2 viruses, and 8 parasites) transmitted in food, chosen because of the frequency in metropolitan France of the foodborne illnesses they cause, their seriousness, their epidemic potential (table 4), and the availability of relevant data.

The morbidity (number of persons made sick and number hospitalized) and mortality (number of deaths) due to food poisoning in metropolitan France during the 1990s and associated with these 23 agents were estimated to determine their importance and to rank them. Various data sources were consulted for this purpose: national, district, and foreign surveillance systems, the medical information systems program (PMSI), the center for death statistics and epidemiology, the national health insurance fund for salaried workers (CnamTS), one-shot studies, and investigations of epidemics in France and in other industrialized countries. Comparison of the estimates from these different sources, followed by a critical analysis, provided a range of values corresponding to the most plausible upper and lower estimates (table 4).

With 238,836 to 269,085 cases estimated annually in this study, foodborne illness appears common in France. Although the figures of estimated viral and parasite infections appear high in relation to bacterial infections, these numbers are not actually comparable because they correspond to different case definitions (laboratory or clinical) that are more or less restrictive (footnote b of table 4).

Salmonella and Campylobacter head the list of foodborne bacterial infections

Salmonella are the most frequent cause of foodborne bacterial infection (causing 30,598-41,139 culture-confirmed cases each year), followed by Campylobacter (12,796-17,322 cases). These two bacteria alone cause 71-85% of the foodborne bacterial illnesses studied. With listeriosis, they also cause most of the cases requiring hospitalization. These bacterial infections are responsible for 84-94% of the deaths, attributable principally to salmonellosis (92-535 estimated annual deaths), listeriosis (78) and, to a lesser extent, Campylobacter (13-18).

Table 4: Morbidity and mortality associated with foodborne infectious agents: the most plausible estimates of the annual mean number of cases, hospitalized cases, and deaths[b] - metropolitan France - 1990

STEC infections	Diseases [a]	% foodborne origin	Estimated mean annual number foodborne		
			Cases [b]	Hospitalized cases	Deaths [c]
Bacteria					
*Bacillus cereus**		100	219 – 701	26 – 84	0
Brucella spp. †	brucellosis	50	28 – 132	58	1
Campylobacter spp. †		80	12,796 – 17,322	2598 – 3516	13 – 18
Clostridium botulinum†	botulism	100	22	17	0 – 1
*Clostridium perfringens**		100	2790 – 8928	33 – 107	2 – 6
Escherichia coli (STEC) *		50	373 – 747	110 – 220	0 – 1
Listeria monocytogenes †	listeriosis	99	304	304	78
Salmonella non – Typhi †	salmonellosis	95	30,598 – 41,139	5691 – 10,202	92 – 535
Salmonella Typhi † §	typhoid fever	80	54	51	0 – 1
Shigella spp. †	shigellosis	10	159 – 233	21 – 69	0 – 0
Staphylococcus aureus *		100	3257 – 10,422	596 – 1907	0
Vibrio spp. †		100	14	3	1
Yersinia spp. †	yersiniosis	90	655 – 1909	155 – 635	4 – 10
Total bacteria			**51,269 – 81,927**	**9663 – 17,173**	**191 – 652**
Virus					
Norovirus ‡		14	70,194	nd	nd
Hepatitis A virus †§	hepatitis A	5	406	52 – 77	2
Total viruses			**70,600**	**52 – 77**	**2**
Parasites					
Anisakis simplex†	anisakiasis	100	8	6	0
Diphyllobothrium latum†		100	3	2	0
Echinococcus granulosus†	cystic echinococcosis	nd	nd	nd	nd
Echinococcus multilocularis†	echinococcosis alveolar	nd	nd	nd	nd
Fasciola hepatica†	liver fluke	100	316 – 357	11	0 – 1
Taenia saginata‖	teniasis	100	64,495	14 – 62	0
*Toxoplasma gondii**	toxoplasmosis	50	51,655	426	35
Trichinella spp.†	trichinellosis	100	40	14	0 – 1
Total parasites			**116,517 – 116,558**	**473 – 521**	**35 – 37**
Total pathogenic agents			**238,836 – 269,085**	**10,188 – 17,771**	**228 – 691**

a: when it has a specific name
b: case definition: † confirmed case (microbiologically or serologically), * symptomatic case (confirmed or not), ‡ cases of norovirus infection (confirmed or not) leading to a consultation with a general practitioner, § indigenous case, ‖ case (confirmed or not) treated with niclosamide.
c: all deaths during infection, without determining attributability to the pathogenic agent studied
nd: not determined

Campylobacter infections

In humans, these infections are most frequently due to the *Campylobacter jejuni* and *Campylobacter coli* species; they appear after an incubation of 2 to 5 days, with gastrointestinal symptoms – diarrhea, abdominal pain, vomiting, and fever. Recovery usually occurs in 2 to 5 days. Complications (mesenteric adenitis, reactive arthritis, Guillain-Barré syndrome, etc.) are rare. Many of these infections are asymptomatic. The diagnosis requires isolation of these *Campylobacter* species. Animals, especially poultry, serve as the reservoir. Transmission is largely foodborne, after eating contaminated food (e.g., chicken, pork, milk, water) raw or inadequately cooked. Direct person-to-person contamination also occurs, through fecal-oral transmission ("dirty hands") or by contact with infected animals.

Norovirus infections

They appear after an incubation period of 12-48 hours with generally moderate gastrointestinal symptoms, including vomiting, diarrhea, nausea, abdominal cramps, and, in young children, a fever above 38°C. Recovery most often occurs within 24-72 hours. The diagnosis is primarily clinical. Norovirus infections are specific to humans, and transmission is principally fecal-oral (another "dirty hands" disease) or by the projection of vomit, direct person-to-person contact or, more rarely, by consumption of contaminated food or water. These most often involve either food contaminated by a person who was sick while handling it or water contaminated by human stool and drunk untreated. Shellfish (oysters) and fruit eaten raw are thus a frequent cause of documented epidemics. Norovirus gastroenteritis occurs at a seasonal rhythm, with a winter upsurge from November through March and peaking from December through February in temperate climates.

Norovirus infections, with an estimated 70,194 cases annually leading to general practitioner visits, are the principal foodborne viral infections.

Of the foodborne parasite infections studied, toxoplasmosis and teniasis (tapeworm) predominate, representing together more than 99% of the parasite infections studied. Toxoplasmosis causes the vast majority of the hospitalizations and deaths. Nonetheless, most of the deaths occurring during toxoplasmosis are probably not directly or exclusively attributable to this infection, which usually occurs in patients with co-morbidity, AIDS in particular.

Globally, the mortality associated with food-borne illness is relatively low (228-691 deaths estimated per year), despite their frequency. We should note here the mortality due to excessive alcohol consumption in France: 23,000 estimated deaths in 1998. Nonetheless, foodborne infections and their consequences (medical services used, losses due to sick time, hospitalization and death) are for the most part avoidable. Convincing proof comes from the prevention and control measures implemented at the level of production, distribution, and consumption of foodstuffs for salmonellosis, listeriosis, and brucellosis: their efficacy has substantially reduced the number of cases and deaths associated with these infections.

Childhood hemolytic uremic syndrome: seven years of surveillance

Childhood hemolytic uremic syndrome (HUS) is rare in France but very serious. The surveillance begun in 1996 and coordinated by InVS shows that most cases are associated with Shiga toxin-producing *Escherichia coli* (STEC) infections. A supplementary case-control study provided information about the risk factors for this contamination; effective prevention and control should focus on them.

Hemolytic uremic syndrome (HUS) is the principal cause of acute kidney failure in children aged 1 month to 3 years. Its case fatality ratio is high, from 3 to 5% according to the study, and it leaves long-term renal sequelae in more than one third of cases. Most cases of *HUS* are due to Shiga toxin-producing *Escherichia coli* (STEC) infections. STEC were recognized as emerging human pathogens in the United States in 1982, following two epidemics of bloody diarrhea associated with eating hamburgers contaminated by them. They cause food poisoning that can include a variety of clinical events: common diarrhea, hemorrhagic colitis, HUS, and thrombocytopenic purpura. Numerous STEC epidemics have been reported in several industrialized countries, some of them large, with high case fatality ratios. STEC is transmitted principally by food. Person-to-person transmission within families or groups and transmission by contact with contaminated ruminants have also been described.

Hemolytic uremic syndrome: combination of acute hemolytic anemia and renal lesions.

Escherichia coli: previously called colibacillus, this germ belongs to the enterobacteria family and is usually found in the intestines of humans and animals. It can cause urinary infections, suppuration, infants' diarrhea, food poisoning, septicemia, etc. STEC are *Escherichia coli* that produce special poisons called Shiga toxins.

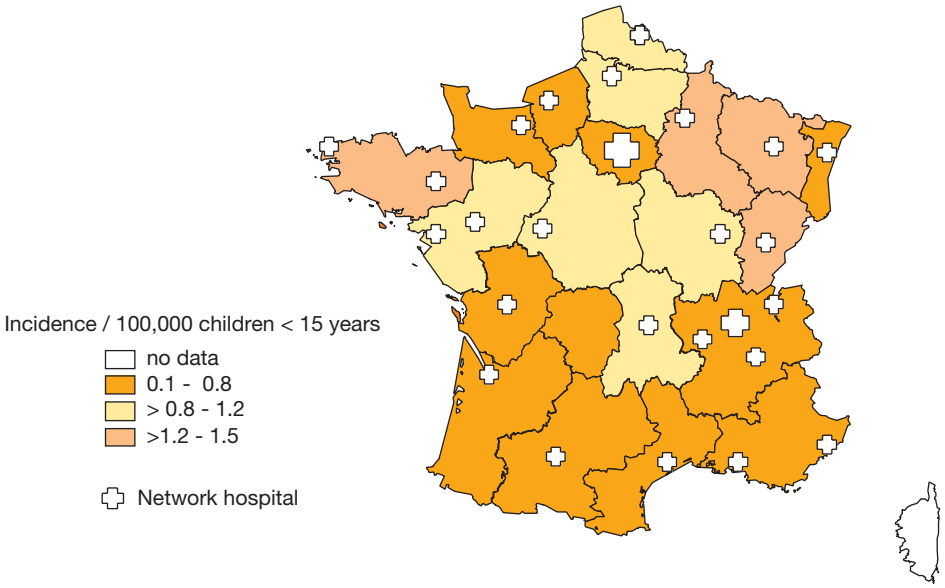
STEC therefore pose a food safety problem in France, as in other industrialized countries. Because French medical laboratories do not routinely look for STEC in stool, surveillance of these infections is based on the HUS surveillance begun in 1996 by InVS, in collaboration with members of the Pediatric Nephrology Society.

Organization of HUS surveillance in France

This surveillance enables us to follow the geographic and temporal trends of HUS in children younger than 15 years in France, to determine their epidemiologic characteristics, and to detect case clusters. It is based on a network of 30 hospital pediatric nephrology departments throughout the country (figure 13) that have participated voluntarily in this surveillance since 1996. They notify InVS of HUS cases by mailing a form including the clinical, microbiological, and epidemiologic information.

STEC infections are confirmed serologically (search for anti-STEC antibodies in the blood), bacteriologically (culturing bacteria from the stool), or by detecting genes coding for Shiga toxins in the stool. A CNR has been named for *Escherichia coli* and *Shigella*,* together with a laboratory;** this should reinforce surveillance and improve diagnosis of STEC infections.

Figure 13: Geographic distribution of HUS surveillance network hospitals and its regional mean incidence annually in children younger than 15 years. France, 1996-2002.



Pediatric nephrology department in the following hospital centers: Amiens, Angers, Angoulême, Annecy, Besançon, Bordeaux, Brest, Clermont-Ferrand, Dijon, Kremlin-Bicêtre, Grenoble, Lille, Lisieux, Lyon (Debrousse, E. Herriot), Marseille, Montpellier, Nancy, Nantes, Nice, Paris (Necker-Enfants Malades, R. Debré, Trousseau), Reims, Rennes, Rouen, Saint-Etienne, Strasbourg, Toulouse, Tours.

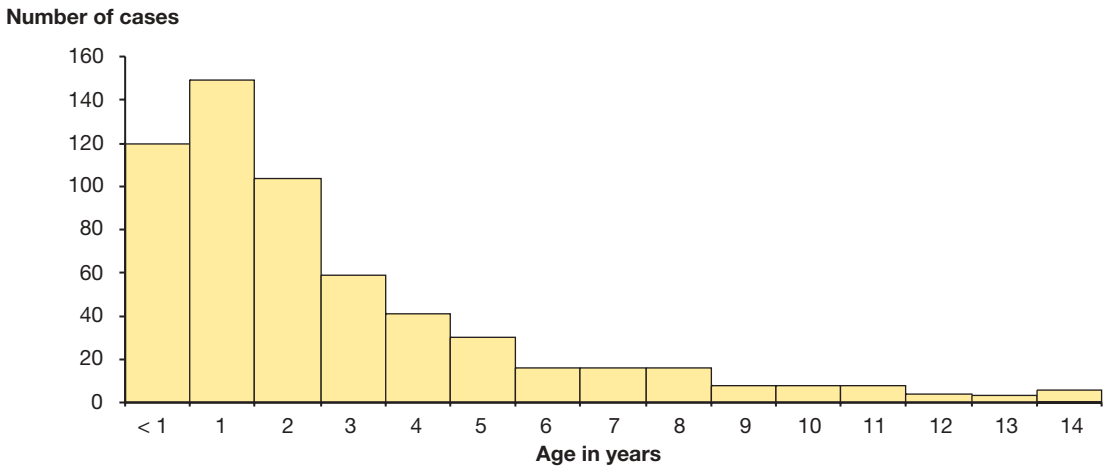
Trends in childhood HUS over the past seven years

Between 1996 and 2002, 591 HUS cases were reported. The annual number of cases reported has remained relatively stable, with a mean of 85 cases per year and a mean annual incidence of 0.74 per 100,000 children younger than 15. In the past seven years, therefore, the incidence of pediatric HUS has stayed stable in France at below 1 case per 100,000. This incidence is of the same order of magnitude as that observed in other European countries.

The geographic analysis (figure 13) shows that the annual mean incidence rate is highest in the regions of Brittany (1.5 per 100,000), Franche-Comté (1.4 per 100,000) and Champagne-Ardennes (1.4 per 100,000); the analysis by age (figure 14) found rates highest among children younger than 2 years (2.6 per 100,000, or 269 cases between 1996 and 2002). The median age of the children

* Pasteur Institute of Paris
** Bacteriology laboratory, Robert Debré Hospital, Paris

Figure 14: Distribution by age of HUS in children younger than 15 years. France, 1996-2002.



affected is 25 months (range: 17 days to 15 years) and 52% are girls. The temporal analysis shows that the majority of HUS observed in France occur as sporadic cases with an upswing every summer: nearly half the cases (49%) occur between June and September (figure 15).

Clinically, 94% of the patients had prodromal diarrhea, bloody for 57%. Seven children died from HUS between 1996 and 2002, for a mean case fatality ratio rate of 1.2%.

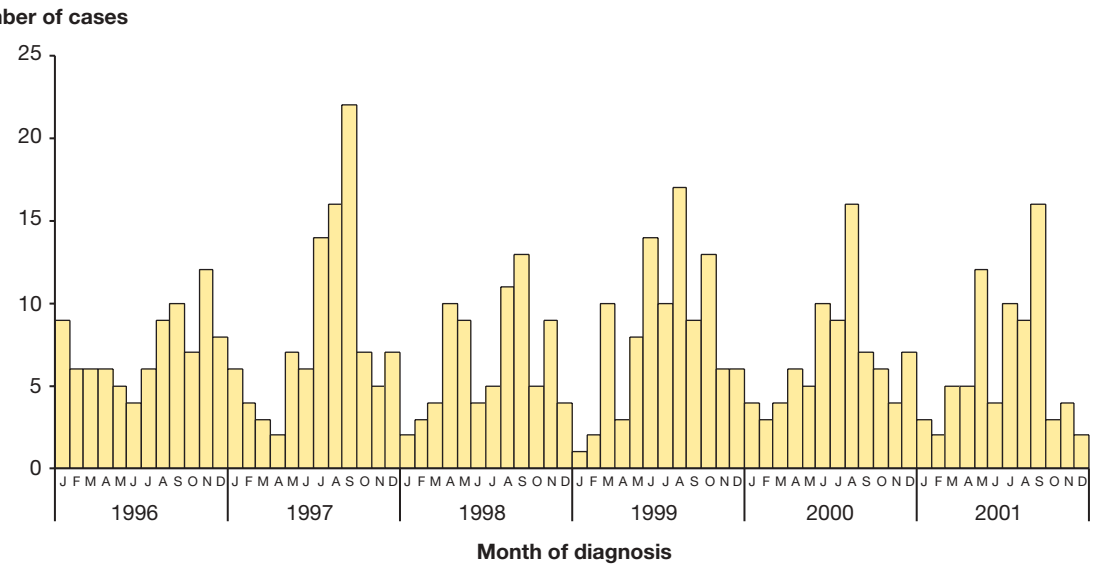
In half the 515 cases of HUS with an etiological diagnosis, disease was associated with a STEC infection; the O157 serogroup was identified most frequently.

Serogroup or serotype or serovar: category in which bacteria or viruses are classified according to their reaction in the presence of serum containing specific antibodies. This serologic variety is one subdivision of species (for example: *Escherichia coli* serogroup O157, meningococcus serogroup C, *Salmonella enterica* serovar Typhimurium).

STEC: its epidemic potential

STEC have demonstrated their epidemic potential in numerous epidemics abroad, sometimes large (United States, Japan, Scotland). In France, two food poisoning epidemics associated with ***Escherichia coli* serogroup O157 and *Escherichia coli* serogroup O148** were detected in 2000 and 2002. Investigation showed that the food responsible was undercooked merguez (lamb sausage) and mutton.

Figure 15: Distribution of HUS cases according to month of onset in children younger than 15 years France, 1996-2002



Risk factors for sporadic cases of HUS

In the absence of specific treatment for HUS and STEC infections, it is important to identify the risk factors for them so that appropriate prevention and control measures may be developed and implemented. We conducted a national case-control study for this purpose: 105 sporadic HUS cases reported in 2000 and 2001 were compared with 196 controls matched for age, sex, and place of residence.

The results indicate that in France consumption of undercooked ground beef, person-to-person transmission in families or institutions (following diarrhea), and contacts with cows between May and September are the principal risk factors for HUS associated with STEC infection in children younger than 15 years.

These results enable us to recommend simple measures aimed at preventing STEC infections in France:

- **Consumption of ground beef must be made safer. A major step is to conduct information campaigns on the risks, especially for children, of eating raw or undercooked ground beef and on the safety resulting from simply cooking it through (70° C for 2 minutes). Frozen ground beef must be cooked without being defrosted first (to avoid the risk of bacterial multiplication in the food).**
- **Hygienic measures for preventing fecal-oral transmission must also be pointed out, together with the need to reinforce them in the case of diarrhea, in institutions and in families.**
- **Contact between young children and cows and cow manure must be avoided.**

Other studies have also been undertaken to explore the risks associated with cow contacts and to identify the factors that might explain why the HUS incidence is higher in some French regions.

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Reinforcement of meningococcal infection surveillance: weekly monitoring and a warning tool for public authorities

Surveillance of invasive meningococcal infection is based on the mandatory reporting and description of all cases. In 2002, two events led InVS to reinforce this surveillance: the increase in the incidence of invasive meningococcal infections of serogroup C and the availability of new anti-meningococcus C vaccines.

Invasive meningococcal infections are rare (approximately 600 cases per year) but very serious diseases: approximately 15% result in death. They hit children in particular, especially infants and adolescents. Each suspicious case must be reported immediately to the district

Invasive: term used to describe a morbid process that rapidly invades an organism. Invasive infectious diseases are characterized by the isolation of the pathogenic agent in a normally sterile site. Meningitis (isolated in the cerebrospinal fluid) and septicemia (isolated in the blood) are the primary types.

health bureau (DDASS) to enable rapid control measures to be taken for the patient's contacts (antibiotic prescription for persons in very close contact with the case in the preceding 10 days). The DDASS inform InVS weekly of the number of these reports, enabling InVS to detect local increases in disease incidence early. Because invasive meningococcal infections are mandatory reporting diseases, the physician also completes a notification form and sends it to the DDASS, which validates it and forwards it to InVS. Analysis of these forms allows us to describe the epidemiology of these diseases and to study their trends over time.

The meningococci responsible for invasive infections most often belong to serogroup B. Less frequently, group C meningococci can also induce invasive infections with an even higher mortality rate; their incidence has recently increased in several European countries, including France, and demonstrated that some strains of this serogroup can induce epidemics.

Current epidemiologic situation in France

The incidence of laboratory-confirmed group C invasive meningococcal infections is increasing: between 1995 and 2001, it went from 0.14 to 0.41 case per 100,000 inhabitants. This situation results from an overall increase in the incidence of invasive meningococcal infections and an increase in the fraction due to group C meningococci: the proportion of group C meningococci in these infections thus rose from 23% to 35% in France between 2000 and 2001.

In this context, a substantial increase was noted in the incidence of invasive meningococcus C infections at the end of 2001 in the district of Puy-de-Dôme: in early 2002 this augmentation, localized in a central strip of the district including the city of Clermont-Ferrand, led to a local vaccination campaign of children aged 2 months to 20 years. At the end of the year, a similar action was undertaken in three contiguous districts in south-western France (Landes, Hautes-Pyrénées, and Pyrénées-Orientales), where the mean incidence rate of invasive meningococcus infections had reached 2.2 cases per 100,000 inhabitants (for the first 40 weeks of 2002), although it was only 0.26 for the rest of France during the same period.

Moreover, since early 2002 new conjugate vaccines against meningococcus C have become available: they may be administered from the age of 2 months, unlike the older polysaccharide vaccines that are generally ineffective in those younger than 2 years.
These new vaccines have proved their efficacy and their epidemiologic effect in the United Kingdom, where a national vaccination campaign for all children aged 2 months to 17 years began in November 1999.

Reinforcement of surveillance in France

Weekly charts, based on the notification forms, allow us to follow for each district the number and incidence of invasive serogroup C meningococcus infections and to identify early the situations for which local vaccination may be appropriate. Based on the vaccination trials in these four districts and on the European data, InVS has proposed the following criteria for an alert threshold at the district level: at least 5 cases, together with an incidence rate of at least 2 cases per 100,000 inhabitants over the previous 52 weeks.
If these conditions are met, a decision-aid group is convoked, consisting of representatives of the Vaccination Advisory Committee (CTV), the DGS, InVS, the meningococci CNR, and the concerned district health bureaus and regional epidemiology unit, as well as a physician expert in infectious diseases. The committee undertakes a more detailed analysis of the epidemiologic situation: it takes into account the recent dynamics of these infections in the district, compared with the regional and national situations, the clinical severity of the infections, and the identity of the meningococci strains circulating locally, to decide whether vaccination is appropriate.

The situation in Europe

An increase in the incidence of invasive meningococcus C infections has been noted in several European countries over the past few years and led five of them to introduce a new conjugate vaccine into babies' vaccination schedules and conduct campaigns for "catch-up" vaccination for older children. These countries are Great Britain, Ireland, Spain, Belgium, and the Netherlands, where the incidence of invasive meningococcus C infections ranged from 1.9 to 4.0 per 100,000 inhabitants at the time these decisions were made.

The High Council of Public Hygiene in France (CSHPF) validated these alert criteria at the end of 2002. Since then, InVS regularly transmits to the DGS the list of districts in which the incidence of invasive meningococcus C infections has exceeded 1 case per 100,000 inhabitants for the past 52 weeks. This new system adds extra input to the standard alert procedures at the DGS for worrisome epidemiologic situations, especially when this limit in any community exceeds the epidemic threshold defined by the July 2002 circular for invasive meningococcal infections (occurrence in less than 3 months of at least 3 cases from identical or undifferentiable strains and an attack rate ≥ 10 per 100,000). These new alert criteria for invasive serogroup C meningococcus infections are subject to modification and will be discussed again, when appropriate, depending on their epidemiologic trend.

BCG vaccination: InVS expertise and its role in the current non-revaccination policy

The French policy of BCG vaccination against tuberculosis relies on generalized primary vaccination of all children (except those with HIV infection) between birth and 6 years, and the systematic revaccination of subjects who are tuberculin-negative. Mandatory vaccination also applies to some occupational categories (jobs in health care and social work). Nonetheless, there is much we do not know or that remains controversial about the efficacy of BCG, its epidemiologic effects, and its place as a tool in the fight against tuberculosis. Within the European Union, only France and Greece today continue to impose generalized primary vaccination and France is now the only country to maintain systematic revaccination. This strategy is expensive and logistically cumbersome. Is it still relevant? Should it be maintained?

To attempt to answer these questions, InVS reviewed and analyzed the available data about BCG efficacy and the epidemiologic situation of tuberculosis in France (data from 1993-1999) to estimate the number of tuberculosis cases prevented by vaccination and by revaccination. This expert assessment was also intended to propose, where appropriate, alternatives to the current vaccination policy. This report was published in 2001.[1] Its principal results were the following:

– available studies confirm the efficacy of BCG vaccination in preventing extrapulmonary forms of tuberculosis in children (meningitis and disseminated tuberculosis). It probably has a real but lesser efficacy in preventing pulmonary forms as well. On the other hand, the efficacy of revaccination appears weak, if it exists at all (data from studies and experiments in other European countries);
– the epidemiologic situation in France comes close to meeting the criteria of the International Union Against Tuberculosis and Lung Diseases for considering the elimination of systematic vaccination of children;
– estimates from French data indicate that the practice of revaccination of tuberculin-negative subjects has an extremely limited impact. Even if revaccination were optimally effective, it would prevent only a dozen cases a year; its cessation would therefore lead, at worst, to an additional dozen cases annually. In a similar epidemiologic context, stopping revaccination in Finland had no negative effect on the incidence of childhood tuberculosis;
– for primary vaccination, the epidemiologic data favor targeting it to regions with an elevated incidence and to populations of children in high-risk settings.

The conclusion of this initial assessment was that: "It appears that we might consider, following a study of the epidemiologic situation of tuberculosis in France, modifying the policy of BCG vaccination.

It is thus appropriate to consider the suppression of revaccination at this time." Following this report, the Vaccination Advisory Committee asked InVS to form a working group including clinical and public health experts to provide the basis for a plan to halt BCG revaccination. This working group, organized by InVS, made recommendations about revaccination and post-vaccine tuberculin testing in children and about revaccination for adults in occupational settings.[2, 3]

Based on this expert assessment, in June 2002 the High Council of Public Hygiene decided in favor of ending revaccination of children and routine post-vaccination tuberculin tests, since their primary purpose is to determine whether revaccination is indicated. Similarly, the suppression of revaccination in tuberculin-negative adults subject to mandatory vaccination because of their job was adopted in November 2002, after a second CSHPF working group approved this recommendation. The Ministry of Health has ratified these provisions modifying French vaccination policy; implementation, however, requires the publication of new regulations, scheduled to be adopted in 2003.

The current epidemiologic situation also makes it possible to consider the usefulness of generalized primary BCG vaccination in children, but the decision in this case is much more complex. It requires a wide-ranging assessment covering not only the epidemiologic and medical aspects but also legal, economic, sociological and ethical considerations. Such an assessment will begin in 2003. In any case, the changes already begun must continue to provide France with a BCG vaccination strategy and an anti-tuberculosis policy more in line with current scientific data, international practice, and the current epidemiologic characteristics of tuberculosis in France.

Other recommendations of the vaccination working group led by InVS [2, 3]

– For children

The group stressed the importance of continuing tuberculin tests conducted by intradermal reaction to investigate tuberculosis cases and recommended the maintenance of screening for tubercular infection in children immigrating to France from countries with high tuberculosis levels, regardless of their vaccination status.

– For adults

Regular clinical and laboratory monitoring that permits the early detection of tuberculosis cases appears to be the most effective strategy for occupational tuberculosis control, together with prevention practices to prevent contamination in healthcare settings.

References:

1 - Impact épidémiologique d'une modification de la politique de vaccination par le BCG en France. Revue de la littérature et analyse des données disponibles. Rapport InVS. Juillet 2001

2 - Lévy-Bruhl D, Barrault Y, Decludt B *et al.* BCG et tests tuberculiniques : évolutions de la politique vaccinale française. *In* : Tuberculose en France : la situation aujourd'hui. *BEH* N°10-11/2003 (numéro thématique) : 61-3

3 - Lévy-Bruhl D, Barrault Y, Decludt B *et al.* Faut-il arrêter le BCG ? *Méd Mal Inf* 2003 ; 33 : 188s-192s

Health impact of air pollution: assessment of regional air quality plans and their evaluation studies

InVS and the regional epidemiology units examined the regional authorities' consideration of health aspects in regional air quality plans and in the studies evaluating the health impact of air pollution.

The 1996 statute on air and rational energy use (L. 30 December 1996) requires each region in France to develop a regional air quality plan (RAQP) that must be based, among other things, on an assessment of the health effects of air pollution. To assist local authorities in this mission, InVS and the West regional epidemiology unit developed a methodological guide for the conduct of health impact assessments of urban air pollution (HIA-AP) in different local contexts: this 1999 guide, based largely on the results of the first phase of an air and health surveillance program in nine French cities (Psas-9), considers the short-term health effects of air pollution in urban areas.*

Once the first RAQPs were nearly all completed, InVS and the regional units sought to assess the extent to which this evaluation tool aided the decision-making process and to examine the influence of local health- and pollution-related factors. To improve the methodological support that InVS and the regional units can furnish local participants, we collected information about their expectations. We analyzed the published RAQPs (their health sections) and surveyed the local participants working in the field of air and health in the 21 regions that developed RAQPs, that is, those working in: the regional health bureaus, the regional epidemiology units, the regional offices of industry, research and the environment (DRIRE), the approved air quality surveillance groups (AASQA), the regional offices of the environmental and energy agency (ADEME), the regional health observatories (ORS), regional councils, and some environmental protection associations.

Problems and expectations

Overall, the RAQPs show the inadequacy of the information and local studies needed for a regional assessment of the health effects of air pollution. Because of their ease of use, the HIA-AP were the only studies performed in many regions: they were conducted in 13 regions, and 10 are currently underway. The principal effect of these local studies, as observed during the survey, was to increase the sensitivity of elected officials to the issue of air and health.

Other more specific interests emerged from the RAQPs: the desire to assess the health impact of pesticides, pollens, and pollution in vulnerable areas such as industrial zones.

What is expected from InVS involves these specific topics but also the more general aspects of information, collaboration, and methodology. They can be summarized in four principal desires:

– simplification of information about InVS study results to make them more accessible to more people (the general public and elected officials);
– better collaboration between the AADQA and public health agencies (InVS, regional epidemiology units, and DRASS) to promote data on air quality;
– information about the health impact of new pollutants (pesticides, benzene) and volatile organic compounds (VOC, PM2.5, and others);
– definitions of new health indicators for the HIA-AP to reflect effects of air pollution (asthma, allergy, bronchitis) less drastic than those currently studied (mortality and hospitalization).

*An updated guide to the assessment of the short- and long-term health impact of urban air pollution was published in March 2003.

The procedure proposed by InVS to assess the health impact of air pollution has proved its usefulness in sensitizing local authorities and improving regional knowledge on this subject. Nonetheless, InVS must continue to develop its expertise about other pollution and health indicators in order to respond to new regional worries and must improve how regional policies take the results of these studies into consideration.

Surveillance of drowning deaths: evaluation and prevention

In France, epidemiologic surveillance of drowning consists of an annual survey conducted by InVS in collaboration with the Ministry of the Interior's civil defense and safety division. More than ten districts, all among the most affected by drownings in swimming pools, volunteered to participate in the first survey, *Drowning 2001*. Its results helped lead to the adoption of a temporary standard for safety barriers around private pools. In 2002, InVS and the Ministry of the Interior set up a more ambitious program to collect epidemiologic data on drowning; it aimed to cover all the drowning deaths in France that summer. The Drowning 2002 survey took place between June and September 2002 throughout France.

Drowning is responsible for more than 500 deaths each year in France. Survivors of near-drownings sometimes suffer very severe sequelae. Numerous studies have shown that many deaths from drownings and sequelae from near-drownings can be avoided. This explains the interest and importance of the Drowning 2002 survey, which should complete French epidemiologic data on this important public health problem.

The figures from the summer of 2002: 2826 accidental drownings caused 252 deaths.

The Drowning 2002 survey recorded, overall, 3141 drownings or near-drownings, 90% accidental; 409 deaths ensued, 252 (62%) from accidental drownings.

Two thirds of the accidents occurred among men, and 49% in persons aged 6 to 24 years. The distribution of these accidents according to type of site (table 5) shows that although drowning incidents in the sea were the most frequent (84.5%), they were less often fatal: professional lifeguards and first aid prevented 75% of these incidents from causing death or even necessitating hospitalization. On the other hand, drowning incidents in rivers and lakes caused death more often. Overall, 121 drowning incidents were reported in private pools, 25 (21%) fatal.

About the Drowning 2002 survey

• ***Definitions:***
– **Drowning** most often causes acute asphyxia due to the penetration of water in the airways. Strictly speaking, drowning involves death.
– **Near drowning** is an accident of the same type that does not cause death.
In this paragraph, presenting the Drowning 2002 survey and its results, the term **drowning** is used in the broad sense of the term, **whether or not death followed**, to designate an event involving "suffocation due to immersion in water." It thus covers fatal drownings and near-drownings.

• ***Sources that participated in the collection of information in the field:***
– those who assisted or dealt with the victims: rescuers from district fire and rescue brigades, emergency paramedical and ambulance crews, lifeguards, police river brigades, and other organized rescue groups;
– physicians and caregivers in hospitals treating drowning victims;
– local staff of the following Ministries: Interior, Sports, and Health; the Consumer Safety Commission, the DDASS, and the regional epidemiology units.

Table 5: Accidental drowning, whether or not death ensued. Distribution by place of drowning. DROWNING 2002 survey

	Drowning, whether or not death ensued N=2826		Drowning followed by death N'=252	
	n	%	n' (% of n) *	%
Pools				
– private family	92	3.2	21 (23%)	8.3
– private institutional	29	1	4 (14%)	1.6
– public/private, fee access	53	1.9	11 (21%)	4.4
Rivers	128	4.5	75 (59%)	29.8
Lakes and ponds	96	3.4	42 (44%)	16.7
Sea (victims died or hospitalized)	387	13.7	87 (4%)	34.5
Sea (other)	2001	70.9		
Other (bathtubs, etc.)	37	1.3	11 (30%)	4.4

* fatality rate

The victims' characteristics and the circumstances varied greatly by place:

– in private pools, 62% of the incidents involved children younger than 6 years. The precipitating circumstances were: lack of surveillance (38%), falls (23%), and not knowing how to swim (14%);
– in public or private pools charging a fee for access, two thirds of the incidents occurred in those younger than 20 years. The most common circumstances involved: a health problem (faintness, epilepsy, or other, 35%), not knowing how to swim (19%), lack of surveillance (16%), and risk-taking behavior (12%);
– in rivers, 71% of the drownings occurred in adults (25 years or older). Most often these drownings were preceded by a fall (35%), alcohol consumption (21%), or a boating accident (14%);
– in lakes and ponds, 59% of the victims were adults (25 years or older). The most common circumstances involved a health problem (faintness, epilepsy, or other, 33%) and falls (13%);
– at sea, 44% of the incidents leading to death or hospitalization occurred among adults older than 45 years, most often associated with a health problem (cardiac malaise or other, 23%), strong currents (19%), exhaustion (17%), swimming in forbidden areas (7%).

The results of this survey made clear for the first time on a national level the number and diversity of drowning incidents according to the setting (e.g., pool, sea), the precipitating events, and the victims' characteristics. These findings have helped to legitimate and reinforce drowning prevention campaigns. This surveillance will also make it possible in the future to assess the consequences of the pool safety law adopted in early 2003.

References:

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Ermanel C, Thélot B. Réseau de surveillance des noyades (Resun). Surveillance épidémiologique des noyades accidentelles en France au cours de l'été 2002. *BEH* n°28/2003 : 125-27

Occupational cancers: first approach towards quantification

The impact of working on health status is important, unequal according to social class, and costly to society. It is nonetheless largely underestimated and poorly recognized in France. The Court of Auditors 2002 report pointed out the substantial underassessment of the cost of occupational diseases in the French social security system. The InVS occupational health department conducted an expert assessment and review of this subject in 2002, commissioned by the committee assigned to assess triennially the proportion of conditions caused by workplace accidents and occupational diseases (AT-MP) in order to update the accounts between these different branches of the health insurance system (article L.176-2, Social Security Code).* This work by InVS represents an initial approach to the quantification of occupational cancers in France.

Although many diseases are due at least in part to occupational exposures, it is essentially only for cancers that epidemiologic data, either international or French, are available to enable a sufficiently reliable estimation of the proportion (or fraction) and the number of cases attributable to these occupational factors in the French male population. For this reason, this InVS study concerns only a limited number of cancers – those officially recognized as occupational diseases in France (by the Social Security administration), with a known causal relation to an occupational carcinogenic hazard listed in IARC's (International Agency for Research on Cancer) group 1 and for which sufficient and credible epidemiologic data exist. For all these reasons, we studied only the following occupational cancers (table 6):
– bronchopulmonary cancers, which account for the second largest number of incident cancers and the most cancer deaths among men in France, and for which some occupational risk factors, such as asbestos exposure, are very clearly established;
– pleural mesothelioma, for which asbestos is the only recognized risk factor and which has since 1998 been the subject of a national surveillance program in France;
– bladder cancer, whose incidence and mortality have increased regularly in France since 1975;
– cancers of the nose and paranasal sinus, which are rare, but whose principal known risk factors are occupational, in particular, exposure to wood dust, the carcinogenic effects of which are well established;
– leukemia, in which benzene exposure has long been known to play a role.

Estimate of the annual number of cases attributable to occupational factors

Only sparse data are available for the direct assessment of cancer cases attributable to occupational exposure in France. Nonetheless, some of the information available enables a reasonable estimate of the cancers and hazards studied (sidebar Methodological Aspects). Table 6 summarizes them; it also shows the number of cancers for which workers' compensation was paid during 1999.

* In 2002, this committee was chaired by Madame Lévy-Rosenwald, Master Counselor at the Court of Auditors; it submitted its report in September 2002.

Methodological aspects

Because most diseases have multifactorial causes, the attributable risk fraction (ARF) for a given factor assesses the proportion of cases of a disease explained by exposure to this risk factor in a specific population (for example, the French population).

It is usually calculated according to the following formula: ARF = Pe (RR-1) / [Pe (RR-1) + 1], where RR is the relative risk of the risk factor for the disease studied (risk of contracting the disease for the subjects exposed to this factor compared with those not exposed), and Pe the proportion of persons exposed to this factor in the population considered. Knowledge of the total number of cases of the disease in the population (N) then enables us to calculate the number of cases attributable to the factor considered (NF), according to the formula: NF = ARF x N.

In this work, the data used to calculate the ARF come from different sources and vary in type according to the cancers and hazards studied:

– We were able to use French data to calculate the ARF directly for pleural mesothelioma and asbestos (national surveillance program data);

– We were able to use French data to calculate the ARF according to the formula above for lung cancers and asbestos, and for nasal-sinus cancers and wood dust. In both cases, the exposure data concern the lifetime prevalence of exposure of the French male population concerned;

– International data were used to estimate the ARFs for the other cancers. We used data only from countries comparable to France in their level of industrialization and from studies whose methodological criteria were considered sufficiently rigorous.

To estimate the number of cancer cases attributable to the occupational risk factors studied (NF), we used the most recent cancer incidence data published for France (the N in the formula NF = ARF x N): those from 1995 for cancers of the lung and bladder and for leukemia, 1997 for nose and paranasal sinus cancers, and 1998 for pleural mesothelioma (legend, table 6).

We thus estimated the annual number of bronchopulmonary cancers in men in France attributable to occupational exposure (to a carcinogen) at between 2433 and 5427 incident cases, depending on the hypotheses considered and based on the attributable fractions reported in international publications. When we apply the same attributable fractions to the CepiDc 1999 data, exposure to an occupational risk factor appears to be responsible for between 2713 and 6051 lung cancer deaths in men.

In view of the available data on the prevalence of asbestos exposure in France, the estimated fraction of bronchopulmonary cancers attributable to this hazard is 12% in men aged 55 years or older and 5% in those aged 35-54 years. This allows us to estimate the overall number of incident cases at more than 2000. The comparison with estimates based on international data (from 1871 to 3742 incident cases) indicates that this estimate is quite realistic. According to CepiDc data, the occupational asbestos exposure accounts for 2086 to 4172 deaths from bronchopulmonary disease, depending on the risk fraction applied.

Pleural mesothelioma attributable to occupational asbestos exposure in French men is assessed at around 550 new cases a year (537-578) according to the national surveillance data, very close to the estimates obtained with the international data.

The only occupational risk factors recognized in France for **bladder cancer** are exposure to some aromatic amines and to tar, oil, and pitch during the manufacture of aluminium by continuous anode electrolysis. Because no lifetime exposure data for men are available in France for these two hazards, the attributable fractions used are those from international publications. They allow us to estimate the annual number of new cases of bladder cancer in the French male population that are attributable to occupational exposure at between 625 and 1110.

Among the sinus and nasal cancers associated with wood dust exposure, the only ones considered to be occupational diseases are cancers of the ethmoid and the paranasal sinuses (Occupational disease table n°47, which does not include cancers of the nasal cavity). Primary cancers of the ethmoid and the paranasal sinuses related to work with nickel matte are also considered (Occupational disease table n°37bis). The existing data on the prevalence of exposure to wood dust in France enable us to estimate at 113 the number of new cases of nasal and paranasal sinus cancers attributable to this occupational risk factor (ARF of 45%) in the French male population.

Ethmoid: irregularly shaped bone of the base of the skull, the upper portion of which forms the ceiling of the nasal cavities and the lateral masses of which help form the internal walls of the eye-socket and the external wall of the nasal cavities.

According to estimates from the international data, 112 to 413 new **leukemia** cases each year in the French male population appear to be attributable to occupational factors.

Table 6: Occupational cancers recognized by the Social Security Administration*: number of cases for which compensation was paid in 1999, and estimates of the number of incident cases attributable to these factors in the French male population, for the cancers and hazards specifically studied (all health insurance funds together)

		OD receiving compensation from SS (a)		Number of attributable cases among men in France		
				Application of attributable AFs		
				international		French
Cancer	**Product implicated**	**OD Table**	**1999 (a)**	**Low hypothesis**	**High hypothesis**	
Leukemia	Benzene	4	16	–	–	–
Leukemia	Ionizing radiation	6	11	–	–	–
Total leukemia	**–**	**–**	**27**	**112 (b)**	**413 (b)**	**–**
Bronchopulmonary cancer	Ionizing radiation	6	7			
Bronchopulmonary cancer	Chromic acid	10ter	6			
Bronchopulmonary cancer	Coal tar	16bis	5			
Bronchopulmonary cancer	Arsenic	20bis	1			
Lung cancer following benign lesions	Asbestos	30 C	107			
Bronchopulmonary cancer	Asbestos	30bis	331	1871 (b)	3742 (b)	2009 (b)
Bronchopulmonary cancer	Nickel	37ter	1			
Bronchopulmonary cancer	Cobalt and tungsten	70ter	0			
Bronchial cancer	Bischloromethyl ether	81 A	0			
Total bronchopulmonary cancers	**–**	**–**	**458**	**2433 (b)**	**5427 (b)**	
Pleural mesothelioma	Asbestos	30 D	267	537 (c)	599 (c)	537–578 (c)
Other primary pleural tumors	Asbestos	30 E	20			
Peritoneal mesothelioma	Asbestos	30 D	11			
Pericardial mesothelioma	Asbestos	30 D	2			
Total mesotheliomas	**Asbestos**		**310**			
Bladder cancer	Aromatic amines	15ter	4	–	422	–
Bladder cancer	Coal tar	16bis	3	–	148	–
Total bladder cancers		**–**	**7**	**625 (b)**	**1110 (b)**	**–**
Cancer of the ethmoid and paranasal sinus	Nickel	37ter	0	18 (d)		–
Cancer of the ethmoid and paranasal sinus	Wood	47	67	40 (d)	–	113 (d)
Total nasal and paranasal sinus	**All factors**	**–**	**67**	**60 (d)**	**102 (d)**	**–**
Hepatocellular carcinoma	Hepatitis B/C	45	0			
Bone sarcoma	Ionizing radiation	6	0			
Angiosarcoma	Vinyl chloride	52	0			

OD. occupational disease
(a) quarterly statistics for workplace safety – CnamTS – Paris, March 2002 – final data entered 21.12.2001, pages 39-56.
(b) Estimated number of cases attributable to occupational factors for incident cases 1995. Source: Le cancer en France, incidence et mortalité, situation en 1995, évolution entre 1975 et 1995, Francim, ministère de la Santé, Paris.
(c) Estimated number of attributable cases based on the incident cases estimated by the national program for mesothelioma surveillance, for 1998, BEH n°03/2002, 2002 : 11-13.
(d) Estimated number of attributable cases for the incidence rate estimated by IARC for 1997: Cancer incidence in five continents, vol VII, Edt DM Parkin, SL Whelan, J. Ferlay, L. Raymond and J. Young. IARC Scientific Publications, n°143, Lyon 1997, p 989.

Comparison of cases indemnified as occupational diseases by the Social Security Administration

Table 6 shows clearly that only a very small fraction of the occupational cancers studied are indemnified as occupational diseases by the Social Security Administration; and the reader must bear in mind that we studied only cancers for which compensation is paid and adequate epidemiologic data exist. This table thus illustrates the extent of this discrepancy and undercompensation in France. Even if we take into account workers affiliated with other health insurance funds, by reducing these estimates by 20%, there would nonetheless be more than 1600 bronchopulmonary cancers and 430 to 460 cases of pleural mesothelioma that should have been indemnified by the Social Security Administration because of their association with occupational asbestos exposure. This undercompensation of occupational cancers appears even greater to the

extent that the incidence of most of the cancers studied tends to increase regularly, so that estimates based on older data are even more substantially underestimated.

Moreover, we note that the role of occupational factors in the onset of cancers is not at all well understood and that the concept of "avoidable cancers" used by decision makers never includes occupational diseases. Rare cancers very strongly associated with a specific hazard and well known to specialists (asbestos and wood dust) are somewhat less ignored. The more frequent a cancer is, however, and the more multifactorial its etiology, the less often its occupational source is considered: this is shown clearly by the treatment of bronchopulmonary cancers due to occupational exposures.

The reasons for this underrecognition and undercompensation are not clearly understood, nor can we yet identify the parts of the French system of occupational disease recognition that may be involved: poor patient information or his (or his family's, in the case of rapid death) refusal to apply, general practitioners' ignorance of occupational etiology and reporting procedures, excessively restrictive tables (delay in treatment, too-short lists of exposed occupations) or their unduly strict application by Social Security offices. Although little epidemiologic or sociological work is available on this subject, some data nonetheless indicate that, at least for some cancers, the bottleneck occurs especially before Social Security involvement, among patients and their general practitioners.

This first attempt to quantify occupational cancers in France shows the extent of their underestimation and undercompensation. The efforts undertaken in recent years to provide information to workers, retirees, and physicians about indemnification of occupational diseases must be continued, together with the exploration of the role of occupational hazards and their health impact. In this framework, Inserm is beginning the Icarus study to examine the occupational risk factors for cancers of the lungs and upper aerodigestive tract, both especially frequent in France. Moreover, a network bringing together university-based occupational medicine institutes, Inserm researchers specializing in the area, and the InVS occupational health department is working to develop a job-exposure matrix that will enable lifetime occupational exposure to chemicals to be assessed in the French population. Other studies in preparation at InVS will analyze mortality by cause (disease) and by occupation. This work should help improve our knowledge of the important public health problem of occupational safety.

Women and occupational risks

This study concerned only men because current data on women's occupational exposure to physicochemical carcinogenic hazards are still very insufficient. Moreover, the statistics furnished by CnamTS do not now allow us to determine the sex of patients receiving compensation for occupational diseases.

Nonetheless the share of occupational factors in cancer among women is very probably substantially underestimated, as it is for men. An Inserm study currently in preparation should soon provide more information about this subject.

Reference:

Imbernon E. Estimation du nombre de cas de certains cancers attribuables à des facteurs professionnels en France. InVS Report, March 2003

Suspected childhood cancer cluster in Vincennes: investigation and epidemiologic follow-up

Late in 1999, three cases of cancer were reported in children attending the Franklin Roosevelt nursery school in Vincennes, a school built on a site that previously held a Kodak industrial plant. Specifically, two cases of leukemia and one of rhabdomyosarcoma were diagnosed between March 1995 and May 1999. In May 2000, after three environmental measurement campaigns in the school and consultation with a group of experts, InVS submitted a report concluding that neither the environmental information nor the epidemiology of the diseases observed justified the suspicion of an association between attendance at the school and the onset of cancer. A year later, the report of a fourth case in the same school (sarcoma, diagnosed in February 2001) strongly upset the local population and led the DGS to request the convocation of a scientific committee, chaired by an InVS representative, to conduct new health, environmental, and epidemiologic investigations. A monitoring committee was also established, chaired by the Prefect of Val-de-Marne and including representatives of the scientific committee, the DDASS, parents, local residents, the Franklin Vigilance Collective, Kodak, the municipality, and the ministries of Health and of the Environment. The mayor of Vincennes decided to transfer the school to a different site, away from the former Kodak plant, at the beginning of the September 2001 school year to protect the children from media pressure.

Epidemiologic investigations

Inserm and InVS are conducting two epidemiologic studies, which will be completed at the end of 2004, one among the 1205 children who have attended the Franklin Roosevelt school since it opened in September 1990 and who will be followed through the age of 15 years or until 31 December 2004 (the cohort study), the other among the population of children in the South Vincennes neighborhood, the area where all the cases lived and which constitutes the school catchment area (incidence study). These investigations required Inserm to construct a childhood cancer registry retrospectively for the Val-de-Marne for 1990-1999. This registry furnishes the reference rates for the general population to which the data in the epidemiologic studies must be compared for interpretation. The childhood cancer registry of the Val-de-Marne included 363 cases counted with excellent exhaustiveness (estimated at 99.7%), indicating an extremely intensive search for cases (average of 3.5 sources per case).

The two epidemiologic studies have confirmed the reported excess of cases: for the 1995-1999 period and relative to the rest of the Val-de-Marne, the cancer incidence rate was higher than expected in the cohort of Franklin school students (3 cases observed compared with 0.4 case expected) and in children in the South Vincennes neighborhood (4 cases observed compared with 0.55 case expected for those aged 0-4 years, and 4 cases observed compared with 0.87 case expected for those 0-14 years). We note that the number of cases expected for this period was 30% higher than the number expected for earlier periods, simply because of the local population increase. The two surveys were always consistent and showed no excess of cases in the pre-alert period (1990-1994).

The incidence study counted 13 cases of cancer among children living in Vincennes. A single case occurred during the 1990-1994 period and 12 cases between 1995 and 1999, 4 of them in South Vincennes: of these 4 cases, 3 are part of the initial school cluster, while the 4th occurred in a newborn. No excess was seen in the rest of the town of Vincennes (outside the South Vincennes neighborhood).

For the post-alert period (2000-2004), the cohort study furnishes partial data, through 31 December 2001, which are also reassuring (no excess of cases). It also shows that no new case of childhood cancer has been added to the four cases already known.

Cluster: unusual aggregation, real or perceived, of health events that are grouped together in time and space.

These two studies therefore showed a cluster of cases that, at this stage, seems clearly limited in time and space. Continued epidemiologic surveillance of the children through 2004 should provide information for the entire post-alert period, that is, the five years following the alert.

Role of environmental investigations in the epidemiologic assessment

The results of the study comparing concentrations in the various possible exposure media in South Vincennes, analyzing samples of groundwater, deep soil, and soil gases, and quantitatively evaluating the health risks will be published in June 2003. When the report was submitted (June 2002), the environmental testing in the school and the neighborhood had not revealed any exposure to high doses of ionizing radiation, the only exposure established with certainty as a cause in several types of childhood cancer. Nor did they uncover the presence of any potential risk factor, that is, of any known or suspected carcinogen for other types of cancer and present on the site at concentrations greater than those normally encountered in the environment. Moreover, the interview with the families of the four schoolchildren showed that they were not all born in the South Vincennes neighborhood, had not attended the same daycare center, and had not played on the same land, that their families had no particular occupational exposure in common, and that their homes did not, according to current knowledge about the site, share any particular exposures. One of the South Vincennes children diagnosed during the alert period had not attended Franklin Roosevelt school. Accordingly, the expert advisory group had no information suggesting that an approach of the "Exposed/Not exposed" type might be useful to compare the risk of childhood cancer measured in an exposed area with that in a non-exposed area.

Should the search for a cause other than chance for this excess have continued?

An extremely strong carcinogen would have been necessary to cause the excess seen in the 1995-1999 period; the only known candidates – antineoplastic chemotherapy and high doses of ionizing radiation – were known to be inapplicable here. The expert advisory group therefore concluded that no known risk factor was likely to explain the excess observed during the alert period and that if an unknown risk factor was involved, it was not specific to the site and therefore a case-control study would not help to discover it.

Case-control study: study comparing the frequency of a past exposure among a group of subjects affected by the disease under study ("cases") and a group of subjects who do not have the disease ("controls"), with the aim of assessing a possible association between the disease studied and exposure.

Epidemiologic research for this investigation

– To construct a Val-de-Marne registry and for the incidence study

Consultation of:

- all cancer centers, university hospital centers in Ile-de-France, and hospital centers in Val-de-Marne:[a] approximately 7000 cases reviewed, with no duplicates;
- approximately 360,000 pathology reports;[b]
- specialists in private practice in Val-de-Marne;[c] 442 mailings, 22 reports;
- the 4 health insurance funds in Val-de-Marne: 192 reports;
- the national registry of childhood leukemia and lymphoma;
- the hospital medical informatics departments and CepiDc at Inserm (the latter 2 sources, anonymous, were used as backup).

(a) Institut Curie, Institut Gustave Roussy, Hôpital Armand Trousseau, Hôpital Necker - Enfants Malades, Hôpital Robert Debré, Hôpital Saint-Vincent de Paul, Hôpital Saint-Louis, Hôpital Jean Verdier, Hôpital Ambroise Paré, Hôpital Antoine Béclère, Centre hospitalier Intercommunal de Créteil, Hôpital du Kremlin-Bicêtre, Hôpital des Quinze-Vingt, Centre hospitalier Intercommunal de Villeneuve Saint-Georges, Hôpital Sainte-Camille de Bry-sur-Marne.
(b) Hôpital Jean Verdier, Hôpital Ambroise Paré, Hôpital Avicenne, Hôpital Antoine Béclère, Hôpital Beaujon, Hôpital Louis Mourier, Centre hospitalier intercommunal de Créteil, Hôpital Henri Mondor, Hôpital du Kremlin-Bicêtre, Fondation ophtalmologique Rothschild, Hôpital Armand Trousseau, Hôpital de la Pitié-Salpétrière, Hôpital Bichat, Hôpital Cochin, Hôpital Européen Georges Pompidou, Hôpital Hôtel Dieu, Hôpital Lariboisière, Hôpital Necker-Enfants Malades, Hôpital des Quinze-Vingt, Hôpital Raymond Poincaré, Hôpital Robert Debré, Hôpital Saint-Antoine, Hôpital Saint-Louis, Hôpital Saint-Vincent de Paul, Hôpital Tenon, Institut Curie, Institut Gustave Roussy, Hôpital Paul Brousse, Centre hospitalier intercommunal de Villeneuve Saint-Georges.
(c) specializing in dermatology, ophthalmology, pediatrics, ENT, orthopedic surgery, endocrinology, nephrology, urology, oncology, internal medicine, anatomopathology, and radiation therapy.

– For the cohort study

- identification of 1205 children who had attended Franklin Roosevelt school between 1 September 1990 and 30 June 2001, based upon the school registry, kept by its directors, and the municipality's school enrolment files;
- establishment of the list of current addresses, found for 93% of them in the files of public and private schools in Vincennes and in the elementary schools of Paris, metropolitan and overseas school districts, by the school health departments, health insurance funds, and students' parents;
- mailing of a questionnaire to the parents of the children in the cohort (except for the known cases): 1038 responses were received;
- for the 164 children whose parents did not respond or who were not identified, verification that they did not appear in either the Val-de-Marne childhood cancer registry or the national registry of childhood leukemia and lymphoma.

The report on these epidemiologic investigations, submitted in June 2002, concluded that "[i]f an exposure of potential risk exists, it remains to be discovered, for South Vincennes as for everywhere else. Today particularly active French and international research is trying to distinguish from chance new risk factors against which prevention might be possible.

It is impossible to distinguish the role of chance and of some unknown risk factor in the excess of cases observed here." The population of children will be followed up routinely through the end of 2004, as initially planned. The results of the studies for the 1990-1999 period do not suggest the need for additional epidemiologic investigations.

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Clavel J, Fourme E, Hartman O, Lacour B, Jougla P, Quénel P. Analyse d'un agrégat de cas de cancers dans l'école Franklin Roosevelt de Vincennes. Rapport final – mai 2002. Rapport Inserm, InVS, juillet 2002.

Gastroenteritis epidemic in Dracy-le-Fort: contamination of the drinking water network

On 20 September 2001, SOS-médecins of Chalon-sur-Saône (a company providing physicians for emergency house calls) reported to the DDASS of Saône-et-Loire several cases of acute gastroenteritis that suggested an outbreak of food poisoning in a hotel in the town of Dracy-le-Fort. The initial investigation, conducted onsite the same day, revealed that the gastroenteritis concerned not only hotel customers but also staff, the local primary school, the local inpatient clinic, and, indeed, the entire community. The extent and character of this epidemic suggested that the drinking water network might be contaminated, since it was the most probable common denominator in terms of exposure. That afternoon, after taking water samples for analytic purposes, the DDASS issued instructions forbidding the consumption of tap water for drinking; these instructions were disseminated that day and the next to the local population. Simultaneously with other measures to deal with the health risk, the DDASS of Saône-et-Loire requested the Center-East regional epidemiology unit to conduct an epidemiologic and environmental expert assessment in collaboration with InVS.

Dracy-le-Fort is a rural municipality of 1100 inhabitants. Part of a water distribution unit serving 26 municipalities, or approximately 16,000 persons, it is located at the end of the network. The Center-East regional epidemiology unit and InVS conducted several types of investigations for descriptive and analytic purposes: a survey of general practitioners in the area of the water distribution unit, two retrospective cohort surveys, one among 33 clients of the hotel in Dracy-le-Fort (participants in a training course), the other among the town's general population (all households listed in the telephone book), microbiological analyses of stool samples from the patients in Dracy-le-Fort, and an environmental survey. These investigations enabled us to confirm and specify the epidemic's characteristics, determine the role of tap water in its onset, identify the infectious agents responsible, and establish their origin and the circumstances of the contamination so that we could recommend appropriate control and prevention measures.

Waterborne epidemic limited to the town of Dracy-le-Fort

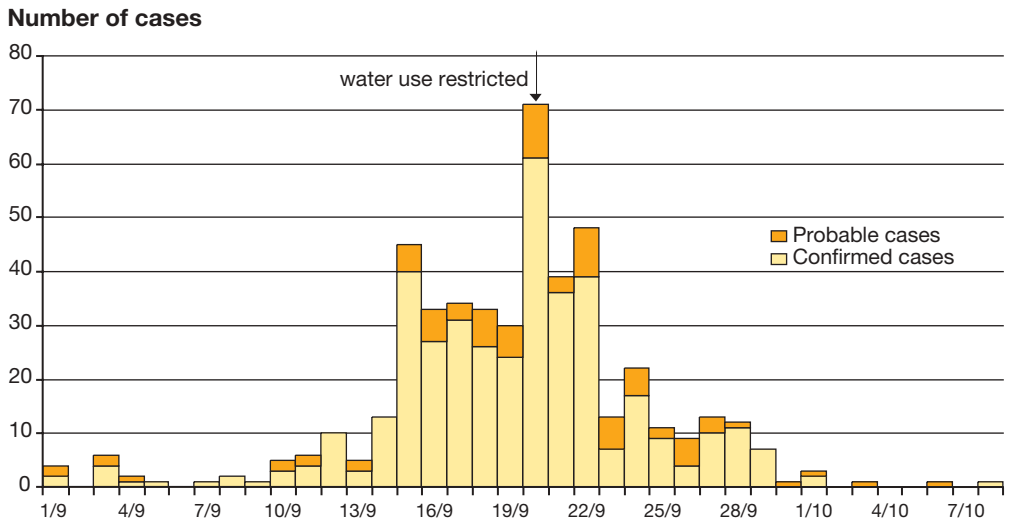
The survey of general practitioners revealed an increase in the number of consultations for gastroenteritis from 14-26 September 2001 (13% of total consultations compared with 1% from 1-13 September) and the high proportion of Dracy-le-Fort inhabitants in this phenomenon. This confirmed the gastroenteritis epidemic and reinforced the waterborne hypothesis, since its geographic range was limited to this town.

The telephone survey of hotel customers ruled out a foodborne source. It revealed an association between consumption of tap water and the onset of acute gastroenteritis, with a high attack rate (79% of the clients became ill).

Attack rate: proportion of persons becoming ill among the exposed population (in this case, those who drank the contaminated water) during an epidemic.

The cohort study in the general population, that is, 291 households in Dracy-le-Fort with 781 persons questioned, confirmed the role of tap water in the onset of gastroenteritis; the risk increased with the quantity of water drunk and the attack rate reached 62% (397 confirmed and 86 probable cases, that is, 483/781). The epidemic curve indicates a progressive augmentation over 9 days beginning on 12 September, peaking on 20 September, and diminishing rapidly thereafter – a change perceptible 4 days after tap water was banned (figure 16). These results, especially the high attack rate, indicate a massive isolated contamination of the drinking water supply network in Dracy-le-Fort.

Figure 16: Distribution of cases among the population of Dracy-le-Fort questioned according to the date of symptom onset (Dracy-le-Fort, Saône-and-Loire, September 2001)



Confirmed cases: diarrhea (≥ 3 liquid stools per day) or vomiting;
Probable cases: diarrhea (1-2 fluid stools per day) or abdominal pain

These investigations underlined the important impact of this epidemic from the health, social, and economic points of view: physician consultation exceeded 50%, 45% of the definite cases were confined to bed for more than 3 days; overall, 794 days of sick time were used.

***Cryptosporidium*, cryptosporidia**: sporozoa parasites pathogenic in humans and animals, which develop inside cells of the gastrointestinal tract and airway. Ubiquitous, frequently encountered among domestic herds, this agent causes cryptosporidiosis, which can be very serious in patients with AIDS. *Cryptosporidium* is the name of a genus (group of species), and cryptosporidia are the forms (points in its life cycle) in which it is disseminated into the environment.

A *Cryptosporidium* epidemic

The stool analyses searched for bacteria, viruses, and parasites and identified several pathogens: *Cryptosporidium parvum* of genotype I (61% of

samples), rotavirus (20%), Enterovirus (14%), *Campylobacter jejuni* (14%), *E. coli* (12%), and adenovirus (6%).

These results led us to conclude that this gastroenteritis epidemic was caused by waterborne *Cryptosporidium parvum*, genotype 1. This genotype (of human origin) as well as the type of viruses and bacteria found in the patients' stools signaled that the drinking water network had been directly contaminated by human fecal material.

Environmental survey

It was rapidly revealed that the local water company as well as the Dracy-le-Fort town hall had recorded several complaints for brownish water after 14 September 2001. Following these complaints, the water company drained the network on 18-19 September 2001. Between 19 September (when the epidemic began) and 31 October 2001, the district health bureau and the water company took 228 water samples from different points of the network. These showed pollution by fecal bacteria: cryptosporidia (genotype not identified) were isolated in 15 samples taken after 24 September. The sample analyses returned to normal after 15 October 2001.

The geographic impact of the water contamination and the distribution of gastroenteritis cases, established by the general practitioners' survey, indicate that the pollution probably originated along the distal portion of the network serving Dracy-le-Fort and thus rule out as causes the raw water, catchment, and treatment. The survey showed an unprotected interconnection between the potable water distribution network and the sewage treatment recycling network. Moreover, the presumed date of contamination, estimated according to the epidemiologic results, coincides with maintenance operations on the plant's sludge mixer.

The most likely hypothesis thus is that the drinking water network was accidentally contaminated following a hazardous manipulation that caused the sewage to flow towards the potable water distribution system; the defects in this interconnection system have been repaired.

The pollution that caused the Dracy-le-Fort epidemic is an example of direct contamination of a water distribution network. It affected only a small part of the network (1 of 26 towns). In this type of accident, affecting the downstream portion of a network, surveillance of treated water at the treatment plant is of course irrelevant. The experience obtained from the investigation of this gastroenteritis epidemic led InVS to make several recommendations:

- **early consideration of complaints about tap water and rapid verification of its quality;**
- **reinforcement of the surveillance and alert system via general practitioners and retail pharmacists (sales of anti-diarrhea agents are a more sensitive indicator than doctors' visits and can be automated);**
- **providing physicians with information about Cryptosporidia infections so that this parasite can be considered and sought more often (at Dracy, testing for Cryptosporidia in patients' stool occurred only after its detection in the water);**
- **identification and formalization of a list of partners able to intervene in an epidemic of this type.**

Crisis management

The water company began draining and disinfecting the network on 19 September 2001 to eliminate the contamination. Chlorination was reinforced from 20 September onward. On 26 September, a chlorination station was installed at Dracy-le-Fort. On 28 September the network was drained at high speed to detach the Cryptosporidia on the biofilm lining the inside of the water pipes. The pipes were drained again on several occasions through 12 October, when the ban on consumption of tap water from the network was lifted.

The analyses of successive water samples show that the fecal bacteria were eliminated from the network within 48 h, after reinforcement of the chlorination; on the other hand, eliminating the cryptosporidia through repeated partial draining of the network took nearly two weeks.

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Municipal solid waste incineration plant in Angers: assessment of the health risks associated with past and present emissions

The Angers solid waste incineration plant, in operation since 1974 and upgraded to comply with European standards (European directives 89/369 and 89/429) in 2000, has a capacity of 101,000 tons/year (3 furnaces burning 5 tons/hour). It is located on the outer edge of the town, near residential neighborhoods and agricultural zones (truck farming) and, according to the local information and surveillance committee, its emissions worried its neighbors. At the suggestion of this committee and the district health bureau, the Prefect of Maine-et-Loire requested a health risk assessment to obtain information for the population and to examine the need for exposure reduction measures. The West regional epidemiology team, in collaboration with InVS, conducted this evaluation to estimate the risks associated with past and present emissions from the incinerator and its nearby furnace.

Local residents worried about the likely health effects – now or later – due to past or present exposure. In such a case – with no health signals and because of the unspecific effects expected from waste incineration emissions, the delayed effects (often with long latency periods), and low individual risks – a quantitative risk assessment was the appropriate procedure.

Assessment methods

Atmospheric emissions from solid waste incineration plants contain many chemical compounds that have different effects, and the emission levels of most have not been measured. In practice, then, we had to address the population concerns but also consider the pollutants whose emission levels were known and for which dose-response relations were available for identified dangers. The following pollutants were considered for the Angers incinerator: hydrogen chloride or hydrochloric gas (HCl), sulphur dioxide (SO_2), particulate matter, metals (lead, mercury, cadmium), and dioxins. Emissions of these pollutants have been measured since 1991.

Quantitative health risk assessment: a structured methodological process that relies on the use of scientific evidence "to define the health effects of exposures of individuals or populations to hazardous materials and situations" (definition of the US National Research Council, 1983). It was designed to provide information for decision making in situations of scientific uncertainty, to overcome limitations on feasibility and interpretation that are inherent in epidemiologic studies in low-risk situations (associations that are difficult if not impossible to demonstrate in these studies). This type of study (also called a health impact assessment) most closely meets the need to provide information to an affected population about the overall risks engendered by environmental exposures. In 1983, the US Academy of Sciences defined the quantitative risk assessment procedure to include four steps: hazard identification, dose-response assessment (selecting the safe and unsafe values), exposure assessment, and risk characterization.

The exposure routes studied were inhalation and ingestion of local products. Multimedia models of atmospheric dispersion and exposure made it possible to estimate the concentrations of pollutants in the atmosphere and the food chain of the exposed populations. These risks were characterized for the individuals who lived in the Angers area between 1974 and 2000 and for those who moved there in 2000.

Health risks for local residents

• **The atmospheric concentrations of metals** associated with the incineration plant before and after its upgrade were low, compared with levels normally observed in the environment. The chimney height (60 m) explains why the environmental concentrations are low, despite a considerable emission flow, especially before the upgrading and particularly for lead. These compounds should therefore not cause any noncarcinogenic health effects in the population. We then considered the carcinogenic effects; the mean individual excess risk (over 70 years) due to cadmium exposure is negligible (1 in a million) and the health impact (over 25 years) is less than 1 additional cancer case in the Angers area.

• **The situation varies more for the respiration of irritating gases** (HCl and SO_2). The "immissions" (that is, the amount of pollutant reaching a

particular location as a result of – and in contrast to – the emissions coming out the chimney) attributable to the incinerator resulted in hazard ratios less than 1. On the other hand, the maximum SO^2 immissions attributable to the furnace before 1985 led to hazard ratios near or above 1 for local residents downwind from the plant in high pressure conditions; the associated hazard is respiratory system irritation, which no longer appears to occur since the change to very low sulphur-content fuel in 1985.

• **The dioxin levels of** the immissions modeled in Angers and attributable to the incineration plant are similar to those observed in urban environments. Before these improvements, the mean overexposure attributable to the incinerator was on the order of one quarter of the mean exposure of the French general population at that time. The hazard ratio was less than 1; with a no-threshold model, the individual excess risk (over 70 years) was 5 per 10,000 and the health impact (over 25 years) 18 cancer cases. After the improvements, the individual excess risk (over 70 years) fell to 8 per 10 million and the health impact (over 30 years) to less than 1 case.

Numerous uncertainties affect the results for dioxins (few emission measurements, its environmental behavior, the dose-response relation). Despite their plausibility and consistency (environmental guidelines and other studies conducted around incinerators), these results must be taken with caution.

The results of this assessment do not require that any particular prevention measures be taken. They show that bringing the Angers incinerator into compliance with European standards reduced exposures substantially. This demonstrates the health benefits that accompany modernization of old incinerators and in particular those that, as in Angers, are located in areas of high population density.

Emissions from the Mennecy paper mill: health risk assessment for the intermediate- and long-term

Since 1997, the inhabitants of Mennecy have complained about strong offensive odors coming from the town's paper mill. These nuisances appeared at the same time as the company implemented a "zero discharge" policy, that is, stopped discharging effluent into the Essonne and recycled it instead. In May 2000, after residents expressed through various neighborhood associations their worries that compounds discharged by the mill, smelly or not, were hazardous to their health, the Prefect of Essonne established a local information committee about the paper mill and created an advisory committee from among its members. To respond to these fears, a quantitative health risk assessment began, with support from InVS.

The concerns of the population living near the Mennecy paper mill involved both the health consequences of prolonged daily exposure to the pollutants discharged, regardless of the smell, and the problem of the odors. Different types of environmental measurements respond to these two types of problems: for the long-term health effects, the environmental concentrations must be measured for a period of one to several weeks, while for the perception of odors, the pollution point must be identified in a time as brief as several minutes. From a practical point of view, these two objectives are incompatible. The study therefore aimed to quantify the intermediate- and long-term health risks run by the population exposed for a prolonged period to the pollutants discharged by the mill.

Assessment stages

The geographic borders of the study area were determined from the location of the complaints. The population concerned was defined as that residing in this area.

Based on the initial assessments conducted, primarily by the national institute of the environment and of industrial risks and the Paris municipal hygiene laboratory, on knowledge of the processes used in the paper mill, and on the laboratory's analytic capacity, the protocol considered three families of pollutants: monocyclic aromatic hydrocarbons, aldehydes and ketones, and volatile organic acids. Overall, 25 pollutants were identified and retained for study because they are measured at emission and at one or more of the sensors located in the study area. While not specific to this industrial activity, these pollutants are representative of the emissions from this paper mill.

A literature review of the health effects and toxicity reference values of these pollutants made it possible to quantify the health risks for 7 of the 25 compounds selected. This quantification relied on three exposure scenarios: for a sedentary adult, a child living, playing, and moving around in the study area, and a child attending the school located in this area but residing outside of it. Long-term (several years) exposure was estimated by calculating the mean weekly concentration of each pollutant for the entire study area and period; for sub-chronic exposure (several weeks), we applied the maximum weekly concentration recorded on one of the sensors.

Characterization of the air quality

The campaign to characterize the air quality in the study area collaborated closely with local stakeholders, to ensure that no place or area raising concerns or questions among the population was neglected.

To characterize not only the air pollution for the entire study area but also the exposure of populations living in this part of town for a long period, environmental samples were taken weekly for 10 consecutive weeks between December 2001 and January 2002.

The laboratory analyses showed that the pollutant concentrations recorded by the various sensors of the study area were homogeneous; they were also of the same order of magnitude as those generally measured in urban air. Accordingly, the portion of air pollution and exposure to it among the population of Mennecy that is attributable to the paper mill is probably very modest. Moreover, the concentrations measured during the week the paper mill was closed did not differ from those measured while it was in operation. They were even slightly higher – a demonstration of the influence of weather conditions on air quality.

Health risks for the population

The results show that the health risks to the population associated with intermediate- and long-term exposure to the compounds examined in this study are all less than or equal to the reference value accepted by numerous national and international bodies. This reference is exceeded only in the most unfavorable scenario, the probability of which is extremely slight, of a sedentary adult living in the study area, staying inside during the day (except for several days a year) and living in the same place for 70 years of his or her life.

Moreover, the risks calculated cannot all be attributed to emissions from the paper mill, since they also reflect exposure to pollutants discharged by all the sources that affect the sensors. The pollution levels recorded during weeks of high paper production do not seem to differ from those measured on days it produced nothing at all.

This procedure enabled us to identify some pollutants for which a lack of information prevented quantification of the health risks and therefore provided future research themes to fill this gap.

Surveillance program to monitor the health consequences of the 2001 chemical factory explosion in Toulouse: early results

The explosion that took place at the AZF site in Toulouse on 21 September 2001 was one of the largest industrial accidents in recent decades, measured either by the power of the blast or the human and property loss. The epidemiologic follow-up program established by InVS and the Midi-Pyrénées DRASS (regional epidemiology unit) began to assess the health consequences the day after the explosion. The objective of this program, organized in three sections, is to assess the intermediate- and long-term health consequences and thereby measure the extent of sequelae that such an event may impose on the health of the population. The experience thus acquired should help to improve the services available to the Toulouse residents affected by this disaster and to populations subject to comparable events in the future.

Consequences of environmental exposures

The explosion released a cloud of atmospheric pollution, composed essentially of nitrogen compounds, that hung over the southwest metropolitan area; nitrate derivatives were also emitted into the Garonne River, which borders the factory, and the blast projected soil particles and fragments from the industrial site into nearby neighborhoods. Because these emissions can cause immediate- or long-term effects in nearby and more distant populations, the analysis of the health risks associated with them took into account these diverse types of pollution simultaneously affecting different media for exposure durations that differed according to the medium. The "environmental health" section of this epidemiologic follow-up system used two methodological approaches concomitantly: a quantitative assessment of health risks based on measurements taken in the environment and the collection of health data from local medical information systems.

According to these two complementary approaches, the population exposure (through inhalation) to the chemicals emitted into the atmosphere (ammonia, nitrogen dioxide, particles, chlorine, nitrogen protoxide, nitric acid) could have caused mild respiratory irritation and transient vascular effects. The levels of asbestos exposure following the explosion should not have presented any health risk to the population. The alert systems did not record any diseases that suggested an unidentified pollutant. We were able to rule out the likelihood of an excess risk in the short and long term from exposure through ingestion – drinking tap water, swallowing soil particles projected from the crater (especially small children), consuming various products grown near the explosion site. Possible exposure to ionizing radiation (from onsite radioactive sources) was also ruled out.

The reassurance provided by these results meant that no specific surveillance or protective measures other than those taken immediately after the disaster were required.

Consequences recorded by existing health systems

The analysis of different data sources shows that the explosion had a major immediate impact on mental health in the population: approximately 5000 persons saw a physician for symptoms related to posttraumatic stress. While its chronic or delayed repercussions on mental health, in the form of either posttraumatic stress or depression, cannot yet be assessed, the extent of these initial consequences suggests there will be substantial long-term repercussions.

Other information also confirms the extent of the catastrophe's traumatic consequences, in particular ocular and auditory (table 7).

The estimate of more than 2000 consultations with general practitioners or pediatricians in the Toulouse metropolitan area for auditory problems alone in the first five weeks after the explosion indicates the importance of the auditory problems

expected in the population. Among the problems reported, we note hearing loss but also increased rates of ear pain and of tinnitus without associated deafness. These injuries may result from the sound of the blast (exposure of the ear to a shock wave) or acoustic trauma (exposure to pressure in the ear that could reach the cochlea, in the inner ear).

Tinnitus: erroneous perception of an auditory sensation (buzzing, whistling, ringing, or crackling).

The only information based on systematic screening for hearing loss comes from the Ministry of Education. It indicates a prevalence on the order of 5%-6% in students in schools near the explosion site.

These observations and the estimated levels of acoustic pressure near the explosion led to a recommendation in July 2002 that systematic hearing tests be performed among those most exposed – that is, those located in a radius of approximately 1.7 km around the site at the moment of the explosion. The Ministry of Education tested the hearing of the preschool and school-age children in the affected areas, and several occupational physicians undertook systematic screening.

Data collection from all of the existing information systems continues to complete and refine this initial assessment, especially of the intermediate-term auditory consequences.

Table 7: Injuries and traumatic consequences of the industrial accident in Toulouse Intermediate report, July 2002

Data sources	Trauma		
	General	Eye	Ear
PMSI (Toulouse UHC)			
Patients hospitalized (226) 21-22/09/01	93%	10%	2%
Disorders in patients discharged the same day (588) 21-22/09/01	88%	– (44% head trauma)	– (44% head trauma)
Heath Insurance (Midi-Pyrénées region)			
2910 injuries listed on 1673 initial medical certificates (of 4900)	68%	1.4%	18%
Estimate of excess cases in the district of Haute Garonne (31) according to healthcare use	–	–	(In planning)
Specialists (Toulouse metropolitan area)			
ENT consultations 21/09-20/10 2001 (581)	–	–	56% deafness 56% tinnitus 46% earaches
OPH consultations 21/09-20/10 2001 (n=?)	–	39 serious wounds (with surgery and hospitalization)	–
Sentinel network (Toulouse metropolitan area): general practitioners and pediatricians			
Consultations 1/10-23/11 2001	~ 120 cases (estimated) of infected wounds	–	~ 200 cases (estimated)
Ministry of Education (for Haute-Garonne 31) Screening in schools in the disaster zone, Nov-Dec 2001			
Nursery and primary school pupils (2971)	–	–	6.3%
Middle and High School students (3327)	–	–	5.5%

PMSI: national medical information program
ENT: ear-nose-throat specialists; OPH: ophthalmologists

Surveys among the most exposed populations

Three series of surveys took place during 2002.

– Among children and adolescents attending school: The Ministry of Education and InVS jointly conducted two surveys. The first, in spring 2002, was part of the European HBSC (Health Behaviour in School-aged Children) study of adolescents aged 11, 13, and 15 years in the Midi-Pyrénées region; a specific section concerning the psychological and school-related consequences of the explosion was completed by 624 students in the disaster area. The other, conducted in autumn 2002, concerned 1000 children selected among sixth-graders (middle school students). Of the children and teens thus questioned, 18% of the first group and 30% of the second said they had consulted at least one mental health professional (psychiatrist, psychologist, intervention team, etc.) after the explosion. According to the posttraumatic stress scale used, 18% of the first group (6 months after the explosion) and 13% of the second (one year after) had symptoms of posttraumatic stress related to the AZF explosion.

– Among AZF employees, workers onsite, and rescue workers: a mail survey is underway (questionnaires being returned).

– Among inhabitants of Toulouse: a survey conducted in collaboration with INSEE, particularly in the most devastated neighborhoods, is also currently collecting data. The results of these surveys will complete this long-term epidemiologic follow-up.

This work has also enabled us to demonstrate the usefulness of epidemiologic activity in emergency situations and the need to organize unhurriedly and in advance both the collaboration between the professionals to be involved in these events and the availability of information essential to respond to the public health questions they raise. In view of the importance of the auditory and psychological (posttraumatic stress, depression, decompensation) effects, the system for treating these problems must be reinforced.

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Fascioliasis from eating cultivated watercress: an epidemic in Nord-Pas-de-Calais

On 15 April 2002, Tourcoing UHC reported 5 cases of fascioliasis – a parasite disease caused by the liver fluke – diagnosed in the past three weeks in four persons living in Nord and a fifth in Pas-de-Calais. The DDASS of both districts, together with the Nord regional epidemiology unit and InVS, undertook an investigation to identify the source of the epidemic and take the necessary measures to control it. Physicians in the region received information by mail, and the population through wide media coverage; these early steps made it possible to identify other possible cases rapidly, treat them as early as possible, and optimize the investigation.

The epidemiologic investigation began by case-finding in conjunction with the two laboratories in the Nord-Pas-de-Calais region that performed fascioliasis serology tests as well as all the local clinical laboratories. This was intended to identify patients with blood count anomalies (white cells ≥

Liver fluke and fascioliasis

The liver fluke *(Fasciola hepatica)* is a parasite whose definitive hosts are ruminants and whose intermediate host is a fresh water snail, *Lymneae truncatula*. Humans intervene in the parasite cycle only accidentally, by ingesting larva released by the snail and encysted on the leaves of aquatic plants (lamb's lettuce, watercress, dandelions, etc.). In humans, fascioliasis develops in two stages: a stage of persistent invasion lasting several weeks, as larva migrate to the hepatic parenchyma, followed in the absence of treatment by a chronic phase during which the parasite, now adult, lives in the bile ducts. Diagnosis during the invasive phase is suggested by signs of foodborne hepatitis associated with blood count anomalies and can be confirmed only by serologic testing. During the chronic stage, the main symptoms involve recurrent biliary complications, and the presence of *F. hepatica* eggs in the stool confirms the diagnosis. Treatment of the infection must begin as early as possible (preferably before the end of the invasive period).

10,000/mm³ and eosinophils ≥ 1000/mm³) so that they could be offered a serologic test if they had symptoms compatible with fascioliasis. An exploratory survey of the first five cases now revealed that they had all eaten watercress and lamb's lettuce (mâche) purchased in supermarkets in the region. A case-control survey of 14 cases identified before 15 June and 23 controls tested the hypothesis of cultivated watercress or lamb's lettuce as the source of the cases – a necessary prerequisite to identifying the premises where the infested greens were grown. The district and regional consumer fraud offices (DDCCRF and DRCCRF) and then the DDASS conducted an administrative inquiry to locate the source of the greens eaten by the patients.

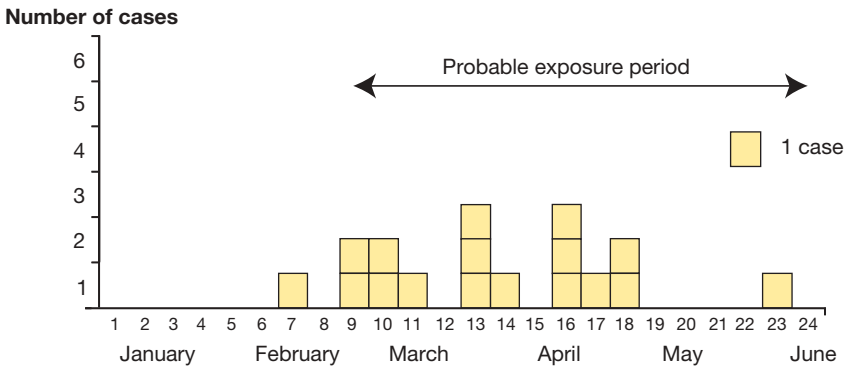
First fascioliasis epidemic in France from the consumption of cultivated watercress

Case-finding enabled us to locate 18 patients (11 in Nord and 7 in Pas-de-Calais), diagnosed directly by a serologic test (including the five cases causing the alert). The search based on blood count anomalies was long and tedious and yielded no other fascioliasis cases; this suggests that the list mentioned above is probably exhaustive because of the early provision of information to physicians and the general public.

The dates the symptoms first occurred are known for 17 cases and ranged from 2 March to 2 June (figure 17). They suggest an infestation between the end of January and beginning of March (incubation period of 15 days to 2 months). The delay between the first signs and diagnosis ranged from 4 to 103 days (median 32 days). These figures show how difficult it is to diagnose this disease, which is often suggested only very late because of its rarity and its unspecific clinical signs.

Incubation: term designating the latency period between infection by a microorganism and the appearance of the first symptoms characterizing the invasive phase.

Figure 17: Weekly distribution of fascioliasis cases according to the date symptoms began, Nord-Pas-de-Calais 2002



The disease most often induced the following symptoms: fatigue (89%), fever (67%), muscle pain (61%), pain in the right hypochondrial region (61%), and pruritus (39%); 11 patients were hospitalized. Of the 18 cases, 17 had eaten raw watercress and the results of the case-control survey showed that fascioliasis was significantly associated with the consumption of raw watercress.

The survey of the supermarkets showed that the watercress purchased by 15 of the 17 cases who had eaten it came from the same producer. The infractions observed at this farm (uncleaned irrigation ditches, no protection against penetration of runoff, nearby cows, etc.) provided further evidence that the infestation of most cases came from this farmer and enabled us to rule out the hypothesis that intensive rain had resulted in contamination of all the watercress farms in the area.

This was the first identified fascioliasis epidemic in France due to consumption of cultivated watercress. Its onset and investigation show that commercial watercress farms can be contaminated. A guide to good practices in cultivating watercress and an updating of the applicable regulations appear necessary to prevent contamination and new epidemics.

Reference:

Mailles A, Vaillant V, Schepens C *et al.* Épidémie de fasciolose dans la Région Nord-Pas-de-Calais, printemps 2002. *BEH* N°09/2003 : 49-50

Q fever epidemic in the Chamonix Valley

In mid-July 2002, general practitioners around Chamonix reported an unexplained illness among adults in this Alpine valley of 9952 inhabitants to the DDASS of Haute-Savoie: continuing elevated fever, major headaches, muscle pain, and elevated transaminase levels. Recovery most often occurred without specific treatment, but several patients were hospitalized at the Annecy Hospital Center. The DDASS, together with the Rhône-Alpes regional epidemiology unit and InVS, set up active case-finding by asking physicians to have Q fever serologic tests performed in patients with these symptoms. After confirmation of the Q fever diagnosis in mid-August, national and European alerts went out and the district office of veterinary services was informed of the situation. The same partners, together with the Rickettsia CNR, conducted an epidemiologic investigation to assess the extent and characteristics of the epidemic and to identify the mode of transmission in order to take appropriate measures to control the epidemic.

Q fever, which occurs in isolated cases and epidemic outbreaks, is a ubiquitous zoonosis due to the *Coxiella Burnetii* microorganism, belonging to the rickettsia family. The most frequent animal reservoirs are cows, sheep, and goats. The disease is transmissible to humans by direct exposure to the birth products of infected females (placenta and abortion products), by inhalation of contaminated aerosols, or by ingestion of unpasteurized contaminated dairy products. In humans, the infection is asymptomatic and benign in half the cases, but chronic forms can cause abortions in pregnant women and endocarditis in persons with cardiac

Zoonosis: infectious disease transmissible in natural conditions from vertebrates to humans, and vice versa (for example: psittacosis, brucellosis).

valve diseases. For this reason, the national alert diffused at confirmation of the diagnosis was aimed at persons who had lived or spent time in the Chamonix Valley since June 2002 and were immunocompromised or pregnant or had cardiac valve diseases. Q fever serologic tests were recommended to this population.

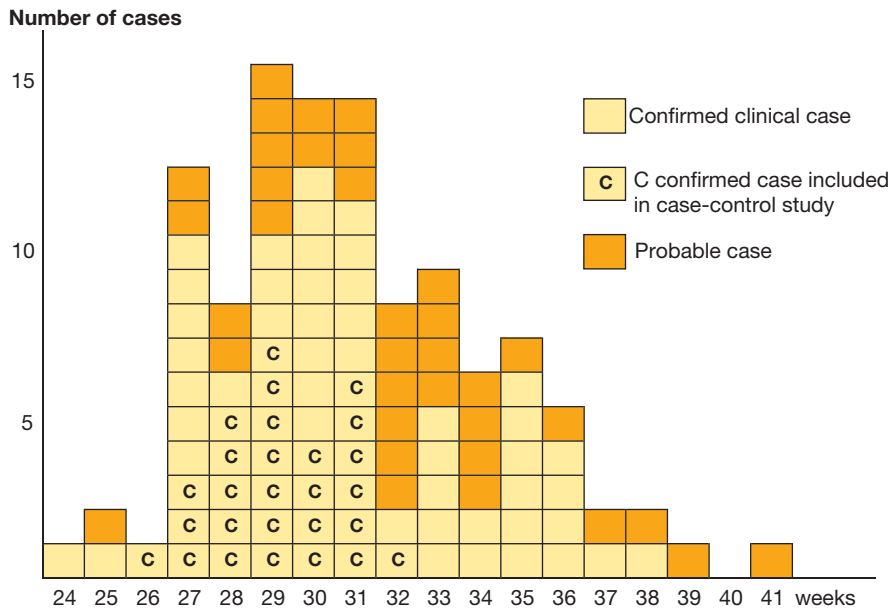
The epidemiologic investigations began by active case-finding among general practitioners, hospitals, and clinical laboratories in the Chamonix Valley and its downstream towns, by an exploratory survey and a case-control study of 27 definite (serologically confirmed) cases and 108 controls. In November 2002, the district veterinary bureau, working with AFSSA, surveyed livestock farmers living or whose herds grazed in the valley to ascertain herd movements, especially since spring 2002.

A broad community epidemic

The results showed a substantial epidemic of Q fever with 88 confirmed cases (including 71 with clinical signs, 6 pregnant women, and 3 patients with valve disease) and 40 probable cases in the Chamonix Valley, and 4 confirmed cases and 1 probable case downstream. The real number of cases is probably higher than the number reported because of the asymptomatic forms and the difficulties of identifying cases among tourists.

Cases occurred from 14 June through 20 September. The number of cases increased rapidly from the beginning of July. The epidemic continued for four months: 62% of the cases began during a 5-week period from early July through early August (figure 18). The epidemic began to weaken during the second week of August.

Figure 18: Number of cases of Q fever by week of onset, Chamonix Valley, summer 2002



– Confirmed clinical cases: person living in or visiting the Chamonix Valley or downstream villages who had a positive serologic test for Q fever and clinical signs.
– Probable case: person living in or visiting the Chamonix Valley or downstream villages in the months before the onset of clinical signs and having had since 1 June 2002 a fever higher than 39°C, accompanied by at least two of the following signs: headaches, muscle pain, nausea, and shivering with elevated transaminase levels.

The case-control study showed that for the entire first phase of the epidemic (the study period for the case-control survey, covering the first epidemic peak between 24 June and 4 July) the disease was significantly associated with close contact with sheep or participation in seasonal sheep migration (transhumance). It found no significant association between the disease and type of occupation, outdoor hobbies, consumption of raw goats' or cows' milk products, direct contacts with animals (pets, livestock, or wild), frequency of movement by neighborhood, or participation in public events.

The survey of farmers revealed that herds had been grazing in valley pastures from early May and had progressively moved to Alpine fields from early June through early August. Three herds of sheep had crossed the town of Chamonix between 30 June and 3 August.

These results suggest that at least the first phase of the epidemic was linked to one or more infected (probably sheep) herds from or migrating through the valley, as in other similar epidemics. Nonetheless, the epidemiologic study did not enable us to identify the infected herd (or herds), a task particularly complex in view of the airborne mode of transmission, the mobility of the herds, the possibility of transmission between herds, and the absence of specific information about their situation and movements.

Based on these epidemiologic results, prevention measures were introduced to restrict the gathering and circulation of herds on their return from the mountains.

In view of the risk that human cases will reappear in the absence of a precise identification of the source of contamination, epidemiologic surveillance will be set up in the spring of 2003. A serologic survey of the animals is underway. It was initially performed on blood samples from a sample of sheep in each herd that passed through the valley and will be completed with samples from sheep giving birth in the herds with positive results; this may help to identify the herds at risk and thus allow measures to avoid a resurgence of cases in humans when the herds return to pasture.

Reference:

Rey S, Thabuis A, Dennetière G *et al.* Investigation d'une épidémie de fièvre Q, vallée de Chamonix, juin-novembre 2002. Journées scientifiques de l'InVS, 3 et 4 décembre 2002. Résumé des présentations. Edition InVS du 23 mars 2003 : présentation 9

Diphtheria: risk of transmission in France from an imported case

Diphtheria is a very serious disease that has disappeared in industrialized countries due to vaccination; its surveillance in France is based on mandatory reporting. Diphtheria had not been reported in France since 1989, but a new case in 2002 led InVS to assess the risk of diphtheria transmission here and to analyze the consequences in terms of vaccination policy.

In France, vaccination against diphtheria has been mandatory for babies since 1938. Three doses are administered at 2, 3, and 4 months, followed by a booster at 15-18 months and then every five years until age 18. Vaccination coverage of babies is excellent (98% of children have received at least three doses by the age of 2 years). The current vaccination calendar does not include boosters for adults, except those traveling in areas where diphtheria persists. The protection

of the adult population, despite the absence of systematic boosters, probably reflects a group immunity conferred by the very high level of coverage in children and whose mechanism is not well understood.

The last reported case of diphtheria in France dated back to 1989. Despite a large epidemic in the countries of the former Soviet Union in the early 1990s (more than 50,000 cases in 1995), the French Vaccination Advisory Committee did not consider it useful to require boosters in adults. This decision was based primarily on the absence of cases detected here over the past decade.

In 2002, a case of diphtheria was diagnosed in Paris and confirmed by the Corynebacteria CNR. It occurred in a young woman from Asia, probably in France for several weeks and therefore infected after her arrival. In compliance with current recommendations, the Paris DDASS, in cooperation with the DGS and InVS, conducted an epidemiologic investigation to identify the persons who had had close contact with the infected young woman – her family and hospital staff – to offer them throat cultures, antibiotics and, if necessary, a booster vaccination. Nonetheless, the identification of her contacts before hospitalization was probably incomplete, because of her family's lack of cooperation. Although no secondary cases were detected in the months thereafter, the failure to identify a *Corynebacterium diphtheriae* carrier among the family contacts makes it impossible to rule out the hypothesis that this strain circulated among her family and friends.

Corynebacteria or Corynebacterium: family of bacteria in which one species is particularly pathogenic in humans: *Corynebacterium diphtheriae*, which causes diphtheria.

In 1998 InVS conducted a seroepidemiologic survey among a representative sample of the national population to estimate the seroprevalence profile of antidiphtheria antibodies in the French population according to age. Its results are troubling: approximately 40% of the women aged 50 years or older do not have these antibodies (positive threshold: 0.01 IU/ml) and are therefore no longer protected against diphtheria. The proportion of unprotected men is lower, because boosters were systematically administered during compulsory military service: it is less than 20% until the age of 70 and remains lower than 30% above this age.

In view of these factors, together with the end of booster vaccinations among young men following the disappearance of mandatory military service, InVS proposed that the DGS rethink the antidiphtheria vaccination strategy. This issue is included in the questions under consideration by a working group set up within the Vaccination Advisory Committee in 2003 to review booster vaccination strategies among adults.

Nosocomial hepatitis C: persistent avoidable infections

The reports of nosocomial infections that health facilities send to InVS revealed several clusters of nosocomial hepatitis C in 2001 and 2002. The investigations that followed indicate that most of these episodes were avoidable.

By 8 January 2003, InVS had received 505 reports of nosocomial infections for the period from 1 August 2001 to 31 December 2002: 8 (1.6%) concerned nosocomial hepatitis C in patients undergoing hemodialysis (4) or who were hospitalized or underwent surgery in the three months before the diagnosis (4); overall, these 8 reports covered 33 cases of hepatitis C.

These reports triggered investigations within the facilities. The nosocomial infection coordinating center assisted in the investigations, as did the HBV and HCV CNRs and InVS on some occasions. The aim was to confirm the nosocomial character of the cases reported, search for other cases, assess hospital practices to find the means of transmission, and analyze the HCV strains

isolated. These investigations confirmed the nosocomial origin of each of the eight reports of nosocomial HCV.

Reports of nosocomial hepatitis C from hemodialysis departments

HCV serologic tests performed as part of the routine laboratory monitoring of dialysis patients identified the cases included in the four reports from hemodialysis centers. Three of the four corresponded to isolated cases of seroconversion and, for two of them, the investigation made it possible to identify the source patient, a known carrier of HCV who received dialysis during the same session.

The fourth report concerned a cluster of nine cases in a hemodialysis center, reported in December 2001 to the southeast nosocomial infection coordinating center. Systematic HCV screening for all the patients in the Béziers hemodialysis unit who underwent dialysis in 2001 identified 22 cases of nosocomial hepatitis C. The center was closed on 22 January 2002 and the patients immediately transferred elsewhere. In view of this serious epidemic of unusual scale, the DGS established a cell of experts. The investigation was conducted by the southeast coordinating center, in collaboration with the DDASS of Hérault, InVS, AFSSAPS, and other experts. It found that three different HCV genotypes were involved: type 2 (13 cases), type 1a (5 cases), and type 1b (4 cases); these 22 cases appeared over a 9-month period (figure 19).

The investigation also showed that HCV transmission occurred principally via staff actions in connecting successive patients to the hemodialysis equipment. Failure to apply standard precautions and rules of hygiene to hemodialysis explains this epidemic, transmitted on the hands of the healthcare staff. It may have been aggravated by stress caused by restructuring in April 2001: during this period, the number of dialysis posts increased from 8 to 12, a change that necessitated the reorganization of treatment in a tiny room in a facility that had too few personnel and too much turnover.

After setting up corrective measures, the hemodialysis center reopened on 25 March 2002. No contamination has been reported since the last case in January 2002.

Reports of nosocomial hepatitis C outside of hemodialysis departments

Two of these four reports corresponded to isolated cases and two to clustered hepatitis C cases. These episodes show how important it is to consider a nosocomial cause when acute hepatitis C is diagnosed, by ascertaining whether the patient was hospitalized in the months before the onset of the infection.

The investigation found the source of contamination for one of the two isolated cases reported. It involved a patient with diabetes hospitalized in a medical department. The practice audit conducted by the Paris-North coordinating center showed that improper use of a blood glucose monitor was a possible source of the contamination. Because blood was placed on a strip already inserted in the monitor, contact was permitted between the patient's finger and the possibly contaminated monitor. The investigation of the second report is underway at the date this report was written: it

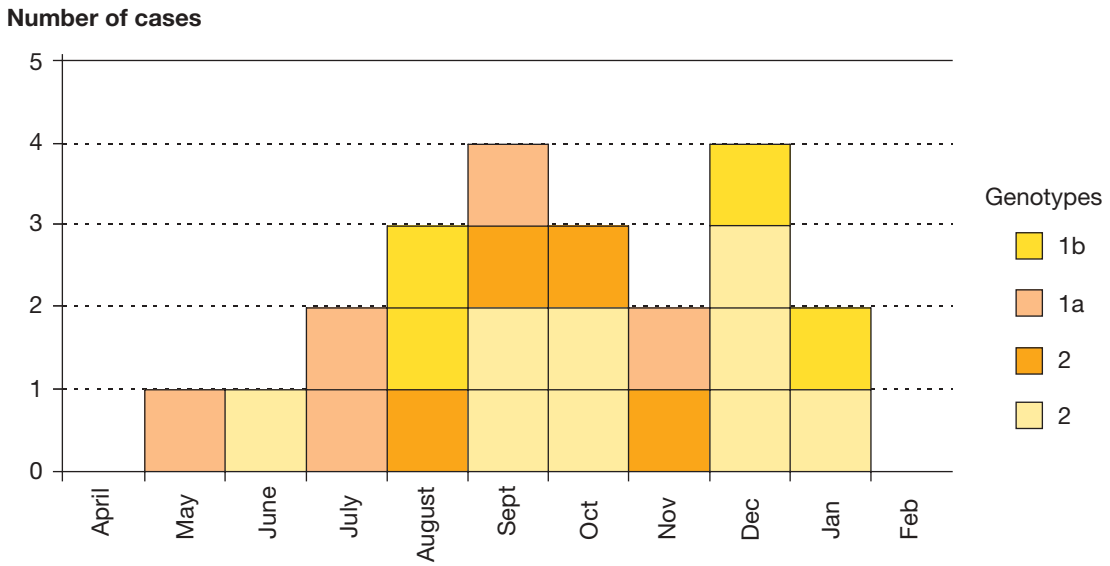
The 26 July 2001 decree and the reporting of nosocomial HCV infections

Nosocomial infection reporting is an alert system intended to supplement the national surveillance networks administered by the alert network for the investigation and surveillance of nosocomial infections (RAISIN). Its action-oriented objective is to detect nosocomial infections sufficiently serious or recurrent to require the implementation of prevention and control measures at the local, regional, or national level. It provides technical assistance to health facilities in formalizing their alert procedures and allows them to call in outside aid if necessary. Unlike surveillance networks, which are voluntary, these reports are a legal obligation defined by the decree of 26 July 2001 and the circular of 30 July 2001.

Among the infections that must be reported are recent cases of hepatitis C of definite or probable nosocomial origin. They meet several of the criteria for reporting defined by the decree: they cause an infrequent and serious nosocomial infection (criterion 1a) and are often associated with procedures that may have exposed other persons to the same risk (criterion 1d). The health facility sends the reporting form simultaneously to the coordinating center (for expert assistance) and to the DDASS (for control); the latter transmit their copy to InVS (for expert assessment and national analysis).

InVS provides back-up methodological support in investigating the cases reported, and cross-checks these data with those received from elsewhere to improve the exhaustiveness of the alerts transmitted (data from the CNR networks and from other agencies, such as AFSSAPS). Finally, the regular analysis of the national data makes it possible to detect emerging infections not considered by the current networks. Reporting, by triggering epidemiologic investigations and specific studies involving all of the participants in the fight against nosocomial infections, reinforces our capacity to control some of them. Documenting them enables the continuous improvement of recommendations directed at healthcare personnel.

Figure 19: Distribution of 22 nosocomial cases of hepatitis C between May 2001 and January 2002 at the Béziers hemodialysis unit



has so far found several possible nosocomial exposures.

Of the two reports of hepatitis C case clusters, the first concerned three patients who underwent surgery during the same orthopedic surgery session. The investigation by the Paris-North coordinating committee showed that the sharing of anesthetic product in multidose vials (without sharing any injectable material) caused the contaminations; this practice disregards the recommendations of the French Society of Anesthesia and Resuscitation. The second report concerned three hepatitis C cases in patients who underwent surgery the same day in the endoscopy and orthopedic theaters of the same establishment. The investigation performed by the Paris-North coordinating center identified general anesthesia as a factor common to the three cases, but the practice audit found no specific abnormality.

The reporting obligation introduced by the decree of 26 July 2001 has facilitated the investigation of hepatitis C cases of definite or probable nosocomial origin and the rapid implementation of appropriate control measures. This new system has so far sparked eight investigations, the results of which have supplemented earlier experience. They have found known causes of HCV contamination in healthcare settings: cross-transmission during hemodialysis sessions and transmission during capillary blood glucose tests. They also point to the risk involved in sharing products or materials, in particular for anesthesia. They have made it possible to modify risky practices in the facilities concerned, to offer screening to other exposed patients, and to develop recommendations for all healthcare professionals.

The effects of reporting go substantially beyond the facilities concerned. The investigation of the Béziers hemodialysis center raised the question of whether similar dysfunctions might exist in other French hemodialysis centers. For this reason, InVS will soon conduct, at the request of the Ministry of Health and in collaboration with the coordinating centers, a two-year national survey to measure the prevalence and incidence of HCV infection and to describe the surveillance methods in hemodialysis centers.

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Germain JM, Gros H, Carbonne A *et al.* Transmission du virus de l'hépatite C potentiellement liée au partage d'un flacon multidoses d'un analgésique central, Eure, 2001. *In* : Numéro thématique – Epidémiologie de l'hépatite C : état des lieux. *BEH* N°16-17/2003 : 102-3

Savey A, Simon F, Lepoutre A *et al.* Investigation de 22 cas de contamination par le virus de l'hépatite C dans un centre d'hémodialyse, Béziers, 2001-2002. *In* : Numéro thématique – Epidémiologie de l'hépatite C : état des lieux. *BEH* N°16-17/2003 : 104-7

Risk of acute lung disease associated with the use of defective bronchoscopes

Following the observation in the United States and in France of a defect (loosening of a piece attached to the end of the biopsy channel) in some bronchoscopes, Olympus recalled bronchoscopes in its BF40, BF240, and BF160 series on 13 March 2002. An alert message sent by AFSSAPS and the DGS to healthcare facilities on 22 March supplemented this recall. At that point, despite a report from a US hospital, no French facility had reported any cases of acute lung disease associated with bronchoscopies with the defective models. Nonetheless, in June 2001, before the defect in this equipment was known, bacterial contamination of these bronchoscopes and of bronchial samples had been identified in a French clinic. A meeting at AFSSAPS on 28 March 2002 decided that InVS and the five nosocomial infection coordinating centers would implement a survey to determine the existence of bacterial lung disease associated with this product defect.

This retrospective survey of healthcare facilities and the professionals using these bronchoscopes set as its principal objective the estimation of the risk of acute respiratory infection associated with the defective bronchoscopes that were the object of the recall; the research was limited to the last 30 patients in each establishment who had undergone a bronchoscopy with a defective apparatus before the recall date. The survey's secondary objective was to seek the existence of typical or atypical mycobacterial infections, in particular *Mycobacterium tuberculosis*, in these patients at the date of the bronchoscopy with the defective equipment, to estimate the prevalence of these infections in bronchoscopy patients. The purpose of this estimate was to quantify the exposure to the risk of possible contamination by mycobacteria during bronchoscopy.

Bronchoscope: apparatus introduced into the trachea and then the bronchi to enable their endoscopic examination and the taking of bronchial samples for biopsy.

Results: the risk of infection

Of 347 facilities surveyed, 211 (61%) responded with information about 114 defective Olympus bronchoscopes (table 8). A questionnaire concerning the patients who had bronchoscopies with a defective Olympus model was completed for 97 (85%) of these bronchoscopes; they covered 1412 patients, or an average of 15 patients per apparatus (table 9). A single case of acute lung disease (0.07%) was diagnosed among these patients, but the germ was not identified; the physician who performed the bronchoscopy considered it improbable that the defective machine caused this lung disease because the patient's mucus already appeared purulent at the time of the bronchoscopy.

These figures indicate that the bronchoscopes could be traced accurately in the facilities that responded to the survey, since the patients were identified for 85% of the defective models. Despite the limitations of this survey (retrospective analysis, heterogeneous data sources, subpopulation of patients), it enabled us to estimate the risk of bacterial infection, which turned out to be very slight.

The results of the bronchoscope samples collected in this survey for 81 (71%) of the defective machines are difficult to interpret given the absence both of positive results for the pathogens usually found in this type of contamination and of information about the conditions in which the samples were taken. These results do not seem to indicate massive contamination of the defective bronchoscopes.

Table 8: Results from 211 facilities

	N	%
Facilities with a series BF40, BF240, BF160 bronchoscope	347	
Facilities responding	211	61%
Olympus bronchoscopes from series BF40, BF240, BF160 used by the responding facilities	455	
Defective bronchoscopes	114	25%
Defective bronchoscopes for which we obtained results of samples	81	71%
Defective bronchoscopes for which a patient was surveyed	97	85%

Table 9: Post-bronchoscopy lung disease and mycobacterial infection at the bronchoscopy

	N
Patients who had a bronchoscopy with a defective apparatus included in the survey	1412
Bacterial lung infections between 2 and 10 days after the bronchoscopy	1*
Patients whose mycobacterial infection status was documented on the date of bronchoscopy	1231
Mycobacterial infection/colonizations at date of bronchoscopy	16
Including *M. tuberculosis*	9
including other mycobacteria	5
including unspecified mycobacteria	2

*lung disease on D7, probably present at bronchoscopy

Mycobacteria results

The status of mycobacterial infection or colonization on the date of bronchoscopy was documented for 1231 patients; 16 (1.3%) had a mycobacterial infection or colonization on that day, 9 (0.7%) due to *Mycobacterium tuberculosis* (table 9).

This result is not surprising, since patients undergoing bronchoscopy usually have risk factors for mycobacterial respiratory infections; moreover, the diagnosis and follow-up of tuberculosis is one possible indication for bronchoscopy. These patients represent a source of potential contamination for patients who subsequently underwent a bronchoscopy with the same equipment. The loosening of a piece of the bronchoscope could have impeded the efficacy of disinfection.

The results of this survey do not indicate an elevated risk of bacterial contamination associated with the defect in the Olympus bronchoscopes, but they do underscore the exposure of patients having bronchoscopies to the risk of cross-contamination by mycobacteria. Flexible endoscopes cannot be sterilized in autoclaves, and their complex design may cause difficulty in their maintenance. This episode points out the importance of good maintenance of endoscopes and of the strict application of official recommendations about disinfection of flexible endoscopes. In addition, the reporting of information about serious incidents linked to defective medical devices is mandatory as part of the medical device monitoring system implemented in 1996.

Epidemic of cutaneous infections of methicillin-resistant *staphylococcus aureus* producing Panton-Valentine leucocidin in the Cotes d'Armor: community and nosocomial transmission

In March 2001, the microbiology laboratory of the Saint-Brieuc Hospital Center in the Côtes d'Armor (Brittany) isolated two strains of *Staphylococcus aureus* resistant to methicillin (MRSA), both with an unusual resistance profile for other antibiotics. These strains came from two patients with cutaneous infections, unrelated to one another but both living in the same town, Lannion. Alerted, the nosocomial infection committee from Lannion Hospital discovered that both patients had been admitted to its maternity ward. Other persons with cutaneous infections were identified among the close friends and family of these patients. In November 2001, analyses by the CNR for staphylococcus toxemia identified an identical strain of MRSA with a gene coding for the Panton-Valentine leucocidin (PVL) in several patients hospitalized or seen in these two hospitals before 9 October 2001. This strain caused cutaneous infections in these patients, but has also been isolated by the CNR in rare but serious cases of necrotizing pneumonia. The Lannion Hospital nosocomial infection committee and the West regional epidemiology unit began an investigation, in collaboration with Saint-Brieuc Hospital, the Côtes d'Armor DDASS, the West coordinating committee, and InVS, to provide a better description of the epidemic and institute control measures.

Panton-Valentine leucocidin (PVL)

This is a toxin secreted by some types of *staphylococcus aureus*. It is a particular virulence factor for unremarkable cutaneous infections (boils, for example), but also more rarely for severe necrotizing pneumonia. This factor is combined here with methicillin resistance, which makes the epidemic more troubling.

The MRSA strain identified in this epidemic produces PVL. These strains seem particularly virulent and easily communicable. The combination of methicillin resistance and this virulence factor (PVL) presents a potential risk of severe bacterial superinfection that can complicate an ordinary viral respiratory infection. This potential risk, considered with both community- and hospital-based transmission, justified the investigations undertaken.

Active hospital- and community-based case-finding began in January 2002. At the Lannion Hospital, the records of mothers and newborns admitted to the maternity ward between October 1999 and February 2001 were examined retrospectively, and the characteristics of the *Staphylococcus aureus* strains isolated from the maternity ward were checked. The maternity ward staff was offered screening for cutaneous infections or nasal colonization by this strain. The case-finding in the community traced the families of cases and identified contacts.

All of the samples taken from cutaneous lesions or by nasal swabs were tested for MRSA, and the strains matching this unusual profile were sent to the CNR for expert assessment.

Results according to data collected by 31 August 2002

This case-finding, conducted for the period 1 October 1999 to 31 August 2002, made it possible to identify 23 cases in 9 households: 15 confirmed cases (65%), 2 probable (9%) and 6 possible (26%).

Case definition in this epidemiologic investigation

A case was defined as any person living in the area of Trégor-Goëlo (Côtes d'Armor) with a clinical picture compatible with a diagnosis of cutaneous staphylococcal infection (folliculitis, furuncle, whitlow, abscess, postpartum mastitis, suppurative wound infection, conjunctivitis with purulent discharge, blepharitis, etc.) diagnosed between 1 October 1999 and 31 August 2002:

– **confirmed case**: isolation of MRSA with a profile determined by the CNR to be identical to that of the strain isolated at Lannion Hospital and expressing the gene coding for PVL;

– **probable case**: isolation of MRSA with an antibiotic resistance profile identical to that of the strain isolated at Lannion Hospital;

– **possible case**: with an epidemiologic link to a confirmed or probable case.

A **household** was defined as a group of persons living under the same roof as a case during the study period. A **contact** was defined as any person without a preexisting, cutaneous infection who lived in the same household as or had close relations with a case.

Twelve cases (4 mothers and 8 newborns) had spent time at the Lannion Hospital maternity ward in the year before the diagnosis of their cutaneous infection. The 23 cases identified lived in 7 towns in the area of Trégor-Goëlo, 11 (48%) of them in Lannion. Six cases (26%) required surgical drainage, 9 (39%) had one or more recurrences. No lung diseases and no deaths were reported. All the strains isolated in these patients belonged to the same epidemic clone, with a similar resistance profile (particularly, sensitivity to gentamicin) and a gene coding for PVL.

Screening of 41 of the 60 staff members of the maternity ward showed no cutaneous lesions or nasal colonization by the strain at issue. Nor was this strain found in any of the 35 strains of *S. aureus* isolated at the maternity ward from clinical samples since April 2001. The negative results of this search, conducted two years after the apparent beginning of the epidemic, do not suggest that the maternity ward is involved in the current transmission of the strain, which has not been isolated in hospitalized patients since September 2000.

The last cases diagnosed were contacts of cases previously identified within the same household. The persistence of these infections in the community may be explained by hand-to-hand transmission within households, possibly promoted by the persistent colonization of some persons by this strain, close contacts, or inadequate hygiene.

This epidemic underlines the importance of basic rules of hygiene, distributed in written form to hospital staff physicians, private practitioners, and clinical laboratories in the region, to encourage them to remind their patients: wash hands and body with antiseptic soap; do not share personal linens (towels, sheets, underwear) and wash them at a temperature above 60°C; regularly clean areas that may be soiled with 1% bleach. To be effective, these measures must be adopted by all members of the household at the same time. It is also recommended to cover infected cutaneous wounds, if possible, and to avoid touching them except during medical care. If necessary, trained workers may visit households to remind them of these rules.

To complete these data, the Côtes d'Armor DDASS, the West coordinating center, and the West regional epidemiology unit conducted an additional study that combined retrospective case-finding and active surveillance by hospital staff physicians, private practitioners, and clinical laboratories. It should also make it possible to determine the origin – community or hospital – of the 12 cases hospitalized in the maternity ward.

This cluster of cutaneous infection cases confirms the community-based transmission of MRSA in France. The combination of methicillin resistance and a virulence factor (PVL) represents a potential risk in the case of more severe infections, especially pulmonary. As of today, the incidence of these infections seen by physicians in private practice remains unknown. It is therefore important to set up studies to characterize these infections better and to identify specific measures to control and prevent them.

Reference:

Lina G, Piémont Y, Godail-Gamot F, Bes M, Peter MO, Gauduchon V, Vandenesch F, Etienne J. Involvement of Panton-Valentine leukocidin-producing *Staphylococcus aureus* in primary skin infections and pneumonia. *Clin Infect Dis* 1999;(29):1128-32.

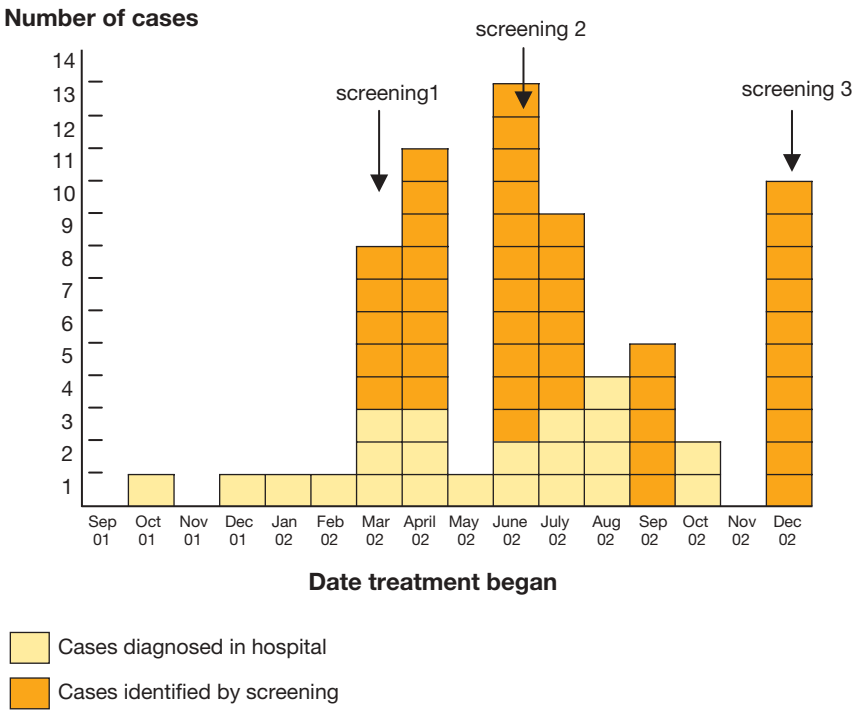
Tuberculosis: epidemic in a hostel for migrant workers in Paris

In March 2002, 13 cases of tuberculosis (2 of them bacilliferous according to bacteriologic examination of the sputum) were discovered in a hostel of African immigrants as part of a program of systematic tuberculosis screening in hostels in Paris, conducted since 1994 by the Paris municipal health department (DASES). This discovery triggered an investigation to find undiagnosed or unreported cases and to propose control and prevention measures.

Bacilliferous: carrying tubercle bacilli in the sputum, therefore contagious.

Four other radiologic screening sessions took place in 2002, with approximately 2590 radiographies taken of more than 1500 persons housed by or having visited this hostel, which has a capacity of 362 beds. These figures illustrate the conditions in the hostel, which caused substantial overcrowding and mobility among those housed there. Active case-finding was undertaken at neighboring hospitals (clinical departments and bacteriology laboratories) and at the Paris DDASS (mandatory reporting). Overall, by the end of 2002, 68 cases of tuberculosis had been identified (figure 20); none of the patients thus screened was lost to follow-up and those who completed their treatment were considered cured. The grouping of the cases in time and space, the presence mainly of early forms of the disease, and the similarities of the isolated strains indicate that the patients were probably contaminated in France. Secondary transmission was amplified inside the hostel because of the living conditions and overcrowding.

Figure 20: Distribution of 68 tuberculosis cases among immigrants who had spent time at the hostel, according to date treatment began, place of diagnosis, and contagious status – Paris 2002



This unprecedented epidemic shows that tuberculosis remains a reality, especially among immigrant populations. Systematic screening made it possible to detect many cases at an early stage and thus to limit morbidity and transmission. Several specific measures of control and prevention were implemented: renovation to combat the unhealthiness of the building, screening in the rooms where many cases were diagnosed. Nonetheless, in view of the high mobility of the population and the incubation period of the disease, this epidemic has probably not ended. For this reason, a permanent medicosocial team began working onsite in the hostel at the end of 2002 to offer tuberculosis screening and treatment as well as information about the disease (recommendation of the High Council of Public Hygiene of France on 15/11/2002).

This epidemic shows the need to sensitize physicians to mandatory reporting and, more generally, to consolidate the battle against tuberculosis, which must be more effective and more reactive; in particular, it requires better communication and liaison between its participants (general practitioners, DDASS, and the tuberculosis department). This reinforcement of the fight against tuberculosis is a special priority in the Paris region, for incidence there is the highest in France.

Reference:

Antoun F, Valin N, Chouaid C et *al.* Epidémie de tuberculose dans un foyer de migrants à Paris en 2002. *In* : Tuberculose en France : la situation aujourd'hui. *BEH* N°10-11/2003 (numéro thématique) : 58-60

Clusters of legionellosis: detection and investigation

Progress in legionellosis surveillance has made it possible to detect more clusters and epidemics, many of which would previously have remained unknown. Several clusters were identified and investigated in 2002. These epidemiologic and microbiological investigations are difficult, tedious, and not always successful. This year, they identified and enabled better control of the sources of contamination causing 2 nosocomial epidemics, at Meaux (22 cases including 4 deaths) and Sarlat (31 cases including 6 deaths); in each city, the source proved to be the hospital's cooling tower. Even when the environmental and bacteriological investigation cannot specify the contamination source, it can allow the district health bureau to identify unreported installations not maintained in compliance with current standards and to sensitize their operators to their regular maintenance, thereby reducing future danger. Accordingly, the Jonzac thermal baths were closed for disinfection after 3 cases of legionellosis were reported among its clients. Similarly, in the Doubs, recommendations were made to the exhibitors at the Pontarlier fair who may have been the source of 5 cases.

Legionellosis can also be contracted while traveling, most often through the drinking water networks in hotels, vacation residences, and campgrounds. This problem led to the establishment of the European Working Group for Legionella Infections (EWGLI), aimed at monitoring travel-related legionellosis. In 2002, the EWGLI network reported 19 clusters (2-4 cases) in French hotels or campgrounds. These

To learn more about EWGLI

This European network makes it possible to identify accommodations that housed persons who came down with legionellosis on returning home from a trip. A procedure makes it possible for national and local authorities to implement control measures in the place of accommodation of a person who fell ill after the trip, even in another European country. Accommodations where clusters occurred must obtain within 6 weeks a certification by the local health authorities that it has taken the appropriate measures of control or the hotel name is placed on the EWGLI web site (www.ewgli.org). This system links European surveillance directly to the action of local public health officials (DDASS) and thus reduces the morbidity and mortality from travel-associated legionellosis.

reports triggered environmental surveys in the local DDASS; 2 hotels were closed until completion of work to resolve their problems.

Because of the improvement in epidemiologic surveillance, ever more clusters of legionellosis are detected: this trend will level off only after effective measures of prevention are implemented. In this context, a CSHPF working group has distributed a guide defining acceptable legionella levels in water, in hospitals, and in places of assembly and presenting practical recommendations for managing the risk of legionella. At the European level, a guide on alert and prevention procedures for travel-associated legionellosis has also been produced.

Influenza epidemic in Madagascar: coordination of the international epidemiologic mission

In mid-July 2002, the health authorities of Madagascar received warning of a large number of deaths from acute respiratory disease in the village of Sahafata (2160 inhabitants), located in the highlands of Fianarantsoa province, approximately 500 km south of the capital, Antananarivo. A new alert was launched at the end of July, in an adjoining district. The investigations conducted by the Madagascar Ministry of Health and the Pasteur Institute there found influenza viruses in the pharyngeal samples collected from patients. On 2 August, the rapidly established national surveillance counted 1291 patients and 156 deaths, in 4 different districts. On 7 August, the Madagascar government requested the assistance of WHO, which mobilized its international epidemic network (GOARN). InVS was asked to coordinate the international team sent to Madagascar, which also included representatives of the CDC, the Paris Pasteur Institute (as the French influenza reference center), and WHO.

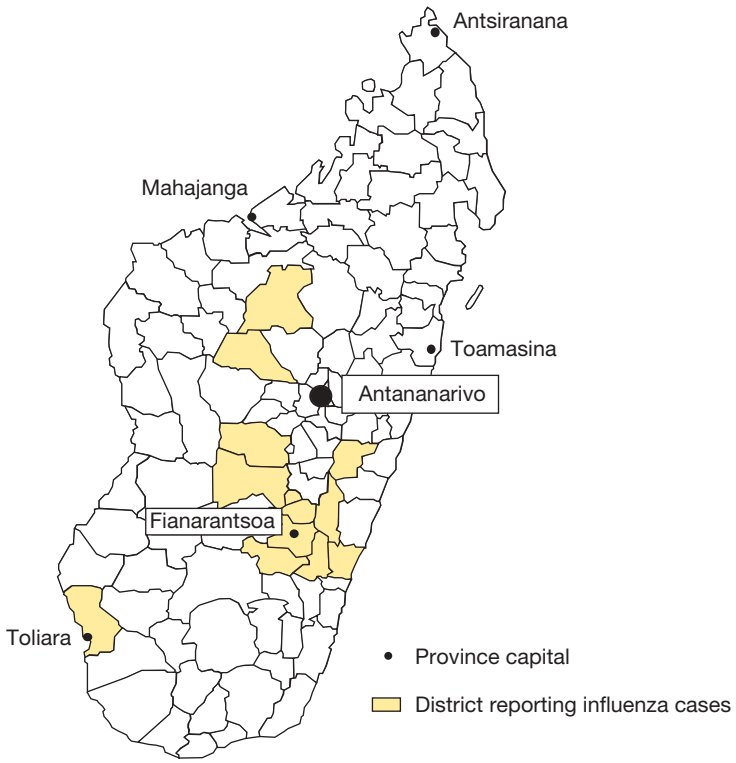
The 6 member team arrived in Antananarivo on 14 August. It remained in Madagascar for 3 weeks, until 5 September, and conducted field investigations in the hardest-hit province, met with local authorities, collected information and samples, and had 152 samples analyzed at the Madagascar Pasteur Institute.

Assessing the extent of the epidemic

According to the influenza surveillance data collected for the entire country by the Ministry of Health, the epidemic peaked during the week of 22 August. On 19 September, 30,304 cumulative cases had been counted, with 754 deaths in 13 of 111 health districts and 4 of the country's 6 provinces (figure 21); 85% of the cases occurred in Fianarantsoa province, a rural area, and only 5% of the deaths occurred in healthcare facilities, where they could have been investigated.

The epidemiologic investigations nonetheless provided a more exact measurement of the nature and extent of the epidemic. The analysis of data collected between 1999 and 2002 by local health centers shows that the number of cases of and deaths from acute respiratory infections peaks each year in winter (Madagascar, in the southern hemisphere, has winter during our summer months) in the highland districts. These winter peaks are therefore not unusual in these regions. The same is true for the presence of influenza A and B viruses, isolated there each year. The influenza viruses isolated in 2002 were type A/Panama/2007/99 (H3N2), like those in circulation throughout the world for many years (this type corresponds to the vaccine strains planned by WHO for the southern hemisphere in 2002 and for the northern hemisphere in 2002–03).

Figure 21: Distribution of cases of influenza in Madagascar, July-August 2002



The particularity of the epidemic in Madagascar is therefore not related to the type of virus, relatively ordinary, but to its exceptional impact on public health. This seems due not to any unusual lethality but to the disease's very high attack rate in the communities in the center of the island. A study in a remote village of the district most affected found that the attack rate of influenza-like illness reached 67%, with mortality estimated at 2%. On the other hand, the Madagascar Pasteur Institute, which surveys influenza virus morbidity and circulation all year long, found no such unusual phenomena in the capital of the province (Fianarantsoa) or in Antananarivo.

Several factors may explain the abnormally high rates of morbidity and mortality of these acute respiratory infections in the rural highlands of Madagascar. Living conditions, in particular overcrowding and malnutrition, together with an especially cold and humid winter, could have promoted influenza transmission within the most vulnerable populations. In the province of Fianarantsoa, 40% of the children younger than 5 years (a population that included 54% of all the deaths) had chronic malnutrition, and most villages had very little access to basic care.

Since the 1997 alert in Hong Kong (chicken influenza), the risk of an influenza pandemic has been a major issue in public health and justifies systematic investigations. This is why this flare-up is rich in information about influenza epidemic control in developing countries and about planning international response to pandemics. Madagascar is one of the poorest countries in the world and had just emerged from a major political crisis that had disrupted the country for months; because the epidemic hit mainly remote areas, the health authorities learned of it late and responded later, despite the surveillance in Antananarivo by the Madagascar Pasteur Institute.

The international team recommended extending influenza surveillance, providing information to the public and healthcare workers about the disease, improving access to care in rural areas, and taking steps to ensure that healthcare facilities have adequate antibiotics for treating bacterial complications. It did not recommend vaccination against influenza, since the epidemic had already spread in August and vaccine distribution was extremely difficult in remote areas. Moreover, the influenza

surveillance system established on this occasion by the Madagascar health authorities appeared needlessly cumbersome and complex. Unable to follow the temporal and geographic extension of the disease, it led to exaggerated and alarmist communication. This project may lead to a long-term collaboration between InVS and Madagascar that would work on reinforcing its alert systems and operational research on influenza.

Reference:

Equipe d'investigation du Réseau mondial d'alerte et de réponse aux épidémies de l'OMS. Épidémie de grippe à Madagascar en juillet et août 2002. *BEH* N°3/2003 : 9-10

CEA employees at Vaujours: a mortality study

From 1957 through 1997, the Atomic Energy Commissariat (CEA) operated Fort Vaujours, which straddled two towns, one in the district of Seine-Saint-Denis and the other in Seine-et-Marne. They tested explosives there, with, in particular, natural and depleted uranium. It was at this military site that CEA conducted the simulations that made it possible to develop the explosive portion of the first French atomic bomb. After the CEA abandoned this site, the prefects of the districts concerned established an interdistrict follow-up committee, to respond to the fears of local officials and neighbors about possible residual soil contamination and to conduct a public inquiry. Responsible for the health-related issues, the Seine-Saint-Denis and Seine-et-Marne DDASS set up a "health" working group. As part of its work, this group sought assistance from the occupational health department of InVS to study the mortality of CEA employees who had worked at Vaujours through 1995.

This study considered the cohort of all workers employed for at least one year at Vaujours between 1955 and 1995. This cohort had already been constructed by CEA and its occupational medicine department as part of an IARC epidemiologic study on the effects of exposure to low doses of ionizing radiation. It included 2473 persons (2010 men and 463 women), 47% of whom still worked at CEA on 1 January 1995. The following information was known for each member of this cohort: date of birth, date of hiring and departure from CEA, occupational category at hiring, and period of presence at Vaujours. Vital status was determined as of 1 January 1995 and found 241 deaths before that date (187 men and 31 women); the cause of death was known for the 218 deaths since 1968. Vital status remained unknown for six subjects.

The InVS occupational health department received the data for this cohort at the end of 2001 and performed an analysis to assess whether the mortality observed in this population (all causes and from cancer) was different from that expected according to the mortality rates of the overall French population. Standardized mortality ratios were thus calculated; they correspond to the ratio of the number of deaths observed and expected (a ratio greater than 1 thus signifies that the observed mortality is higher than expected). Their 95% confidence intervals were calculated to assess their statistical significance (see table 10).

Table 10: Observed and expected mortality in the cohort of CEA employees who worked at Vaujours (1968-1994)

Cohort population	Cause of death	Deaths		SMR:* deaths observed/ deaths expected	95% CI
		expected	observed		
Men	all causes	316	187	0.59	0.51-0.68
	tumor	110	70	0.63	0.49-0.80
	no tumor	206	117	0.57	0.47-0.68
Women	all causes	28	31	1.10	0.75-1.56
	tumor	11	20	1.86	1.14-2.88
	no tumor	17	11	0.65	0.32-1.16

* Standardized mortality ratio (SMR)
95% CI: 95% confidence interval. If the interval does not contain the value 1, the ratio is significantly different from 1: we can thus conclude that the mortality of the population studied is different from that of the general population (or, alternatively, the difference in mortality observed may be due to chance).

Mortality study results

Tumors were the leading cause of death observed in the cohort (37%), followed by circulatory system diseases (23%), and injuries and accidents (17%). This distribution of causes of death is perfectly normal for this type of occupational population.

Of the 70 tumor-related deaths in men, the most common were bronchopulmonary (17%) and gastrointestinal (17%) cancers; the number of deaths observed was significantly lower than the number expected (table 10).

Twenty women died from cancer: breast cancer was the most frequent type (7 deaths). There was a slight, but not significant, excess of deaths from all causes, compared with the number expected. Only 11 cancer deaths were expected; thus the 20 observed constituted a significant excess. Additional analyses showed that this significant excess of cancer deaths was in fact specific to women engineers and managers, among whom there were 7 cancer deaths compared with the slightly more than 1 expected (SMR=4.76: 95% CI: 1.91-9.82). These 7 deaths came from the following types of tumors: 3 breast cancers, 1 ovarian cancer, 1 malignant skin melanoma, 1 lymphocytic-histiocytic lymphoma, and 1 cancer with the site unspecified. The strongest excess corresponded to a brief presence at Vaujours (5 deaths compared with less than 1 expected for presence less than 6 years, 2 deaths compared with slightly more than 1 expected for a longer presence).

To interpret these results, we must bear in mind that excess cancer deaths, especially from breast cancer, among women in high social categories are observed consistently in the epidemiologic literature. The fact that the excess is much more marked for a short work period than for a long duration runs counter to the idea of a relation with working at the site.

The mortality analysis for the CEA employee population reveals no unexpected results. The excess of cancer deaths among women does not appear to be associated with their presence at Vaujours. These results, included in the final report of the "health" group, were presented to the follow-up committee at its last public meeting, during which the conclusions from other studies, about radioactivity, chemical pollution, and groundwater pollution, were also reported. No results warranting concern came out of any of these studies, but several analyses had yet to be performed.

Asbestos in automobiles: risk assessment among auto mechanics

Decree 96-1133, which forbids any transfer or sale of products, material, or devices containing asbestos, came into effect on 1 January 1997. This ban did not concern the resale of used automobiles or of farm and forest vehicles and equipment made before 1997, for a transition period of five years and subsequently prolonged for another year. At the expiration of this moratorium, decree 2002-1528, dated 24 December 2002, continued the dispensation for used vehicles and equipment, except for those with brake pads containing asbestos. Preceding this decision, the public authorities sought expert recommendations. Following a referral from the Department of Labor Relations (dated 17 October 2002) the InVS occupational health department conducted a quantitative evaluation of the risks of lung cancer and pleural mesothelioma associated with asbestos in automotive vehicles among mechanics who work on these vehicles.

Given the very short deadline allotted (two weeks), this evaluation could be based only on available, rapidly accessible information. 1999 census data (from INSEE, the national statistics institute) made it possible to select 242,360 men, aged 16-60 years, who worked as automobile mechanics (that is, whose activity sector or occupation and social category are among those related to automobile repair) and might be exposed to asbestos.

Mechanics' exposure is essentially associated with working on brittle parts, which can cause asbestos fibers (mainly chrysotile) to spread throughout the workplace. These parts are mainly brake linings for both disk and drum brakes from before 1997 (for French cars) as well as clutch linings. The other parts that may contain asbestos (cylinder head gaskets, oil pan gaskets, alternator rings, manifold and fluid circuit gaskets, flange gaskets, and bituminous coatings) cause very little dust emission and are taken apart only very rarely (every 10 to 20 years). Trucks have still other parts that may contain asbestos, including torque limitation linings and brake lever shaft linings.

Several exposure scenarios explored

It was impossible to calculate the levels of asbestos exposure directly from the dust level measures corresponding to the various tasks of automobile mechanics (information too variable or unavailable). We used data from a vast epidemiologic survey of occupational exposures conducted by the Ministry of Labor in 1994 (Sumer survey) to assess the proportion of time spent exposed to asbestos during a work week in a population of mechanics: 70% of them were exposed less than 2 hours a week, 17% from 2 to 10 hours, 11% more than 10 hours, and 2% for an unknown duration.

These data were used to apply several exposure scenarios to the calculations. They combine different levels associated with the tasks performed, different distributions of workers exposed to asbestos, and several periods. Some information about the changes in the automobile fleet in France, the vehicles with parts likely to release asbestos, and the frequency of these parts' replacement made it possible to estimate the natural extinction period for the asbestos-releasing automobile fleet, that is, the time by which they would essentially disappear if no governmental measures were taken. Weekly exposure, expressed in fibers/ml (fibers inhaled on average during a work week), was calculated, followed by cumulative exposure, expressed in fibers/ml/year. To be conservative, these calculations assumed that each mechanic was exposed from the age of 18 years and that his exposure continued at the latest until the age of 65 years.

To assess the carcinogenic effects of chrysotile asbestos (the main type in automobiles), we applied in this work the models used by the Inserm expert advisory group on the health effects of asbestos exposure and by international health authorities. Applying them to the population of

242,360 selected mechanics, we were able to calculate a "lifetime" (between 20 and 80 years) risk of death from lung cancer (taking into account asbestos exposure, the population age structure, and the distribution of deaths from other causes) and the number of lifetime incident mesothelioma cases attributable to asbestos.

Results transmitted to the DRT and the DGS

One of the scenarios appeared to be the most realistic: it assumes that all the mechanics were exposed to asbestos, that this exposure ranged from 0.06 to 0.25 fibers/ml weekly on average for the period before 1997 (date when the sale of new vehicles containing asbestos was banned in France), and from 0.01 to 0.06 fibers/ml weekly for the period from 1998 through 2010. The "natural" extinction of exposure in 2010 seems realistic, in view of the data on changes in the French automobile fleet.

Table 11 presents the risk calculations for the population selected, taking these hypotheses into account and considering that the mechanics have been exposed to asbestos for their entire working life (from age 18 at the earliest through age 65 at the latest).

According to this scenario, for a fiber level per task of 1/ml (plausible median exposure level) corresponding to a mean weekly exposure level of 0.12 f/ml/week for the personnel concerned for the entire pre-1998 period and a mean level of 0.03 f/ml/week for the 1998-2010 period, the (lifetime) cancer (lung cancer and mesothelioma) deaths due to pre-2003 – and thus inevitable – asbestos exposure among these mechanics total 604; if no steps are taken to modify the French automobile fleet before 2010, another 42 deaths can be foreseen.

As a reminder, according to the general French population mortality rate in 1998 (Inserm data), 13,487 "lifetime" lung cancer deaths are expected in this population of automobile mechanics without considering asbestos exposure.

Table 11: Quantitative evaluation of the risk of mesothelioma and lung cancer associated with asbestos exposure in automobile mechanics

Mean weekly exposure level in the population of mechanics f/ml		Lifetime deaths due to exposure before 2003	Lifetime deaths due to exposure if it continues through 2010	Deaths avoided by ending exposure in 2002
		$N_{p1} + N_{m1} = N_1$	$N_{p2} + N_{m2} = N_2$	$N_3 = N_2 - N_1$
Before 1997	1998-2010			
0.06	0.01	160.3 + 141.3 = **301.6**	176.6 + 146.3 = **322.9**	**21.3**
0.12	0.03	320.7 + 282.6 = **603.3**	353.2 + 292.5 = **645.7**	**42.1**
0.25	0.06	641.4 + 565 = **1206.4**	706.5 + 585 = **1291.5**	**85.1**

Np = Number of lifetime deaths from lung cancer
Nm = Number of lifetime deaths from pleural mesothelioma

Suspected childhood cancer cluster in Vincennes: investigation and epidemiologic follow-up

Late in 1999, three cases of cancer were reported in children attending the Franklin Roosevelt nursery school in Vincennes, a school built on a site that previously held a Kodak industrial plant. Specifically, two cases of leukemia and one of rhabdomyosarcoma were diagnosed between March 1995 and May 1999. In May 2000, after three environmental measurement campaigns in the school and consultation with a group of experts, InVS submitted a report concluding that neither the environmental information nor the epidemiology of the diseases observed justified the suspicion of an association between attendance at the school and the onset of cancer. A year later, the report of a fourth case in the same school (sarcoma, diagnosed in February 2001) strongly upset the local population and led the DGS to request the convocation of a scientific committee, chaired by an InVS representative, to conduct new health, environmental, and epidemiologic investigations. A monitoring committee was also established, chaired by the Prefect of Val-de-Marne and including representatives of the scientific committee, the DDASS, parents, local residents, the Franklin Vigilance Collective, Kodak, the municipality, and the ministries of Health and of the Environment. The mayor of Vincennes decided to transfer the school to a different site, away from the former Kodak plant, at the beginning of the September 2001 school year to protect the children from media pressure.

Epidemiologic investigations

Inserm and InVS are conducting two epidemiologic studies, which will be completed at the end of 2004, one among the 1205 children who have attended the Franklin Roosevelt school since it opened in September 1990 and who will be followed through the age of 15 years or until 31 December 2004 (the cohort study), the other among the population of children in the South Vincennes neighborhood, the area where all the cases lived and which constitutes the school catchment area (incidence study). These investigations required Inserm to construct a childhood cancer registry retrospectively for the Val-de-Marne for 1990-1999. This registry furnishes the reference rates for the general population to which the data in the epidemiologic studies must be compared for interpretation. The childhood cancer registry of the Val-de-Marne included 363 cases counted with excellent exhaustiveness (estimated at 99.7%), indicating an extremely intensive search for cases (average of 3.5 sources per case).

The two epidemiologic studies have confirmed the reported excess of cases: for the 1995-1999 period and relative to the rest of the Val-de-Marne, the cancer incidence rate was higher than expected in the cohort of Franklin school students (3 cases observed compared with 0.4 case expected) and in children in the South Vincennes neighborhood (4 cases observed compared with 0.55 case expected for those aged 0-4 years, and 4 cases observed compared with 0.87 case expected for those 0-14 years). We note that the number of cases expected for this period was 30% higher than the number expected for earlier periods, simply because of the local population increase. The two surveys were always consistent and showed no excess of cases in the pre-alert period (1990-1994).

The incidence study counted 13 cases of cancer among children living in Vincennes. A single case occurred during the 1990-1994 period and 12 cases between 1995 and 1999, 4 of them in South Vincennes: of these 4 cases, 3 are part of the initial school cluster, while the 4th occurred in a newborn. No excess was seen in the rest of the town of Vincennes (outside the South Vincennes neighborhood).

For the post-alert period (2000-2004), the cohort study furnishes partial data, through 31 December 2001, which are also reassuring (no excess of cases). It also shows that no new case of childhood cancer has been added to the four cases already known.

Cluster: unusual aggregation, real or perceived, of health events that are grouped together in time and space.

These two studies therefore showed a cluster of cases that, at this stage, seems clearly limited in time and space. Continued epidemiologic surveillance of the children through 2004 should provide information for the entire post-alert period, that is, the five years following the alert.

Role of environmental investigations in the epidemiologic assessment

The results of the study comparing concentrations in the various possible exposure media in South Vincennes, analyzing samples of groundwater, deep soil, and soil gases, and quantitatively evaluating the health risks will be published in June 2003. When the report was submitted (June 2002), the environmental testing in the school and the neighborhood had not revealed any exposure to high doses of ionizing radiation, the only exposure established with certainty as a cause in several types of childhood cancer. Nor did they uncover the presence of any potential risk factor, that is, of any known or suspected carcinogen for other types of cancer and present on the site at concentrations greater than those normally encountered in the environment. Moreover, the interview with the families of the four schoolchildren showed that they were not all born in the South Vincennes neighborhood, had not attended the same daycare center, and had not played on the same land, that their families had no particular occupational exposure in common, and that their homes did not, according to current knowledge about the site, share any particular exposures. One of the South Vincennes children diagnosed during the alert period had not attended Franklin Roosevelt school. Accordingly, the expert advisory group had no information suggesting that an approach of the "Exposed/Not exposed" type might be useful to compare the risk of childhood cancer measured in an exposed area with that in a non-exposed area.

Should the search for a cause other than chance for this excess have continued?

An extremely strong carcinogen would have been necessary to cause the excess seen in the 1995-1999 period; the only known candidates – antineoplastic chemotherapy and high doses of ionizing radiation – were known to be inapplicable here. The expert advisory group therefore concluded that no known risk factor was likely to explain the excess observed during the alert period and that if an unknown risk factor was involved, it was not specific to the site and therefore a case-control study would not help to discover it.

Case-control study: study comparing the frequency of a past exposure among a group of subjects affected by the disease under study ("cases") and a group of subjects who do not have the disease ("controls"), with the aim of assessing a possible association between the disease studied and exposure.

Epidemiologic research for this investigation

– To construct a Val-de-Marne registry and for the incidence study

Consultation of:

- all cancer centers, university hospital centers in Ile-de-France, and hospital centers in Val-de-Marne:[a] approximately 7000 cases reviewed, with no duplicates;
- approximately 360,000 pathology reports;[b]
- specialists in private practice in Val-de-Marne;[c] 442 mailings, 22 reports;
- the 4 health insurance funds in Val-de-Marne: 192 reports;
- the national registry of childhood leukemia and lymphoma;
- the hospital medical informatics departments and CepiDc at Inserm (the latter 2 sources, anonymous, were used as backup).

(a) Institut Curie, Institut Gustave Roussy, Hôpital Armand Trousseau, Hôpital Necker - Enfants Malades, Hôpital Robert Debré, Hôpital Saint-Vincent de Paul, Hôpital Saint-Louis, Hôpital Jean Verdier, Hôpital Ambroise Paré, Hôpital Antoine Béclère, Centre hospitalier Intercommunal de Créteil, Hôpital du Kremlin-Bicêtre, Hôpital des Quinze-Vingt, Centre hospitalier Intercommunal de Villeneuve Saint-Georges, Hôpital Sainte-Camille de Bry-sur-Marne.
(b) Hôpital Jean Verdier, Hôpital Ambroise Paré, Hôpital Avicenne, Hôpital Antoine Béclère, Hôpital Beaujon, Hôpital Louis Mourier, Centre hospitalier intercommunal de Créteil, Hôpital Henri Mondor, Hôpital du Kremlin-Bicêtre, Fondation ophtalmologique Rothschild, Hôpital Armand Trousseau, Hôpital de la Pitié-Salpétrière, Hôpital Bichat, Hôpital Cochin, Hôpital Européen Georges Pompidou, Hôpital Hôtel Dieu, Hôpital Lariboisière, Hôpital Necker-Enfants Malades, Hôpital des Quinze-Vingt, Hôpital Raymond Poincaré, Hôpital Robert Debré, Hôpital Saint-Antoine, Hôpital Saint-Louis, Hôpital Saint-Vincent de Paul, Hôpital Tenon, Institut Curie, Institut Gustave Roussy, Hôpital Paul Brousse, Centre hospitalier intercommunal de Villeneuve Saint-Georges.
(c) specializing in dermatology, ophthalmology, pediatrics, ENT, orthopedic surgery, endocrinology, nephrology, urology, oncology, internal medicine, anatomopathology, and radiation therapy.

– For the cohort study

- identification of 1205 children who had attended Franklin Roosevelt school between 1 September 1990 and 30 June 2001, based upon the school registry, kept by its directors, and the municipality's school enrolment files;
- establishment of the list of current addresses, found for 93% of them in the files of public and private schools in Vincennes and in the elementary schools of Paris, metropolitan and overseas school districts, by the school health departments, health insurance funds, and students' parents;
- mailing of a questionnaire to the parents of the children in the cohort (except for the known cases): 1038 responses were received;
- for the 164 children whose parents did not respond or who were not identified, verification that they did not appear in either the Val-de-Marne childhood cancer registry or the national registry of childhood leukemia and lymphoma.

The report on these epidemiologic investigations, submitted in June 2002, concluded that "[i]f an exposure of potential risk exists, it remains to be discovered, for South Vincennes as for everywhere else. Today particularly active French and international research is trying to distinguish from chance new risk factors against which prevention might be possible.

It is impossible to distinguish the role of chance and of some unknown risk factor in the excess of cases observed here." The population of children will be followed up routinely through the end of 2004, as initially planned. The results of the studies for the 1990-1999 period do not suggest the need for additional epidemiologic investigations.

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Clavel J, Fourme E, Hartman O, Lacour B, Jougla P, Quénel P. Analyse d'un agrégat de cas de cancers dans l'école Franklin Roosevelt de Vincennes. Rapport final – mai 2002. Rapport Inserm, InVS, juillet 2002.

Gastroenteritis epidemic in Dracy-le-Fort: contamination of the drinking water network

On 20 September 2001, SOS-médecins of Chalon-sur-Saône (a company providing physicians for emergency house calls) reported to the DDASS of Saône-et-Loire several cases of acute gastroenteritis that suggested an outbreak of food poisoning in a hotel in the town of Dracy-le-Fort. The initial investigation, conducted onsite the same day, revealed that the gastroenteritis concerned not only hotel customers but also staff, the local primary school, the local inpatient clinic, and, indeed, the entire community. The extent and character of this epidemic suggested that the drinking water network might be contaminated, since it was the most probable common denominator in terms of exposure. That afternoon, after taking water samples for analytic purposes, the DDASS issued instructions forbidding the consumption of tap water for drinking; these instructions were disseminated that day and the next to the local population. Simultaneously with other measures to deal with the health risk, the DDASS of Saône-et-Loire requested the Center-East regional epidemiology unit to conduct an epidemiologic and environmental expert assessment in collaboration with InVS.

Dracy-le-Fort is a rural municipality of 1100 inhabitants. Part of a water distribution unit serving 26 municipalities, or approximately 16,000 persons, it is located at the end of the network. The Center-East regional epidemiology unit and InVS conducted several types of investigations for descriptive and analytic purposes: a survey of general practitioners in the area of the water distribution unit, two retrospective cohort surveys, one among 33 clients of the hotel in Dracy-le-Fort (participants in a training course), the other among the town's general population (all households listed in the telephone book), microbiological analyses of stool samples from the patients in Dracy-le-Fort, and an environmental survey. These investigations enabled us to confirm and specify the epidemic's characteristics, determine the role of tap water in its onset, identify the infectious agents responsible, and establish their origin and the circumstances of the contamination so that we could recommend appropriate control and prevention measures.

Waterborne epidemic limited to the town of Dracy-le-Fort

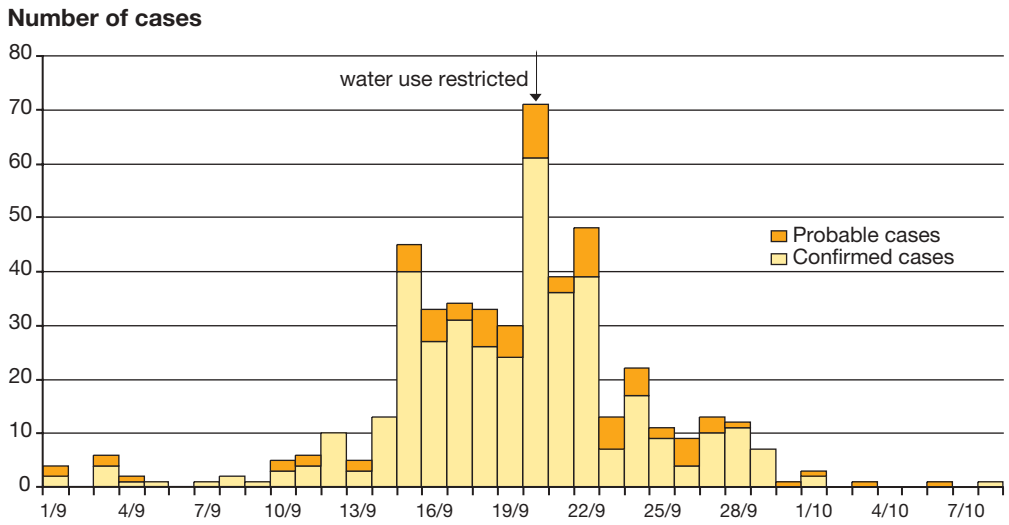
The survey of general practitioners revealed an increase in the number of consultations for gastroenteritis from 14-26 September 2001 (13% of total consultations compared with 1% from 1-13 September) and the high proportion of Dracy-le-Fort inhabitants in this phenomenon. This confirmed the gastroenteritis epidemic and reinforced the waterborne hypothesis, since its geographic range was limited to this town.

The telephone survey of hotel customers ruled out a foodborne source. It revealed an association between consumption of tap water and the onset of acute gastroenteritis, with a high attack rate (79% of the clients became ill).

Attack rate: proportion of persons becoming ill among the exposed population (in this case, those who drank the contaminated water) during an epidemic.

The cohort study in the general population, that is, 291 households in Dracy-le-Fort with 781 persons questioned, confirmed the role of tap water in the onset of gastroenteritis; the risk increased with the quantity of water drunk and the attack rate reached 62% (397 confirmed and 86 probable cases, that is, 483/781). The epidemic curve indicates a progressive augmentation over 9 days beginning on 12 September, peaking on 20 September, and diminishing rapidly thereafter – a change perceptible 4 days after tap water was banned (figure 16). These results, especially the high attack rate, indicate a massive isolated contamination of the drinking water supply network in Dracy-le-Fort.

Figure 16: Distribution of cases among the population of Dracy-le-Fort questioned according to the date of symptom onset (Dracy-le-Fort, Saône-and-Loire, September 2001)



Confirmed cases: diarrhea (≥ 3 liquid stools per day) or vomiting;
Probable cases: diarrhea (1-2 fluid stools per day) or abdominal pain

These investigations underlined the important impact of this epidemic from the health, social, and economic points of view: physician consultation exceeded 50%, 45% of the definite cases were confined to bed for more than 3 days; overall, 794 days of sick time were used.

***Cryptosporidium*, cryptosporidia**: sporozoa parasites pathogenic in humans and animals, which develop inside cells of the gastrointestinal tract and airway. Ubiquitous, frequently encountered among domestic herds, this agent causes cryptosporidiosis, which can be very serious in patients with AIDS. *Cryptosporidium* is the name of a genus (group of species), and cryptosporidia are the forms (points in its life cycle) in which it is disseminated into the environment.

A *Cryptosporidium* epidemic

The stool analyses searched for bacteria, viruses, and parasites and identified several pathogens: *Cryptosporidium parvum* of genotype I (61% of

samples), rotavirus (20%), Enterovirus (14%), *Campylobacter jejuni* (14%), *E. coli* (12%), and adenovirus (6%).

These results led us to conclude that this gastroenteritis epidemic was caused by waterborne *Cryptosporidium parvum*, genotype 1. This genotype (of human origin) as well as the type of viruses and bacteria found in the patients' stools signaled that the drinking water network had been directly contaminated by human fecal material.

Environmental survey

It was rapidly revealed that the local water company as well as the Dracy-le-Fort town hall had recorded several complaints for brownish water after 14 September 2001. Following these complaints, the water company drained the network on 18-19 September 2001. Between 19 September (when the epidemic began) and 31 October 2001, the district health bureau and the water company took 228 water samples from different points of the network. These showed pollution by fecal bacteria: cryptosporidia (genotype not identified) were isolated in 15 samples taken after 24 September. The sample analyses returned to normal after 15 October 2001.

The geographic impact of the water contamination and the distribution of gastroenteritis cases, established by the general practitioners' survey, indicate that the pollution probably originated along the distal portion of the network serving Dracy-le-Fort and thus rule out as causes the raw water, catchment, and treatment. The survey showed an unprotected interconnection between the potable water distribution network and the sewage treatment recycling network. Moreover, the presumed date of contamination, estimated according to the epidemiologic results, coincides with maintenance operations on the plant's sludge mixer.

The most likely hypothesis thus is that the drinking water network was accidentally contaminated following a hazardous manipulation that caused the sewage to flow towards the potable water distribution system; the defects in this interconnection system have been repaired.

The pollution that caused the Dracy-le-Fort epidemic is an example of direct contamination of a water distribution network. It affected only a small part of the network (1 of 26 towns). In this type of accident, affecting the downstream portion of a network, surveillance of treated water at the treatment plant is of course irrelevant. The experience obtained from the investigation of this gastroenteritis epidemic led InVS to make several recommendations:

- **early consideration of complaints about tap water and rapid verification of its quality;**
- **reinforcement of the surveillance and alert system via general practitioners and retail pharmacists (sales of anti-diarrhea agents are a more sensitive indicator than doctors' visits and can be automated);**
- **providing physicians with information about Cryptosporidia infections so that this parasite can be considered and sought more often (at Dracy, testing for Cryptosporidia in patients' stool occurred only after its detection in the water);**
- **identification and formalization of a list of partners able to intervene in an epidemic of this type.**

Crisis management

The water company began draining and disinfecting the network on 19 September 2001 to eliminate the contamination. Chlorination was reinforced from 20 September onward. On 26 September, a chlorination station was installed at Dracy-le-Fort. On 28 September the network was drained at high speed to detach the Cryptosporidia on the biofilm lining the inside of the water pipes. The pipes were drained again on several occasions through 12 October, when the ban on consumption of tap water from the network was lifted.

The analyses of successive water samples show that the fecal bacteria were eliminated from the network within 48 h, after reinforcement of the chlorination; on the other hand, eliminating the cryptosporidia through repeated partial draining of the network took nearly two weeks.

Reference:

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Municipal solid waste incineration plant in Angers: assessment of the health risks associated with past and present emissions

The Angers solid waste incineration plant, in operation since 1974 and upgraded to comply with European standards (European directives 89/369 and 89/429) in 2000, has a capacity of 101,000 tons/year (3 furnaces burning 5 tons/hour). It is located on the outer edge of the town, near residential neighborhoods and agricultural zones (truck farming) and, according to the local information and surveillance committee, its emissions worried its neighbors. At the suggestion of this committee and the district health bureau, the Prefect of Maine-et-Loire requested a health risk assessment to obtain information for the population and to examine the need for exposure reduction measures. The West regional epidemiology team, in collaboration with InVS, conducted this evaluation to estimate the risks associated with past and present emissions from the incinerator and its nearby furnace.

Local residents worried about the likely health effects – now or later – due to past or present exposure. In such a case – with no health signals and because of the unspecific effects expected from waste incineration emissions, the delayed effects (often with long latency periods), and low individual risks – a quantitative risk assessment was the appropriate procedure.

Assessment methods

Atmospheric emissions from solid waste incineration plants contain many chemical compounds that have different effects, and the emission levels of most have not been measured. In practice, then, we had to address the population concerns but also consider the pollutants whose emission levels were known and for which dose-response relations were available for identified dangers. The following pollutants were considered for the Angers incinerator: hydrogen chloride or hydrochloric gas (HCl), sulphur dioxide (SO_2), particulate matter, metals (lead, mercury, cadmium), and dioxins. Emissions of these pollutants have been measured since 1991.

Quantitative health risk assessment: a structured methodological process that relies on the use of scientific evidence "to define the health effects of exposures of individuals or populations to hazardous materials and situations" (definition of the US National Research Council, 1983). It was designed to provide information for decision making in situations of scientific uncertainty, to overcome limitations on feasibility and interpretation that are inherent in epidemiologic studies in low-risk situations (associations that are difficult if not impossible to demonstrate in these studies). This type of study (also called a health impact assessment) most closely meets the need to provide information to an affected population about the overall risks engendered by environmental exposures. In 1983, the US Academy of Sciences defined the quantitative risk assessment procedure to include four steps: hazard identification, dose-response assessment (selecting the safe and unsafe values), exposure assessment, and risk characterization.

The exposure routes studied were inhalation and ingestion of local products. Multimedia models of atmospheric dispersion and exposure made it possible to estimate the concentrations of pollutants in the atmosphere and the food chain of the exposed populations. These risks were characterized for the individuals who lived in the Angers area between 1974 and 2000 and for those who moved there in 2000.

Health risks for local residents

• **The atmospheric concentrations of metals** associated with the incineration plant before and after its upgrade were low, compared with levels normally observed in the environment. The chimney height (60 m) explains why the environmental concentrations are low, despite a considerable emission flow, especially before the upgrading and particularly for lead. These compounds should therefore not cause any noncarcinogenic health effects in the population. We then considered the carcinogenic effects; the mean individual excess risk (over 70 years) due to cadmium exposure is negligible (1 in a million) and the health impact (over 25 years) is less than 1 additional cancer case in the Angers area.

• **The situation varies more for the respiration of irritating gases** (HCl and SO_2). The "immissions" (that is, the amount of pollutant reaching a

particular location as a result of – and in contrast to – the emissions coming out the chimney) attributable to the incinerator resulted in hazard ratios less than 1. On the other hand, the maximum SO^2 immissions attributable to the furnace before 1985 led to hazard ratios near or above 1 for local residents downwind from the plant in high pressure conditions; the associated hazard is respiratory system irritation, which no longer appears to occur since the change to very low sulphur-content fuel in 1985.

• **The dioxin levels of** the immissions modeled in Angers and attributable to the incineration plant are similar to those observed in urban environments. Before these improvements, the mean overexposure attributable to the incinerator was on the order of one quarter of the mean exposure of the French general population at that time. The hazard ratio was less than 1; with a no-threshold model, the individual excess risk (over 70 years) was 5 per 10,000 and the health impact (over 25 years) 18 cancer cases. After the improvements, the individual excess risk (over 70 years) fell to 8 per 10 million and the health impact (over 30 years) to less than 1 case.

Numerous uncertainties affect the results for dioxins (few emission measurements, its environmental behavior, the dose-response relation). Despite their plausibility and consistency (environmental guidelines and other studies conducted around incinerators), these results must be taken with caution.

The results of this assessment do not require that any particular prevention measures be taken. They show that bringing the Angers incinerator into compliance with European standards reduced exposures substantially. This demonstrates the health benefits that accompany modernization of old incinerators and in particular those that, as in Angers, are located in areas of high population density.

Emissions from the Mennecy paper mill: health risk assessment for the intermediate- and long-term

Since 1997, the inhabitants of Mennecy have complained about strong offensive odors coming from the town's paper mill. These nuisances appeared at the same time as the company implemented a "zero discharge" policy, that is, stopped discharging effluent into the Essonne and recycled it instead. In May 2000, after residents expressed through various neighborhood associations their worries that compounds discharged by the mill, smelly or not, were hazardous to their health, the Prefect of Essonne established a local information committee about the paper mill and created an advisory committee from among its members. To respond to these fears, a quantitative health risk assessment began, with support from InVS.

The concerns of the population living near the Mennecy paper mill involved both the health consequences of prolonged daily exposure to the pollutants discharged, regardless of the smell, and the problem of the odors. Different types of environmental measurements respond to these two types of problems: for the long-term health effects, the environmental concentrations must be measured for a period of one to several weeks, while for the perception of odors, the pollution point must be identified in a time as brief as several minutes. From a practical point of view, these two objectives are incompatible. The study therefore aimed to quantify the intermediate- and long-term health risks run by the population exposed for a prolonged period to the pollutants discharged by the mill.

Assessment stages

The geographic borders of the study area were determined from the location of the complaints. The population concerned was defined as that residing in this area.

Based on the initial assessments conducted, primarily by the national institute of the environment and of industrial risks and the Paris municipal hygiene laboratory, on knowledge of the processes used in the paper mill, and on the laboratory's analytic capacity, the protocol considered three families of pollutants: monocyclic aromatic hydrocarbons, aldehydes and ketones, and volatile organic acids. Overall, 25 pollutants were identified and retained for study because they are measured at emission and at one or more of the sensors located in the study area. While not specific to this industrial activity, these pollutants are representative of the emissions from this paper mill.

A literature review of the health effects and toxicity reference values of these pollutants made it possible to quantify the health risks for 7 of the 25 compounds selected. This quantification relied on three exposure scenarios: for a sedentary adult, a child living, playing, and moving around in the study area, and a child attending the school located in this area but residing outside of it. Long-term (several years) exposure was estimated by calculating the mean weekly concentration of each pollutant for the entire study area and period; for sub-chronic exposure (several weeks), we applied the maximum weekly concentration recorded on one of the sensors.

Characterization of the air quality

The campaign to characterize the air quality in the study area collaborated closely with local stakeholders, to ensure that no place or area raising concerns or questions among the population was neglected.

To characterize not only the air pollution for the entire study area but also the exposure of populations living in this part of town for a long period, environmental samples were taken weekly for 10 consecutive weeks between December 2001 and January 2002.

The laboratory analyses showed that the pollutant concentrations recorded by the various sensors of the study area were homogeneous; they were also of the same order of magnitude as those generally measured in urban air. Accordingly, the portion of air pollution and exposure to it among the population of Mennecy that is attributable to the paper mill is probably very modest. Moreover, the concentrations measured during the week the paper mill was closed did not differ from those measured while it was in operation. They were even slightly higher – a demonstration of the influence of weather conditions on air quality.

Health risks for the population

The results show that the health risks to the population associated with intermediate- and long-term exposure to the compounds examined in this study are all less than or equal to the reference value accepted by numerous national and international bodies. This reference is exceeded only in the most unfavorable scenario, the probability of which is extremely slight, of a sedentary adult living in the study area, staying inside during the day (except for several days a year) and living in the same place for 70 years of his or her life.

Moreover, the risks calculated cannot all be attributed to emissions from the paper mill, since they also reflect exposure to pollutants discharged by all the sources that affect the sensors. The pollution levels recorded during weeks of high paper production do not seem to differ from those measured on days it produced nothing at all.

This procedure enabled us to identify some pollutants for which a lack of information prevented quantification of the health risks and therefore provided future research themes to fill this gap.

Surveillance program to monitor the health consequences of the 2001 chemical factory explosion in Toulouse: early results

The explosion that took place at the AZF site in Toulouse on 21 September 2001 was one of the largest industrial accidents in recent decades, measured either by the power of the blast or the human and property loss. The epidemiologic follow-up program established by InVS and the Midi-Pyrénées DRASS (regional epidemiology unit) began to assess the health consequences the day after the explosion. The objective of this program, organized in three sections, is to assess the intermediate- and long-term health consequences and thereby measure the extent of sequelae that such an event may impose on the health of the population. The experience thus acquired should help to improve the services available to the Toulouse residents affected by this disaster and to populations subject to comparable events in the future.

Consequences of environmental exposures

The explosion released a cloud of atmospheric pollution, composed essentially of nitrogen compounds, that hung over the southwest metropolitan area; nitrate derivatives were also emitted into the Garonne River, which borders the factory, and the blast projected soil particles and fragments from the industrial site into nearby neighborhoods. Because these emissions can cause immediate- or long-term effects in nearby and more distant populations, the analysis of the health risks associated with them took into account these diverse types of pollution simultaneously affecting different media for exposure durations that differed according to the medium. The "environmental health" section of this epidemiologic follow-up system used two methodological approaches concomitantly: a quantitative assessment of health risks based on measurements taken in the environment and the collection of health data from local medical information systems.

According to these two complementary approaches, the population exposure (through inhalation) to the chemicals emitted into the atmosphere (ammonia, nitrogen dioxide, particles, chlorine, nitrogen protoxide, nitric acid) could have caused mild respiratory irritation and transient vascular effects. The levels of asbestos exposure following the explosion should not have presented any health risk to the population. The alert systems did not record any diseases that suggested an unidentified pollutant. We were able to rule out the likelihood of an excess risk in the short and long term from exposure through ingestion – drinking tap water, swallowing soil particles projected from the crater (especially small children), consuming various products grown near the explosion site. Possible exposure to ionizing radiation (from onsite radioactive sources) was also ruled out.

The reassurance provided by these results meant that no specific surveillance or protective measures other than those taken immediately after the disaster were required.

Consequences recorded by existing health systems

The analysis of different data sources shows that the explosion had a major immediate impact on mental health in the population: approximately 5000 persons saw a physician for symptoms related to posttraumatic stress. While its chronic or delayed repercussions on mental health, in the form of either posttraumatic stress or depression, cannot yet be assessed, the extent of these initial consequences suggests there will be substantial long-term repercussions.

Other information also confirms the extent of the catastrophe's traumatic consequences, in particular ocular and auditory (table 7).

The estimate of more than 2000 consultations with general practitioners or pediatricians in the Toulouse metropolitan area for auditory problems alone in the first five weeks after the explosion indicates the importance of the auditory problems

expected in the population. Among the problems reported, we note hearing loss but also increased rates of ear pain and of tinnitus without associated deafness. These injuries may result from the sound of the blast (exposure of the ear to a shock wave) or acoustic trauma (exposure to pressure in the ear that could reach the cochlea, in the inner ear).

Tinnitus: erroneous perception of an auditory sensation (buzzing, whistling, ringing, or crackling).

The only information based on systematic screening for hearing loss comes from the Ministry of Education. It indicates a prevalence on the order of 5%-6% in students in schools near the explosion site.

These observations and the estimated levels of acoustic pressure near the explosion led to a recommendation in July 2002 that systematic hearing tests be performed among those most exposed – that is, those located in a radius of approximately 1.7 km around the site at the moment of the explosion. The Ministry of Education tested the hearing of the preschool and school-age children in the affected areas, and several occupational physicians undertook systematic screening.

Data collection from all of the existing information systems continues to complete and refine this initial assessment, especially of the intermediate-term auditory consequences.

Table 7: Injuries and traumatic consequences of the industrial accident in Toulouse Intermediate report, July 2002

Data sources	Trauma		
	General	Eye	Ear
PMSI (Toulouse UHC)			
Patients hospitalized (226) 21-22/09/01	93%	10%	2%
Disorders in patients discharged the same day (588) 21-22/09/01	88%	– (44% head trauma)	– (44% head trauma)
Heath Insurance (Midi-Pyrénées region)			
2910 injuries listed on 1673 initial medical certificates (of 4900)	68%	1.4%	18%
Estimate of excess cases in the district of Haute Garonne (31) according to healthcare use	–	–	(In planning)
Specialists (Toulouse metropolitan area)			
ENT consultations 21/09-20/10 2001 (581)	–	–	56% deafness 56% tinnitus 46% earaches
OPH consultations 21/09-20/10 2001 (n=?)	–	39 serious wounds (with surgery and hospitalization)	–
Sentinel network (Toulouse metropolitan area): general practitioners and pediatricians			
Consultations 1/10-23/11 2001	~ 120 cases (estimated) of infected wounds	–	~ 200 cases (estimated)
Ministry of Education (for Haute-Garonne 31) Screening in schools in the disaster zone, Nov-Dec 2001			
Nursery and primary school pupils (2971)	–	–	6.3%
Middle and High School students (3327)	–	–	5.5%

PMSI: national medical information program
ENT: ear-nose-throat specialists; OPH: ophthalmologists

Surveys among the most exposed populations

Three series of surveys took place during 2002.

– Among children and adolescents attending school: The Ministry of Education and InVS jointly conducted two surveys. The first, in spring 2002, was part of the European HBSC (Health Behaviour in School-aged Children) study of adolescents aged 11, 13, and 15 years in the Midi-Pyrénées region; a specific section concerning the psychological and school-related consequences of the explosion was completed by 624 students in the disaster area. The other, conducted in autumn 2002, concerned 1000 children selected among sixth-graders (middle school students). Of the children and teens thus questioned, 18% of the first group and 30% of the second said they had consulted at least one mental health professional (psychiatrist, psychologist, intervention team, etc.) after the explosion. According to the posttraumatic stress scale used, 18% of the first group (6 months after the explosion) and 13% of the second (one year after) had symptoms of posttraumatic stress related to the AZF explosion.

– Among AZF employees, workers onsite, and rescue workers: a mail survey is underway (questionnaires being returned).

– Among inhabitants of Toulouse: a survey conducted in collaboration with INSEE, particularly in the most devastated neighborhoods, is also currently collecting data. The results of these surveys will complete this long-term epidemiologic follow-up.

This work has also enabled us to demonstrate the usefulness of epidemiologic activity in emergency situations and the need to organize unhurriedly and in advance both the collaboration between the professionals to be involved in these events and the availability of information essential to respond to the public health questions they raise. In view of the importance of the auditory and psychological (posttraumatic stress, depression, decompensation) effects, the system for treating these problems must be reinforced.

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Institut de veille sanitaire, Cellule interrégionale d'épidémiologie Midi-Pyrénées. Suivi épidémiologique des conséquences sanitaires de l'explosion de l'usine AZF – Rapport intermédiaire juin 2002. Rapport InVS/CIRE 9 juillet 2002

Cassadou S, Ricoux C, Gourier-Fréry C *et al.* Conséquences sanitaires de l'explosion à l'usine de Grande Paroisse le 21 Septembre 2001 - Rapport final sur les conséquences des expositions environnementales, Mars 2003. Rapport InVS/CIRE 19 mars 2003

Fascioliasis from eating cultivated watercress: an epidemic in Nord-Pas-de-Calais

On 15 April 2002, Tourcoing UHC reported 5 cases of fascioliasis – a parasite disease caused by the liver fluke – diagnosed in the past three weeks in four persons living in Nord and a fifth in Pas-de-Calais. The DDASS of both districts, together with the Nord regional epidemiology unit and InVS, undertook an investigation to identify the source of the epidemic and take the necessary measures to control it. Physicians in the region received information by mail, and the population through wide media coverage; these early steps made it possible to identify other possible cases rapidly, treat them as early as possible, and optimize the investigation.

The epidemiologic investigation began by case-finding in conjunction with the two laboratories in the Nord-Pas-de-Calais region that performed fascioliasis serology tests as well as all the local clinical laboratories. This was intended to identify patients with blood count anomalies (white cells ≥

Liver fluke and fascioliasis

The liver fluke *(Fasciola hepatica)* is a parasite whose definitive hosts are ruminants and whose intermediate host is a fresh water snail, *Lymneae truncatula*. Humans intervene in the parasite cycle only accidentally, by ingesting larva released by the snail and encysted on the leaves of aquatic plants (lamb's lettuce, watercress, dandelions, etc.). In humans, fascioliasis develops in two stages: a stage of persistent invasion lasting several weeks, as larva migrate to the hepatic parenchyma, followed in the absence of treatment by a chronic phase during which the parasite, now adult, lives in the bile ducts. Diagnosis during the invasive phase is suggested by signs of foodborne hepatitis associated with blood count anomalies and can be confirmed only by serologic testing. During the chronic stage, the main symptoms involve recurrent biliary complications, and the presence of *F. hepatica* eggs in the stool confirms the diagnosis. Treatment of the infection must begin as early as possible (preferably before the end of the invasive period).

10,000/mm³ and eosinophils ≥ 1000/mm³) so that they could be offered a serologic test if they had symptoms compatible with fascioliasis. An exploratory survey of the first five cases now revealed that they had all eaten watercress and lamb's lettuce (mâche) purchased in supermarkets in the region. A case-control survey of 14 cases identified before 15 June and 23 controls tested the hypothesis of cultivated watercress or lamb's lettuce as the source of the cases – a necessary prerequisite to identifying the premises where the infested greens were grown. The district and regional consumer fraud offices (DDCCRF and DRCCRF) and then the DDASS conducted an administrative inquiry to locate the source of the greens eaten by the patients.

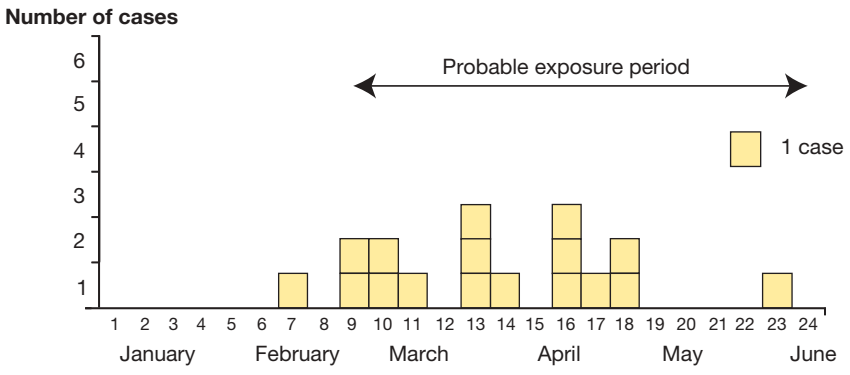
First fascioliasis epidemic in France from the consumption of cultivated watercress

Case-finding enabled us to locate 18 patients (11 in Nord and 7 in Pas-de-Calais), diagnosed directly by a serologic test (including the five cases causing the alert). The search based on blood count anomalies was long and tedious and yielded no other fascioliasis cases; this suggests that the list mentioned above is probably exhaustive because of the early provision of information to physicians and the general public.

The dates the symptoms first occurred are known for 17 cases and ranged from 2 March to 2 June (figure 17). They suggest an infestation between the end of January and beginning of March (incubation period of 15 days to 2 months). The delay between the first signs and diagnosis ranged from 4 to 103 days (median 32 days). These figures show how difficult it is to diagnose this disease, which is often suggested only very late because of its rarity and its unspecific clinical signs.

Incubation: term designating the latency period between infection by a microorganism and the appearance of the first symptoms characterizing the invasive phase.

Figure 17: Weekly distribution of fascioliasis cases according to the date symptoms began, Nord-Pas-de-Calais 2002



The disease most often induced the following symptoms: fatigue (89%), fever (67%), muscle pain (61%), pain in the right hypochondrial region (61%), and pruritus (39%); 11 patients were hospitalized. Of the 18 cases, 17 had eaten raw watercress and the results of the case-control survey showed that fascioliasis was significantly associated with the consumption of raw watercress.

The survey of the supermarkets showed that the watercress purchased by 15 of the 17 cases who had eaten it came from the same producer. The infractions observed at this farm (uncleaned irrigation ditches, no protection against penetration of runoff, nearby cows, etc.) provided further evidence that the infestation of most cases came from this farmer and enabled us to rule out the hypothesis that intensive rain had resulted in contamination of all the watercress farms in the area.

This was the first identified fascioliasis epidemic in France due to consumption of cultivated watercress. Its onset and investigation show that commercial watercress farms can be contaminated. A guide to good practices in cultivating watercress and an updating of the applicable regulations appear necessary to prevent contamination and new epidemics.

Reference:

Mailles A, Vaillant V, Schepens C *et al.* Épidémie de fasciolose dans la Région Nord-Pas-de-Calais, printemps 2002. *BEH* N°09/2003 : 49-50

Q fever epidemic in the Chamonix Valley

In mid-July 2002, general practitioners around Chamonix reported an unexplained illness among adults in this Alpine valley of 9952 inhabitants to the DDASS of Haute-Savoie: continuing elevated fever, major headaches, muscle pain, and elevated transaminase levels. Recovery most often occurred without specific treatment, but several patients were hospitalized at the Annecy Hospital Center. The DDASS, together with the Rhône-Alpes regional epidemiology unit and InVS, set up active case-finding by asking physicians to have Q fever serologic tests performed in patients with these symptoms. After confirmation of the Q fever diagnosis in mid-August, national and European alerts went out and the district office of veterinary services was informed of the situation. The same partners, together with the Rickettsia CNR, conducted an epidemiologic investigation to assess the extent and characteristics of the epidemic and to identify the mode of transmission in order to take appropriate measures to control the epidemic.

Q fever, which occurs in isolated cases and epidemic outbreaks, is a ubiquitous zoonosis due to the *Coxiella Burnetii* microorganism, belonging to the rickettsia family. The most frequent animal reservoirs are cows, sheep, and goats. The disease is transmissible to humans by direct exposure to the birth products of infected females (placenta and abortion products), by inhalation of contaminated aerosols, or by ingestion of unpasteurized contaminated dairy products. In humans, the infection is asymptomatic and benign in half the cases, but chronic forms can cause abortions in pregnant women and endocarditis in persons with cardiac

Zoonosis: infectious disease transmissible in natural conditions from vertebrates to humans, and vice versa (for example: psittacosis, brucellosis).

valve diseases. For this reason, the national alert diffused at confirmation of the diagnosis was aimed at persons who had lived or spent time in the Chamonix Valley since June 2002 and were immunocompromised or pregnant or had cardiac valve diseases. Q fever serologic tests were recommended to this population.

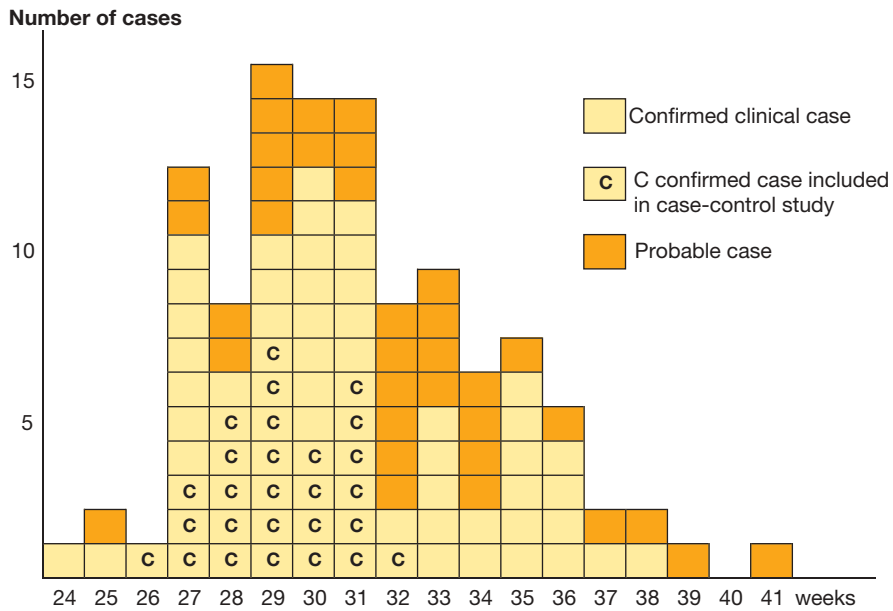
The epidemiologic investigations began by active case-finding among general practitioners, hospitals, and clinical laboratories in the Chamonix Valley and its downstream towns, by an exploratory survey and a case-control study of 27 definite (serologically confirmed) cases and 108 controls. In November 2002, the district veterinary bureau, working with AFSSA, surveyed livestock farmers living or whose herds grazed in the valley to ascertain herd movements, especially since spring 2002.

A broad community epidemic

The results showed a substantial epidemic of Q fever with 88 confirmed cases (including 71 with clinical signs, 6 pregnant women, and 3 patients with valve disease) and 40 probable cases in the Chamonix Valley, and 4 confirmed cases and 1 probable case downstream. The real number of cases is probably higher than the number reported because of the asymptomatic forms and the difficulties of identifying cases among tourists.

Cases occurred from 14 June through 20 September. The number of cases increased rapidly from the beginning of July. The epidemic continued for four months: 62% of the cases began during a 5-week period from early July through early August (figure 18). The epidemic began to weaken during the second week of August.

Figure 18: Number of cases of Q fever by week of onset, Chamonix Valley, summer 2002



– Confirmed clinical cases: person living in or visiting the Chamonix Valley or downstream villages who had a positive serologic test for Q fever and clinical signs.
– Probable case: person living in or visiting the Chamonix Valley or downstream villages in the months before the onset of clinical signs and having had since 1 June 2002 a fever higher than 39°C, accompanied by at least two of the following signs: headaches, muscle pain, nausea, and shivering with elevated transaminase levels.

The case-control study showed that for the entire first phase of the epidemic (the study period for the case-control survey, covering the first epidemic peak between 24 June and 4 July) the disease was significantly associated with close contact with sheep or participation in seasonal sheep migration (transhumance). It found no significant association between the disease and type of occupation, outdoor hobbies, consumption of raw goats' or cows' milk products, direct contacts with animals (pets, livestock, or wild), frequency of movement by neighborhood, or participation in public events.

The survey of farmers revealed that herds had been grazing in valley pastures from early May and had progressively moved to Alpine fields from early June through early August. Three herds of sheep had crossed the town of Chamonix between 30 June and 3 August.

These results suggest that at least the first phase of the epidemic was linked to one or more infected (probably sheep) herds from or migrating through the valley, as in other similar epidemics. Nonetheless, the epidemiologic study did not enable us to identify the infected herd (or herds), a task particularly complex in view of the airborne mode of transmission, the mobility of the herds, the possibility of transmission between herds, and the absence of specific information about their situation and movements.

Based on these epidemiologic results, prevention measures were introduced to restrict the gathering and circulation of herds on their return from the mountains.

In view of the risk that human cases will reappear in the absence of a precise identification of the source of contamination, epidemiologic surveillance will be set up in the spring of 2003. A serologic survey of the animals is underway. It was initially performed on blood samples from a sample of sheep in each herd that passed through the valley and will be completed with samples from sheep giving birth in the herds with positive results; this may help to identify the herds at risk and thus allow measures to avoid a resurgence of cases in humans when the herds return to pasture.

Reference:

Rey S, Thabuis A, Dennetière G *et al.* Investigation d'une épidémie de fièvre Q, vallée de Chamonix, juin-novembre 2002. Journées scientifiques de l'InVS, 3 et 4 décembre 2002. Résumé des présentations. Edition InVS du 23 mars 2003 : présentation 9

Diphtheria: risk of transmission in France from an imported case

Diphtheria is a very serious disease that has disappeared in industrialized countries due to vaccination; its surveillance in France is based on mandatory reporting. Diphtheria had not been reported in France since 1989, but a new case in 2002 led InVS to assess the risk of diphtheria transmission here and to analyze the consequences in terms of vaccination policy.

In France, vaccination against diphtheria has been mandatory for babies since 1938. Three doses are administered at 2, 3, and 4 months, followed by a booster at 15-18 months and then every five years until age 18. Vaccination coverage of babies is excellent (98% of children have received at least three doses by the age of 2 years). The current vaccination calendar does not include boosters for adults, except those traveling in areas where diphtheria persists. The protection

of the adult population, despite the absence of systematic boosters, probably reflects a group immunity conferred by the very high level of coverage in children and whose mechanism is not well understood.

The last reported case of diphtheria in France dated back to 1989. Despite a large epidemic in the countries of the former Soviet Union in the early 1990s (more than 50,000 cases in 1995), the French Vaccination Advisory Committee did not consider it useful to require boosters in adults. This decision was based primarily on the absence of cases detected here over the past decade.

In 2002, a case of diphtheria was diagnosed in Paris and confirmed by the Corynebacteria CNR. It occurred in a young woman from Asia, probably in France for several weeks and therefore infected after her arrival. In compliance with current recommendations, the Paris DDASS, in cooperation with the DGS and InVS, conducted an epidemiologic investigation to identify the persons who had had close contact with the infected young woman – her family and hospital staff – to offer them throat cultures, antibiotics and, if necessary, a booster vaccination. Nonetheless, the identification of her contacts before hospitalization was probably incomplete, because of her family's lack of cooperation. Although no secondary cases were detected in the months thereafter, the failure to identify a *Corynebacterium diphtheriae* carrier among the family contacts makes it impossible to rule out the hypothesis that this strain circulated among her family and friends.

Corynebacteria or Corynebacterium: family of bacteria in which one species is particularly pathogenic in humans: *Corynebacterium diphtheriae*, which causes diphtheria.

In 1998 InVS conducted a seroepidemiologic survey among a representative sample of the national population to estimate the seroprevalence profile of antidiphtheria antibodies in the French population according to age. Its results are troubling: approximately 40% of the women aged 50 years or older do not have these antibodies (positive threshold: 0.01 IU/ml) and are therefore no longer protected against diphtheria. The proportion of unprotected men is lower, because boosters were systematically administered during compulsory military service: it is less than 20% until the age of 70 and remains lower than 30% above this age.

In view of these factors, together with the end of booster vaccinations among young men following the disappearance of mandatory military service, InVS proposed that the DGS rethink the antidiphtheria vaccination strategy. This issue is included in the questions under consideration by a working group set up within the Vaccination Advisory Committee in 2003 to review booster vaccination strategies among adults.

Nosocomial hepatitis C: persistent avoidable infections

The reports of nosocomial infections that health facilities send to InVS revealed several clusters of nosocomial hepatitis C in 2001 and 2002. The investigations that followed indicate that most of these episodes were avoidable.

By 8 January 2003, InVS had received 505 reports of nosocomial infections for the period from 1 August 2001 to 31 December 2002: 8 (1.6%) concerned nosocomial hepatitis C in patients undergoing hemodialysis (4) or who were hospitalized or underwent surgery in the three months before the diagnosis (4); overall, these 8 reports covered 33 cases of hepatitis C.

These reports triggered investigations within the facilities. The nosocomial infection coordinating center assisted in the investigations, as did the HBV and HCV CNRs and InVS on some occasions. The aim was to confirm the nosocomial character of the cases reported, search for other cases, assess hospital practices to find the means of transmission, and analyze the HCV strains

isolated. These investigations confirmed the nosocomial origin of each of the eight reports of nosocomial HCV.

Reports of nosocomial hepatitis C from hemodialysis departments

HCV serologic tests performed as part of the routine laboratory monitoring of dialysis patients identified the cases included in the four reports from hemodialysis centers. Three of the four corresponded to isolated cases of seroconversion and, for two of them, the investigation made it possible to identify the source patient, a known carrier of HCV who received dialysis during the same session.

The fourth report concerned a cluster of nine cases in a hemodialysis center, reported in December 2001 to the southeast nosocomial infection coordinating center. Systematic HCV screening for all the patients in the Béziers hemodialysis unit who underwent dialysis in 2001 identified 22 cases of nosocomial hepatitis C. The center was closed on 22 January 2002 and the patients immediately transferred elsewhere. In view of this serious epidemic of unusual scale, the DGS established a cell of experts. The investigation was conducted by the southeast coordinating center, in collaboration with the DDASS of Hérault, InVS, AFSSAPS, and other experts. It found that three different HCV genotypes were involved: type 2 (13 cases), type 1a (5 cases), and type 1b (4 cases); these 22 cases appeared over a 9-month period (figure 19).

The investigation also showed that HCV transmission occurred principally via staff actions in connecting successive patients to the hemodialysis equipment. Failure to apply standard precautions and rules of hygiene to hemodialysis explains this epidemic, transmitted on the hands of the healthcare staff. It may have been aggravated by stress caused by restructuring in April 2001: during this period, the number of dialysis posts increased from 8 to 12, a change that necessitated the reorganization of treatment in a tiny room in a facility that had too few personnel and too much turnover.

After setting up corrective measures, the hemodialysis center reopened on 25 March 2002. No contamination has been reported since the last case in January 2002.

Reports of nosocomial hepatitis C outside of hemodialysis departments

Two of these four reports corresponded to isolated cases and two to clustered hepatitis C cases. These episodes show how important it is to consider a nosocomial cause when acute hepatitis C is diagnosed, by ascertaining whether the patient was hospitalized in the months before the onset of the infection.

The investigation found the source of contamination for one of the two isolated cases reported. It involved a patient with diabetes hospitalized in a medical department. The practice audit conducted by the Paris-North coordinating center showed that improper use of a blood glucose monitor was a possible source of the contamination. Because blood was placed on a strip already inserted in the monitor, contact was permitted between the patient's finger and the possibly contaminated monitor. The investigation of the second report is underway at the date this report was written: it

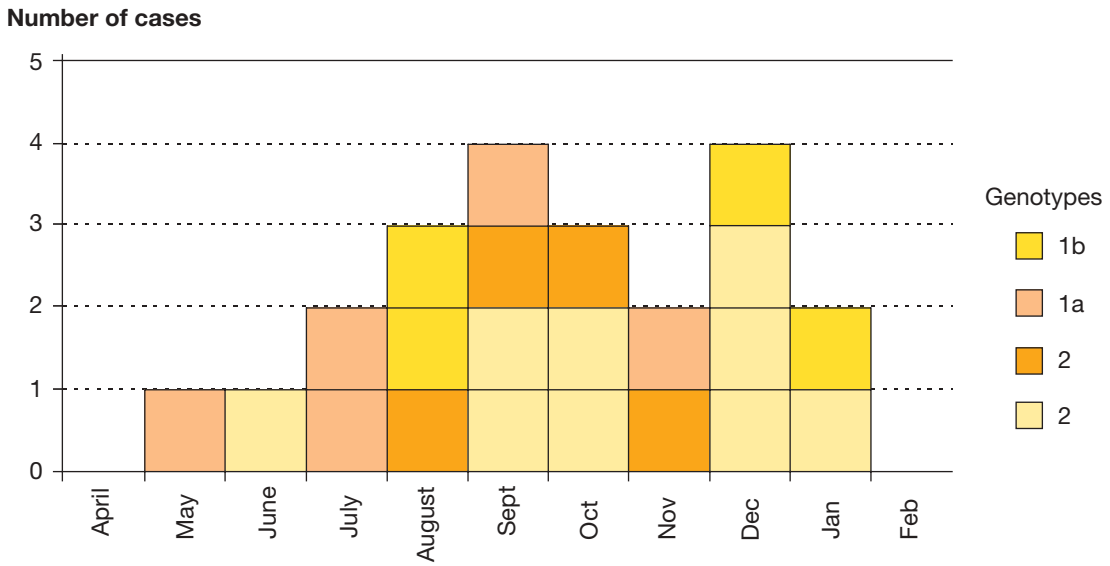
The 26 July 2001 decree and the reporting of nosocomial HCV infections

Nosocomial infection reporting is an alert system intended to supplement the national surveillance networks administered by the alert network for the investigation and surveillance of nosocomial infections (RAISIN). Its action-oriented objective is to detect nosocomial infections sufficiently serious or recurrent to require the implementation of prevention and control measures at the local, regional, or national level. It provides technical assistance to health facilities in formalizing their alert procedures and allows them to call in outside aid if necessary. Unlike surveillance networks, which are voluntary, these reports are a legal obligation defined by the decree of 26 July 2001 and the circular of 30 July 2001.

Among the infections that must be reported are recent cases of hepatitis C of definite or probable nosocomial origin. They meet several of the criteria for reporting defined by the decree: they cause an infrequent and serious nosocomial infection (criterion 1a) and are often associated with procedures that may have exposed other persons to the same risk (criterion 1d). The health facility sends the reporting form simultaneously to the coordinating center (for expert assistance) and to the DDASS (for control); the latter transmit their copy to InVS (for expert assessment and national analysis).

InVS provides back-up methodological support in investigating the cases reported, and cross-checks these data with those received from elsewhere to improve the exhaustiveness of the alerts transmitted (data from the CNR networks and from other agencies, such as AFSSAPS). Finally, the regular analysis of the national data makes it possible to detect emerging infections not considered by the current networks. Reporting, by triggering epidemiologic investigations and specific studies involving all of the participants in the fight against nosocomial infections, reinforces our capacity to control some of them. Documenting them enables the continuous improvement of recommendations directed at healthcare personnel.

Figure 19: Distribution of 22 nosocomial cases of hepatitis C between May 2001 and January 2002 at the Béziers hemodialysis unit



has so far found several possible nosocomial exposures.

Of the two reports of hepatitis C case clusters, the first concerned three patients who underwent surgery during the same orthopedic surgery session. The investigation by the Paris-North coordinating committee showed that the sharing of anesthetic product in multidose vials (without sharing any injectable material) caused the contaminations; this practice disregards the recommendations of the French Society of Anesthesia and Resuscitation. The second report concerned three hepatitis C cases in patients who underwent surgery the same day in the endoscopy and orthopedic theaters of the same establishment. The investigation performed by the Paris-North coordinating center identified general anesthesia as a factor common to the three cases, but the practice audit found no specific abnormality.

The reporting obligation introduced by the decree of 26 July 2001 has facilitated the investigation of hepatitis C cases of definite or probable nosocomial origin and the rapid implementation of appropriate control measures. This new system has so far sparked eight investigations, the results of which have supplemented earlier experience. They have found known causes of HCV contamination in healthcare settings: cross-transmission during hemodialysis sessions and transmission during capillary blood glucose tests. They also point to the risk involved in sharing products or materials, in particular for anesthesia. They have made it possible to modify risky practices in the facilities concerned, to offer screening to other exposed patients, and to develop recommendations for all healthcare professionals.

The effects of reporting go substantially beyond the facilities concerned. The investigation of the Béziers hemodialysis center raised the question of whether similar dysfunctions might exist in other French hemodialysis centers. For this reason, InVS will soon conduct, at the request of the Ministry of Health and in collaboration with the coordinating centers, a two-year national survey to measure the prevalence and incidence of HCV infection and to describe the surveillance methods in hemodialysis centers.

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Germain JM, Gros H, Carbonne A *et al.* Transmission du virus de l'hépatite C potentiellement liée au partage d'un flacon multidoses d'un analgésique central, Eure, 2001. *In* : Numéro thématique – Epidémiologie de l'hépatite C : état des lieux. *BEH* N°16-17/2003 : 102-3

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Risk of acute lung disease associated with the use of defective bronchoscopes

Following the observation in the United States and in France of a defect (loosening of a piece attached to the end of the biopsy channel) in some bronchoscopes, Olympus recalled bronchoscopes in its BF40, BF240, and BF160 series on 13 March 2002. An alert message sent by AFSSAPS and the DGS to healthcare facilities on 22 March supplemented this recall. At that point, despite a report from a US hospital, no French facility had reported any cases of acute lung disease associated with bronchoscopies with the defective models. Nonetheless, in June 2001, before the defect in this equipment was known, bacterial contamination of these bronchoscopes and of bronchial samples had been identified in a French clinic. A meeting at AFSSAPS on 28 March 2002 decided that InVS and the five nosocomial infection coordinating centers would implement a survey to determine the existence of bacterial lung disease associated with this product defect.

This retrospective survey of healthcare facilities and the professionals using these bronchoscopes set as its principal objective the estimation of the risk of acute respiratory infection associated with the defective bronchoscopes that were the object of the recall; the research was limited to the last 30 patients in each establishment who had undergone a bronchoscopy with a defective apparatus before the recall date. The survey's secondary objective was to seek the existence of typical or atypical mycobacterial infections, in particular *Mycobacterium tuberculosis*, in these patients at the date of the bronchoscopy with the defective equipment, to estimate the prevalence of these infections in bronchoscopy patients. The purpose of this estimate was to quantify the exposure to the risk of possible contamination by mycobacteria during bronchoscopy.

Bronchoscope: apparatus introduced into the trachea and then the bronchi to enable their endoscopic examination and the taking of bronchial samples for biopsy.

Results: the risk of infection

Of 347 facilities surveyed, 211 (61%) responded with information about 114 defective Olympus bronchoscopes (table 8). A questionnaire concerning the patients who had bronchoscopies with a defective Olympus model was completed for 97 (85%) of these bronchoscopes; they covered 1412 patients, or an average of 15 patients per apparatus (table 9). A single case of acute lung disease (0.07%) was diagnosed among these patients, but the germ was not identified; the physician who performed the bronchoscopy considered it improbable that the defective machine caused this lung disease because the patient's mucus already appeared purulent at the time of the bronchoscopy.

These figures indicate that the bronchoscopes could be traced accurately in the facilities that responded to the survey, since the patients were identified for 85% of the defective models. Despite the limitations of this survey (retrospective analysis, heterogeneous data sources, subpopulation of patients), it enabled us to estimate the risk of bacterial infection, which turned out to be very slight.

The results of the bronchoscope samples collected in this survey for 81 (71%) of the defective machines are difficult to interpret given the absence both of positive results for the pathogens usually found in this type of contamination and of information about the conditions in which the samples were taken. These results do not seem to indicate massive contamination of the defective bronchoscopes.

Table 8: Results from 211 facilities

	N	%
Facilities with a series BF40, BF240, BF160 bronchoscope	347	
Facilities responding	211	61%
Olympus bronchoscopes from series BF40, BF240, BF160 used by the responding facilities	455	
Defective bronchoscopes	114	25%
Defective bronchoscopes for which we obtained results of samples	81	71%
Defective bronchoscopes for which a patient was surveyed	97	85%

Table 9: Post-bronchoscopy lung disease and mycobacterial infection at the bronchoscopy

	N
Patients who had a bronchoscopy with a defective apparatus included in the survey	1412
Bacterial lung infections between 2 and 10 days after the bronchoscopy	1*
Patients whose mycobacterial infection status was documented on the date of bronchoscopy	1231
Mycobacterial infection/colonizations at date of bronchoscopy	16
Including *M. tuberculosis*	9
including other mycobacteria	5
including unspecified mycobacteria	2

*lung disease on D7, probably present at bronchoscopy

Mycobacteria results

The status of mycobacterial infection or colonization on the date of bronchoscopy was documented for 1231 patients; 16 (1.3%) had a mycobacterial infection or colonization on that day, 9 (0.7%) due to *Mycobacterium tuberculosis* (table 9).

This result is not surprising, since patients undergoing bronchoscopy usually have risk factors for mycobacterial respiratory infections; moreover, the diagnosis and follow-up of tuberculosis is one possible indication for bronchoscopy. These patients represent a source of potential contamination for patients who subsequently underwent a bronchoscopy with the same equipment. The loosening of a piece of the bronchoscope could have impeded the efficacy of disinfection.

The results of this survey do not indicate an elevated risk of bacterial contamination associated with the defect in the Olympus bronchoscopes, but they do underscore the exposure of patients having bronchoscopies to the risk of cross-contamination by mycobacteria. Flexible endoscopes cannot be sterilized in autoclaves, and their complex design may cause difficulty in their maintenance. This episode points out the importance of good maintenance of endoscopes and of the strict application of official recommendations about disinfection of flexible endoscopes. In addition, the reporting of information about serious incidents linked to defective medical devices is mandatory as part of the medical device monitoring system implemented in 1996.

Epidemic of cutaneous infections of methicillin-resistant *staphylococcus aureus* producing Panton-Valentine leucocidin in the Cotes d'Armor: community and nosocomial transmission

In March 2001, the microbiology laboratory of the Saint-Brieuc Hospital Center in the Côtes d'Armor (Brittany) isolated two strains of *Staphylococcus aureus* resistant to methicillin (MRSA), both with an unusual resistance profile for other antibiotics. These strains came from two patients with cutaneous infections, unrelated to one another but both living in the same town, Lannion. Alerted, the nosocomial infection committee from Lannion Hospital discovered that both patients had been admitted to its maternity ward. Other persons with cutaneous infections were identified among the close friends and family of these patients. In November 2001, analyses by the CNR for staphylococcus toxemia identified an identical strain of MRSA with a gene coding for the Panton-Valentine leucocidin (PVL) in several patients hospitalized or seen in these two hospitals before 9 October 2001. This strain caused cutaneous infections in these patients, but has also been isolated by the CNR in rare but serious cases of necrotizing pneumonia. The Lannion Hospital nosocomial infection committee and the West regional epidemiology unit began an investigation, in collaboration with Saint-Brieuc Hospital, the Côtes d'Armor DDASS, the West coordinating committee, and InVS, to provide a better description of the epidemic and institute control measures.

Panton-Valentine leucocidin (PVL)

This is a toxin secreted by some types of *staphylococcus aureus*. It is a particular virulence factor for unremarkable cutaneous infections (boils, for example), but also more rarely for severe necrotizing pneumonia. This factor is combined here with methicillin resistance, which makes the epidemic more troubling.

The MRSA strain identified in this epidemic produces PVL. These strains seem particularly virulent and easily communicable. The combination of methicillin resistance and this virulence factor (PVL) presents a potential risk of severe bacterial superinfection that can complicate an ordinary viral respiratory infection. This potential risk, considered with both community- and hospital-based transmission, justified the investigations undertaken.

Active hospital- and community-based case-finding began in January 2002. At the Lannion Hospital, the records of mothers and newborns admitted to the maternity ward between October 1999 and February 2001 were examined retrospectively, and the characteristics of the *Staphylococcus aureus* strains isolated from the maternity ward were checked. The maternity ward staff was offered screening for cutaneous infections or nasal colonization by this strain. The case-finding in the community traced the families of cases and identified contacts.

All of the samples taken from cutaneous lesions or by nasal swabs were tested for MRSA, and the strains matching this unusual profile were sent to the CNR for expert assessment.

Results according to data collected by 31 August 2002

This case-finding, conducted for the period 1 October 1999 to 31 August 2002, made it possible to identify 23 cases in 9 households: 15 confirmed cases (65%), 2 probable (9%) and 6 possible (26%).

Case definition in this epidemiologic investigation

A case was defined as any person living in the area of Trégor-Goëlo (Côtes d'Armor) with a clinical picture compatible with a diagnosis of cutaneous staphylococcal infection (folliculitis, furuncle, whitlow, abscess, postpartum mastitis, suppurative wound infection, conjunctivitis with purulent discharge, blepharitis, etc.) diagnosed between 1 October 1999 and 31 August 2002:

– **confirmed case**: isolation of MRSA with a profile determined by the CNR to be identical to that of the strain isolated at Lannion Hospital and expressing the gene coding for PVL;

– **probable case**: isolation of MRSA with an antibiotic resistance profile identical to that of the strain isolated at Lannion Hospital;

– **possible case**: with an epidemiologic link to a confirmed or probable case.

A **household** was defined as a group of persons living under the same roof as a case during the study period. A **contact** was defined as any person without a preexisting, cutaneous infection who lived in the same household as or had close relations with a case.

Twelve cases (4 mothers and 8 newborns) had spent time at the Lannion Hospital maternity ward in the year before the diagnosis of their cutaneous infection. The 23 cases identified lived in 7 towns in the area of Trégor-Goëlo, 11 (48%) of them in Lannion. Six cases (26%) required surgical drainage, 9 (39%) had one or more recurrences. No lung diseases and no deaths were reported. All the strains isolated in these patients belonged to the same epidemic clone, with a similar resistance profile (particularly, sensitivity to gentamicin) and a gene coding for PVL.

Screening of 41 of the 60 staff members of the maternity ward showed no cutaneous lesions or nasal colonization by the strain at issue. Nor was this strain found in any of the 35 strains of *S. aureus* isolated at the maternity ward from clinical samples since April 2001. The negative results of this search, conducted two years after the apparent beginning of the epidemic, do not suggest that the maternity ward is involved in the current transmission of the strain, which has not been isolated in hospitalized patients since September 2000.

The last cases diagnosed were contacts of cases previously identified within the same household. The persistence of these infections in the community may be explained by hand-to-hand transmission within households, possibly promoted by the persistent colonization of some persons by this strain, close contacts, or inadequate hygiene.

This epidemic underlines the importance of basic rules of hygiene, distributed in written form to hospital staff physicians, private practitioners, and clinical laboratories in the region, to encourage them to remind their patients: wash hands and body with antiseptic soap; do not share personal linens (towels, sheets, underwear) and wash them at a temperature above 60°C; regularly clean areas that may be soiled with 1% bleach. To be effective, these measures must be adopted by all members of the household at the same time. It is also recommended to cover infected cutaneous wounds, if possible, and to avoid touching them except during medical care. If necessary, trained workers may visit households to remind them of these rules.

To complete these data, the Côtes d'Armor DDASS, the West coordinating center, and the West regional epidemiology unit conducted an additional study that combined retrospective case-finding and active surveillance by hospital staff physicians, private practitioners, and clinical laboratories. It should also make it possible to determine the origin – community or hospital – of the 12 cases hospitalized in the maternity ward.

This cluster of cutaneous infection cases confirms the community-based transmission of MRSA in France. The combination of methicillin resistance and a virulence factor (PVL) represents a potential risk in the case of more severe infections, especially pulmonary. As of today, the incidence of these infections seen by physicians in private practice remains unknown. It is therefore important to set up studies to characterize these infections better and to identify specific measures to control and prevent them.

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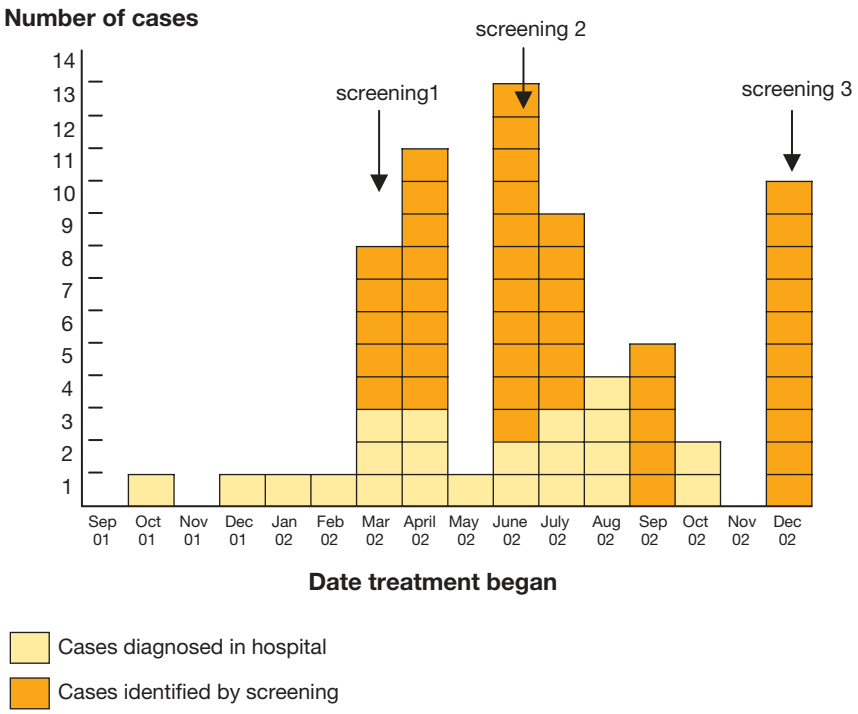
Tuberculosis: epidemic in a hostel for migrant workers in Paris

In March 2002, 13 cases of tuberculosis (2 of them bacilliferous according to bacteriologic examination of the sputum) were discovered in a hostel of African immigrants as part of a program of systematic tuberculosis screening in hostels in Paris, conducted since 1994 by the Paris municipal health department (DASES). This discovery triggered an investigation to find undiagnosed or unreported cases and to propose control and prevention measures.

Bacilliferous: carrying tubercle bacilli in the sputum, therefore contagious.

Four other radiologic screening sessions took place in 2002, with approximately 2590 radiographies taken of more than 1500 persons housed by or having visited this hostel, which has a capacity of 362 beds. These figures illustrate the conditions in the hostel, which caused substantial overcrowding and mobility among those housed there. Active case-finding was undertaken at neighboring hospitals (clinical departments and bacteriology laboratories) and at the Paris DDASS (mandatory reporting). Overall, by the end of 2002, 68 cases of tuberculosis had been identified (figure 20); none of the patients thus screened was lost to follow-up and those who completed their treatment were considered cured. The grouping of the cases in time and space, the presence mainly of early forms of the disease, and the similarities of the isolated strains indicate that the patients were probably contaminated in France. Secondary transmission was amplified inside the hostel because of the living conditions and overcrowding.

Figure 20: Distribution of 68 tuberculosis cases among immigrants who had spent time at the hostel, according to date treatment began, place of diagnosis, and contagious status – Paris 2002



This unprecedented epidemic shows that tuberculosis remains a reality, especially among immigrant populations. Systematic screening made it possible to detect many cases at an early stage and thus to limit morbidity and transmission. Several specific measures of control and prevention were implemented: renovation to combat the unhealthiness of the building, screening in the rooms where many cases were diagnosed. Nonetheless, in view of the high mobility of the population and the incubation period of the disease, this epidemic has probably not ended. For this reason, a permanent medicosocial team began working onsite in the hostel at the end of 2002 to offer tuberculosis screening and treatment as well as information about the disease (recommendation of the High Council of Public Hygiene of France on 15/11/2002).

This epidemic shows the need to sensitize physicians to mandatory reporting and, more generally, to consolidate the battle against tuberculosis, which must be more effective and more reactive; in particular, it requires better communication and liaison between its participants (general practitioners, DDASS, and the tuberculosis department). This reinforcement of the fight against tuberculosis is a special priority in the Paris region, for incidence there is the highest in France.

Reference:

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Clusters of legionellosis: detection and investigation

Progress in legionellosis surveillance has made it possible to detect more clusters and epidemics, many of which would previously have remained unknown. Several clusters were identified and investigated in 2002. These epidemiologic and microbiological investigations are difficult, tedious, and not always successful. This year, they identified and enabled better control of the sources of contamination causing 2 nosocomial epidemics, at Meaux (22 cases including 4 deaths) and Sarlat (31 cases including 6 deaths); in each city, the source proved to be the hospital's cooling tower. Even when the environmental and bacteriological investigation cannot specify the contamination source, it can allow the district health bureau to identify unreported installations not maintained in compliance with current standards and to sensitize their operators to their regular maintenance, thereby reducing future danger. Accordingly, the Jonzac thermal baths were closed for disinfection after 3 cases of legionellosis were reported among its clients. Similarly, in the Doubs, recommendations were made to the exhibitors at the Pontarlier fair who may have been the source of 5 cases.

Legionellosis can also be contracted while traveling, most often through the drinking water networks in hotels, vacation residences, and campgrounds. This problem led to the establishment of the European Working Group for Legionella Infections (EWGLI), aimed at monitoring travel-related legionellosis. In 2002, the EWGLI network reported 19 clusters (2-4 cases) in French hotels or campgrounds. These

To learn more about EWGLI

This European network makes it possible to identify accommodations that housed persons who came down with legionellosis on returning home from a trip. A procedure makes it possible for national and local authorities to implement control measures in the place of accommodation of a person who fell ill after the trip, even in another European country. Accommodations where clusters occurred must obtain within 6 weeks a certification by the local health authorities that it has taken the appropriate measures of control or the hotel name is placed on the EWGLI web site (www.ewgli.org). This system links European surveillance directly to the action of local public health officials (DDASS) and thus reduces the morbidity and mortality from travel-associated legionellosis.

reports triggered environmental surveys in the local DDASS; 2 hotels were closed until completion of work to resolve their problems.

Because of the improvement in epidemiologic surveillance, ever more clusters of legionellosis are detected: this trend will level off only after effective measures of prevention are implemented. In this context, a CSHPF working group has distributed a guide defining acceptable legionella levels in water, in hospitals, and in places of assembly and presenting practical recommendations for managing the risk of legionella. At the European level, a guide on alert and prevention procedures for travel-associated legionellosis has also been produced.

Influenza epidemic in Madagascar: coordination of the international epidemiologic mission

In mid-July 2002, the health authorities of Madagascar received warning of a large number of deaths from acute respiratory disease in the village of Sahafata (2160 inhabitants), located in the highlands of Fianarantsoa province, approximately 500 km south of the capital, Antananarivo. A new alert was launched at the end of July, in an adjoining district. The investigations conducted by the Madagascar Ministry of Health and the Pasteur Institute there found influenza viruses in the pharyngeal samples collected from patients. On 2 August, the rapidly established national surveillance counted 1291 patients and 156 deaths, in 4 different districts. On 7 August, the Madagascar government requested the assistance of WHO, which mobilized its international epidemic network (GOARN). InVS was asked to coordinate the international team sent to Madagascar, which also included representatives of the CDC, the Paris Pasteur Institute (as the French influenza reference center), and WHO.

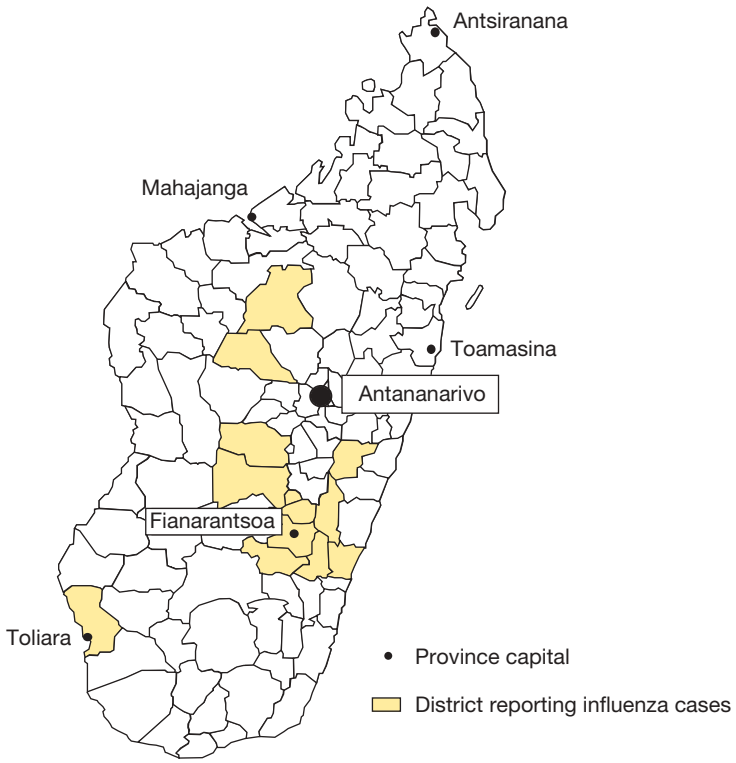
The 6 member team arrived in Antananarivo on 14 August. It remained in Madagascar for 3 weeks, until 5 September, and conducted field investigations in the hardest-hit province, met with local authorities, collected information and samples, and had 152 samples analyzed at the Madagascar Pasteur Institute.

Assessing the extent of the epidemic

According to the influenza surveillance data collected for the entire country by the Ministry of Health, the epidemic peaked during the week of 22 August. On 19 September, 30,304 cumulative cases had been counted, with 754 deaths in 13 of 111 health districts and 4 of the country's 6 provinces (figure 21); 85% of the cases occurred in Fianarantsoa province, a rural area, and only 5% of the deaths occurred in healthcare facilities, where they could have been investigated.

The epidemiologic investigations nonetheless provided a more exact measurement of the nature and extent of the epidemic. The analysis of data collected between 1999 and 2002 by local health centers shows that the number of cases of and deaths from acute respiratory infections peaks each year in winter (Madagascar, in the southern hemisphere, has winter during our summer months) in the highland districts. These winter peaks are therefore not unusual in these regions. The same is true for the presence of influenza A and B viruses, isolated there each year. The influenza viruses isolated in 2002 were type A/Panama/2007/99 (H3N2), like those in circulation throughout the world for many years (this type corresponds to the vaccine strains planned by WHO for the southern hemisphere in 2002 and for the northern hemisphere in 2002–03).

Figure 21: Distribution of cases of influenza in Madagascar, July-August 2002



The particularity of the epidemic in Madagascar is therefore not related to the type of virus, relatively ordinary, but to its exceptional impact on public health. This seems due not to any unusual lethality but to the disease's very high attack rate in the communities in the center of the island. A study in a remote village of the district most affected found that the attack rate of influenza-like illness reached 67%, with mortality estimated at 2%. On the other hand, the Madagascar Pasteur Institute, which surveys influenza virus morbidity and circulation all year long, found no such unusual phenomena in the capital of the province (Fianarantsoa) or in Antananarivo.

Several factors may explain the abnormally high rates of morbidity and mortality of these acute respiratory infections in the rural highlands of Madagascar. Living conditions, in particular overcrowding and malnutrition, together with an especially cold and humid winter, could have promoted influenza transmission within the most vulnerable populations. In the province of Fianarantsoa, 40% of the children younger than 5 years (a population that included 54% of all the deaths) had chronic malnutrition, and most villages had very little access to basic care.

Since the 1997 alert in Hong Kong (chicken influenza), the risk of an influenza pandemic has been a major issue in public health and justifies systematic investigations. This is why this flare-up is rich in information about influenza epidemic control in developing countries and about planning international response to pandemics. Madagascar is one of the poorest countries in the world and had just emerged from a major political crisis that had disrupted the country for months; because the epidemic hit mainly remote areas, the health authorities learned of it late and responded later, despite the surveillance in Antananarivo by the Madagascar Pasteur Institute.

The international team recommended extending influenza surveillance, providing information to the public and healthcare workers about the disease, improving access to care in rural areas, and taking steps to ensure that healthcare facilities have adequate antibiotics for treating bacterial complications. It did not recommend vaccination against influenza, since the epidemic had already spread in August and vaccine distribution was extremely difficult in remote areas. Moreover, the influenza

surveillance system established on this occasion by the Madagascar health authorities appeared needlessly cumbersome and complex. Unable to follow the temporal and geographic extension of the disease, it led to exaggerated and alarmist communication. This project may lead to a long-term collaboration between InVS and Madagascar that would work on reinforcing its alert systems and operational research on influenza.

Reference:

Equipe d'investigation du Réseau mondial d'alerte et de réponse aux épidémies de l'OMS. Épidémie de grippe à Madagascar en juillet et août 2002. *BEH* N°3/2003 : 9-10

CEA employees at Vaujours: a mortality study

From 1957 through 1997, the Atomic Energy Commissariat (CEA) operated Fort Vaujours, which straddled two towns, one in the district of Seine-Saint-Denis and the other in Seine-et-Marne. They tested explosives there, with, in particular, natural and depleted uranium. It was at this military site that CEA conducted the simulations that made it possible to develop the explosive portion of the first French atomic bomb. After the CEA abandoned this site, the prefects of the districts concerned established an interdistrict follow-up committee, to respond to the fears of local officials and neighbors about possible residual soil contamination and to conduct a public inquiry. Responsible for the health-related issues, the Seine-Saint-Denis and Seine-et-Marne DDASS set up a "health" working group. As part of its work, this group sought assistance from the occupational health department of InVS to study the mortality of CEA employees who had worked at Vaujours through 1995.

This study considered the cohort of all workers employed for at least one year at Vaujours between 1955 and 1995. This cohort had already been constructed by CEA and its occupational medicine department as part of an IARC epidemiologic study on the effects of exposure to low doses of ionizing radiation. It included 2473 persons (2010 men and 463 women), 47% of whom still worked at CEA on 1 January 1995. The following information was known for each member of this cohort: date of birth, date of hiring and departure from CEA, occupational category at hiring, and period of presence at Vaujours. Vital status was determined as of 1 January 1995 and found 241 deaths before that date (187 men and 31 women); the cause of death was known for the 218 deaths since 1968. Vital status remained unknown for six subjects.

The InVS occupational health department received the data for this cohort at the end of 2001 and performed an analysis to assess whether the mortality observed in this population (all causes and from cancer) was different from that expected according to the mortality rates of the overall French population. Standardized mortality ratios were thus calculated; they correspond to the ratio of the number of deaths observed and expected (a ratio greater than 1 thus signifies that the observed mortality is higher than expected). Their 95% confidence intervals were calculated to assess their statistical significance (see table 10).

Table 10: Observed and expected mortality in the cohort of CEA employees who worked at Vaujours (1968-1994)

Cohort population	Cause of death	Deaths		SMR:* deaths observed/ deaths expected	95% CI
		expected	observed		
Men	all causes	316	187	0.59	0.51-0.68
	tumor	110	70	0.63	0.49-0.80
	no tumor	206	117	0.57	0.47-0.68
Women	all causes	28	31	1.10	0.75-1.56
	tumor	11	20	1.86	1.14-2.88
	no tumor	17	11	0.65	0.32-1.16

* Standardized mortality ratio (SMR)
95% CI: 95% confidence interval. If the interval does not contain the value 1, the ratio is significantly different from 1: we can thus conclude that the mortality of the population studied is different from that of the general population (or, alternatively, the difference in mortality observed may be due to chance).

Mortality study results

Tumors were the leading cause of death observed in the cohort (37%), followed by circulatory system diseases (23%), and injuries and accidents (17%). This distribution of causes of death is perfectly normal for this type of occupational population.

Of the 70 tumor-related deaths in men, the most common were bronchopulmonary (17%) and gastrointestinal (17%) cancers; the number of deaths observed was significantly lower than the number expected (table 10).

Twenty women died from cancer: breast cancer was the most frequent type (7 deaths). There was a slight, but not significant, excess of deaths from all causes, compared with the number expected. Only 11 cancer deaths were expected; thus the 20 observed constituted a significant excess. Additional analyses showed that this significant excess of cancer deaths was in fact specific to women engineers and managers, among whom there were 7 cancer deaths compared with the slightly more than 1 expected (SMR=4.76: 95% CI: 1.91-9.82). These 7 deaths came from the following types of tumors: 3 breast cancers, 1 ovarian cancer, 1 malignant skin melanoma, 1 lymphocytic-histiocytic lymphoma, and 1 cancer with the site unspecified. The strongest excess corresponded to a brief presence at Vaujours (5 deaths compared with less than 1 expected for presence less than 6 years, 2 deaths compared with slightly more than 1 expected for a longer presence).

To interpret these results, we must bear in mind that excess cancer deaths, especially from breast cancer, among women in high social categories are observed consistently in the epidemiologic literature. The fact that the excess is much more marked for a short work period than for a long duration runs counter to the idea of a relation with working at the site.

The mortality analysis for the CEA employee population reveals no unexpected results. The excess of cancer deaths among women does not appear to be associated with their presence at Vaujours. These results, included in the final report of the "health" group, were presented to the follow-up committee at its last public meeting, during which the conclusions from other studies, about radioactivity, chemical pollution, and groundwater pollution, were also reported. No results warranting concern came out of any of these studies, but several analyses had yet to be performed.

Asbestos in automobiles: risk assessment among auto mechanics

Decree 96-1133, which forbids any transfer or sale of products, material, or devices containing asbestos, came into effect on 1 January 1997. This ban did not concern the resale of used automobiles or of farm and forest vehicles and equipment made before 1997, for a transition period of five years and subsequently prolonged for another year. At the expiration of this moratorium, decree 2002-1528, dated 24 December 2002, continued the dispensation for used vehicles and equipment, except for those with brake pads containing asbestos. Preceding this decision, the public authorities sought expert recommendations. Following a referral from the Department of Labor Relations (dated 17 October 2002) the InVS occupational health department conducted a quantitative evaluation of the risks of lung cancer and pleural mesothelioma associated with asbestos in automotive vehicles among mechanics who work on these vehicles.

Given the very short deadline allotted (two weeks), this evaluation could be based only on available, rapidly accessible information. 1999 census data (from INSEE, the national statistics institute) made it possible to select 242,360 men, aged 16-60 years, who worked as automobile mechanics (that is, whose activity sector or occupation and social category are among those related to automobile repair) and might be exposed to asbestos.

Mechanics' exposure is essentially associated with working on brittle parts, which can cause asbestos fibers (mainly chrysotile) to spread throughout the workplace. These parts are mainly brake linings for both disk and drum brakes from before 1997 (for French cars) as well as clutch linings. The other parts that may contain asbestos (cylinder head gaskets, oil pan gaskets, alternator rings, manifold and fluid circuit gaskets, flange gaskets, and bituminous coatings) cause very little dust emission and are taken apart only very rarely (every 10 to 20 years). Trucks have still other parts that may contain asbestos, including torque limitation linings and brake lever shaft linings.

Several exposure scenarios explored

It was impossible to calculate the levels of asbestos exposure directly from the dust level measures corresponding to the various tasks of automobile mechanics (information too variable or unavailable). We used data from a vast epidemiologic survey of occupational exposures conducted by the Ministry of Labor in 1994 (Sumer survey) to assess the proportion of time spent exposed to asbestos during a work week in a population of mechanics: 70% of them were exposed less than 2 hours a week, 17% from 2 to 10 hours, 11% more than 10 hours, and 2% for an unknown duration.

These data were used to apply several exposure scenarios to the calculations. They combine different levels associated with the tasks performed, different distributions of workers exposed to asbestos, and several periods. Some information about the changes in the automobile fleet in France, the vehicles with parts likely to release asbestos, and the frequency of these parts' replacement made it possible to estimate the natural extinction period for the asbestos-releasing automobile fleet, that is, the time by which they would essentially disappear if no governmental measures were taken. Weekly exposure, expressed in fibers/ml (fibers inhaled on average during a work week), was calculated, followed by cumulative exposure, expressed in fibers/ml/year. To be conservative, these calculations assumed that each mechanic was exposed from the age of 18 years and that his exposure continued at the latest until the age of 65 years.

To assess the carcinogenic effects of chrysotile asbestos (the main type in automobiles), we applied in this work the models used by the Inserm expert advisory group on the health effects of asbestos exposure and by international health authorities. Applying them to the population of

242,360 selected mechanics, we were able to calculate a "lifetime" (between 20 and 80 years) risk of death from lung cancer (taking into account asbestos exposure, the population age structure, and the distribution of deaths from other causes) and the number of lifetime incident mesothelioma cases attributable to asbestos.

Results transmitted to the DRT and the DGS

One of the scenarios appeared to be the most realistic: it assumes that all the mechanics were exposed to asbestos, that this exposure ranged from 0.06 to 0.25 fibers/ml weekly on average for the period before 1997 (date when the sale of new vehicles containing asbestos was banned in France), and from 0.01 to 0.06 fibers/ml weekly for the period from 1998 through 2010. The "natural" extinction of exposure in 2010 seems realistic, in view of the data on changes in the French automobile fleet.

Table 11 presents the risk calculations for the population selected, taking these hypotheses into account and considering that the mechanics have been exposed to asbestos for their entire working life (from age 18 at the earliest through age 65 at the latest).

According to this scenario, for a fiber level per task of 1/ml (plausible median exposure level) corresponding to a mean weekly exposure level of 0.12 f/ml/week for the personnel concerned for the entire pre-1998 period and a mean level of 0.03 f/ml/week for the 1998-2010 period, the (lifetime) cancer (lung cancer and mesothelioma) deaths due to pre-2003 – and thus inevitable – asbestos exposure among these mechanics total 604; if no steps are taken to modify the French automobile fleet before 2010, another 42 deaths can be foreseen.

As a reminder, according to the general French population mortality rate in 1998 (Inserm data), 13,487 "lifetime" lung cancer deaths are expected in this population of automobile mechanics without considering asbestos exposure.

Table 11: Quantitative evaluation of the risk of mesothelioma and lung cancer associated with asbestos exposure in automobile mechanics

Mean weekly exposure level in the population of mechanics f/ml		Lifetime deaths due to exposure before 2003	Lifetime deaths due to exposure if it continues through 2010	Deaths avoided by ending exposure in 2002
		$N_{p1} + N_{m1} = N_1$	$N_{p2} + N_{m2} = N_2$	$N_3 = N_2 - N_1$
Before 1997	1998-2010			
0.06	0.01	160.3 + 141.3 = **301.6**	176.6 + 146.3 = **322.9**	**21.3**
0.12	0.03	320.7 + 282.6 = **603.3**	353.2 + 292.5 = **645.7**	**42.1**
0.25	0.06	641.4 + 565 = **1206.4**	706.5 + 585 = **1291.5**	**85.1**

Np = Number of lifetime deaths from lung cancer
Nm = Number of lifetime deaths from pleural mesothelioma

Surveillance of carbon monoxide (CO) poisoning

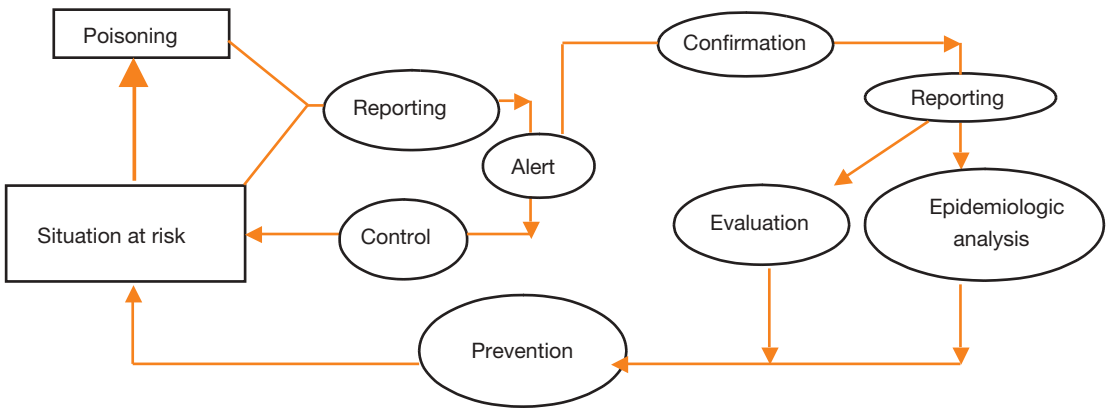
Carbon monoxide is the most common cause of severe acute poisoning in France where it causes several thousand acute poisonings and several hundred deaths each year. Efforts to monitor these incidents epidemiologically began several years ago, but inadequacies in the existing systems have led to incomplete and sometimes contradictory data. At the request of the DGS, a working group met in 2001-2002 to reexamine the entire system and propose a more functional, consistent, and effective replacement. The CSHPF approved the committee's recommendations on 12 December 2002.* InVS is now responsible for the implementation of this new system to improve the surveillance of CO poisoning and thereby also its prevention.

The objectives of the new surveillance system for CO poisoning are threefold:
– **identify** cases and situations at risk (including premises where incidents have already occurred but also other types of situations) to correct them and prevent poisoning;
– **describe** the distribution of CO poisoning in time and space and according to different risk factors, in order to assess the importance of this public health problem and to direct primary prevention strategies:
– **assess** remedial actions, medical management, and prevention policies.
The inclusion of at-risk situations in surveillance, which opens the way to a screening policy, is one of the most important changes in the new system; others include the standardization of definitions and data collection tools and the ability to assign technical investigations to experts in risk situations.

Primary prevention: all measures aimed at preventing the onset of a disease or poisoning. It is distinguished from secondary prevention, which consists of minimizing the disease effects and preventing its aggravation.

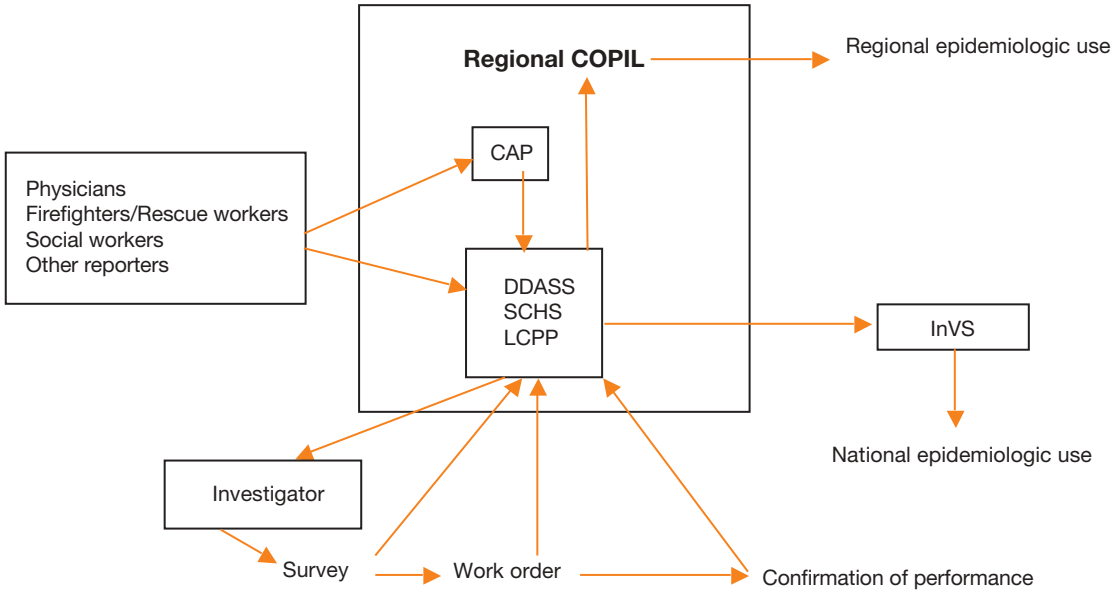
To meet these objectives, a reporting system will be established to provide epidemiologic surveillance (figure 22). This system will resemble the main lines of the mandatory disease reporting system but will differ as to some of the reporters (fire and rescue departments, among others) and participants (poison centers). One of the principal difficulties of this project is the organization of these partnerships (figure 23), with their complex regulatory and financial aspects. **Current plans call for this new CO poisoning surveillance system to be implemented in two experimental regions by the spring of 2004 and for it to be extended nationwide at the end of that year.**

Figure 22: The new system of reporting cases and situations at risk of CO poisoning



* publication pending in the Official Bulletin of the Ministry of Health, the Family and Handicapped Persons

Figure 23: Essential partnerships for the new system for surveillance of CO poisoning



Reference:

Salines G, Ledoyen D, Thierry B. Un nouveau système de surveillance des intoxications au monoxyde de carbone. Journées scientifiques de l'InVS, 3 et 4 décembre 2002. Résumé des présentations, poster. Edition InVS du 23 mars 2003 : poster n°25

Exposure to ionizing radiation for medical reasons: action plan

At the request of the DGS, InVS has for nearly two years led a working group on activities to monitor patients' exposure to ionizing radiation for medical purposes. It submitted its conclusions in September 2002.

The objectives of this surveillance system are to:
– follow changes over time in the distribution of medical irradiation practices and of received doses so that we can identify the populations particularly exposed, orient prevention policies, assess their efficacy, and facilitate the production of information useful for developing epidemiologic studies;
– monitor the possible health consequences of exposure to ionizing radiation and thus the efficacy of the prevention measures recommended and assess the health benefits and risks produced by these policies.

Ionizing radiation: all electromagnetic or particle radiation capable of producing ions directly or indirectly in passing through matter. They include X, alpha, beta, and gamma rays. They are used in medicine for radiography and radiation therapy and, more generally, in radiology.

The working group focused especially on the development of epidemiologic surveillance activities. Its principal recommendations include:

1. creation and development of the logistic conditions needed to implement a surveillance system for medical exposure to ionizing radiation;
2. implementation of a surveillance system for medical exposure to ionizing radiation, with priority to interventional radiology, CT, childhood exposure, and screening activities (mammography);
3. reinforcement of the surveillance of effects possibly associated with ionizing radiation (beginning with cancer) and examination of the possible use of exposure information for this purpose;
4. development of research on the effects of medical exposure to ionizing radiation;
5. development of training and information activities for various participants and structuring of the science watch.

In all cases, these recommendations will require the participation and coordination of numerous partners and the availability of human and financial resources.

Based on these propositions, the Directorate of nuclear safety and radioprotection (DGSNR) has, in collaboration with InVS and IRSN, prepared a national action plan. It assigns to InVS specific responsibility for the system needed to improve knowledge about the frequency of radiologic examinations and their distribution in various population categories. InVS will also conduct field studies to explore the area of interventional radiology and assess the feasibility of surveillance of the doses received by patients and their related complications (radiation burns and epidermitis).

Within InVS, health surveillance related to ionizing radiation exposure must be integrated into cancer surveillance systems. A study is already underway to assess the feasibility of national surveillance of these exposures in thyroid cancer. InVS is also assessing the possibility of a unique health identification code system to facilitate this double surveillance of cancer and the exposure to ionizing radiation associated with it.

To make the knowledge provided by the science watch more accessible to various participants in radioprotection, InVS is also setting up a regular program of critical analysis of recent scientific articles on subjects related to public health and surveillance in this domain.

Reference:

Exposition aux rayonnements ionisants d'origine médicale. Propositions pour la mise en place et le développement d'activités de surveillance épidémiologique en population générale. Rapport InVS - Département santé environnement. September 2002

Indoor Air Quality Observatory

The objectives of the Indoor Air Quality Observatory (OQAI) (run by the construction science and technique center, CSTB) are to learn more about air quality inside buildings, to assess the exposure of populations that spend time in them, and to identify the agents and conditions that present a health risk for these occupants. The system is quite extensive, and InVS's participation in its scientific council gives it an overall vision of the work underway. The environmental health department is participating in the following themes:

– development of methods and tools for a measurement campaign to assess air quality in different types of homes in 2003. This national campaign will include a sample of 720 homes, representative of French housing; its elaboration is based on the information obtained in a 2001 pilot phase involving 90 housing units. The pollutants measured were selected through a ranking based on health criteria but which also took technical and budgetary constraints into account;

– development of methods to assess exposure from the data that will be collected during this national campaign. Through a contract with CSTB, InVS is responsible for organizing and conducting this work, which must simultaneously take into account long-term exposures and those of short duration but greater intensity. It will rely on data from measurements as well as from space-time activity budget information collected during the pilot study. It will focus especially on two indoor pollutants, benzene and carbon monoxide. Other pollutants will be measured (aldehydes, glycol ethers, NO_2, allergens, molds, etc.) and may be the object of similar analyses;

– consideration of the health consequences associated with residential air quality. Possible research directions include the (recurrent) complaints of residents or children in public premises and all of the effects considered together as "sick building syndrome." This early analysis relies on a literature review, the collection of available data from the relevant departments (DDASS, Paris municipal hygiene laboratory, etc.), and information systems already in place. It is intended to help determine the magnitude of the appropriate studies.

The Indoor Air Quality Observatory is a broad program whose goals match ours. Significant involvement by the InVS environmental health department includes participation in developing the public health aspects of the system. This work should help fulfill two goals: to identify the agents for which population exposure should be monitored and to analyze the relevance of the surveillance of specific diseases or of epidemiologic studies that might better characterize the health risks related to indoor environments. It requires multiple partnerships and must thus maintain adequate funding if it is to meet these goals.

Towards a national cancer surveillance system following the model chosen for thyroid cancers

The current surveillance of cancers in France does not meet the needs of the intensified fight against cancer that President Chirac has named as one of the three priorities of his administration. Three* of the Minister of Health's 70 recommendations for the government's plan against cancer involve the improvement of this epidemiologic information system. Accordingly, InVS has proposed a national cancer surveillance system, to be based on the model chosen for the surveillance of thyroid cancer after a long (two and a half years) and intensive multidisciplinary assessment.

* A.1 Improve our knowledge of the changes in the disease over time:
1 – support the cancer registries and develop InVS's national epidemiology system;
2 – develop regional epidemiologic analyses and technical assistance for regional health policies within InVS;
3 – develop a partnership between InVS and IARC for international action programs: surveillance system.

While the current surveillance system (essentially based on registries and the Inserm CepiDc) provides national cancer statistics, reveals their changes over time, and makes it possible to compare France with other, especially European, countries, it is not adequate for these new surveillance aims. It is difficult to use for monitoring programs below the national level (e.g., regional health programs) or for planning healthcare services regionally. It is even less able to provide needed information about environmental risks that may occur anywhere in the country, despite recent expectations of both the authorities and the public. Some cancers must be monitored nationally (cancers related to environmental exposure, sites for which screening is feasible).

To meet these new goals, InVS proposes a national cancer surveillance system based on the recommendations of the multidisciplinary "thyroid" committee for strengthening the surveillance of thyroid cancers.

From the surveillance of thyroid cancers...

The incidence of thyroid cancer in France has been increasing regularly (6% per year); although this augmentation began before the accident at Chernobyl in 1986, it is often perceived by the public as one of its consequences. The surveillance system based on cancer registries (which cover 13% of the general population and 44% of children younger than 15 years) cannot monitor the entire country.

In March 2000, at the request of the DGS, InVS began to consider how to improve the national surveillance of thyroid cancers. Towards this end, it coordinated a multidisciplinary committee assigned to make recommendations on this subject. The committee's final report, transmitted by InVS to the relevant ministerial departments in October 2002, presented various surveillance scenarios assessed in terms of their feasibility, cost, and efficacy. The proposal selected by the Cancer Policy Committee in its report, made public in January 2003, and by the Ministers of Health and of Research involves the establishment of national thyroid cancer surveillance, based initially on a two-level system (figure 24):

– a so-called "routine" level: a continuous, permanent, national follow-up of incident cases recorded with anonymous codes by the PMSI (existing national medical information system), with exhaustiveness validated in the regions covered by registries;
– an alert level triggered by a suspected case cluster in a limited geographic zone or at the request of the population or authorities.

This system will be progressively completed by integration into the first level of surveillance of data from cytopathology reports.

InVS is responsible for validating this two-level surveillance system, for testing the procedures for its implementation for thyroid cancer at pilot sites, and for adapting them for progressive application to the follow-up of other cancers that justify national surveillance.

... To a national cancer surveillance system

This system should result in successfully fulfilling the following three objectives:

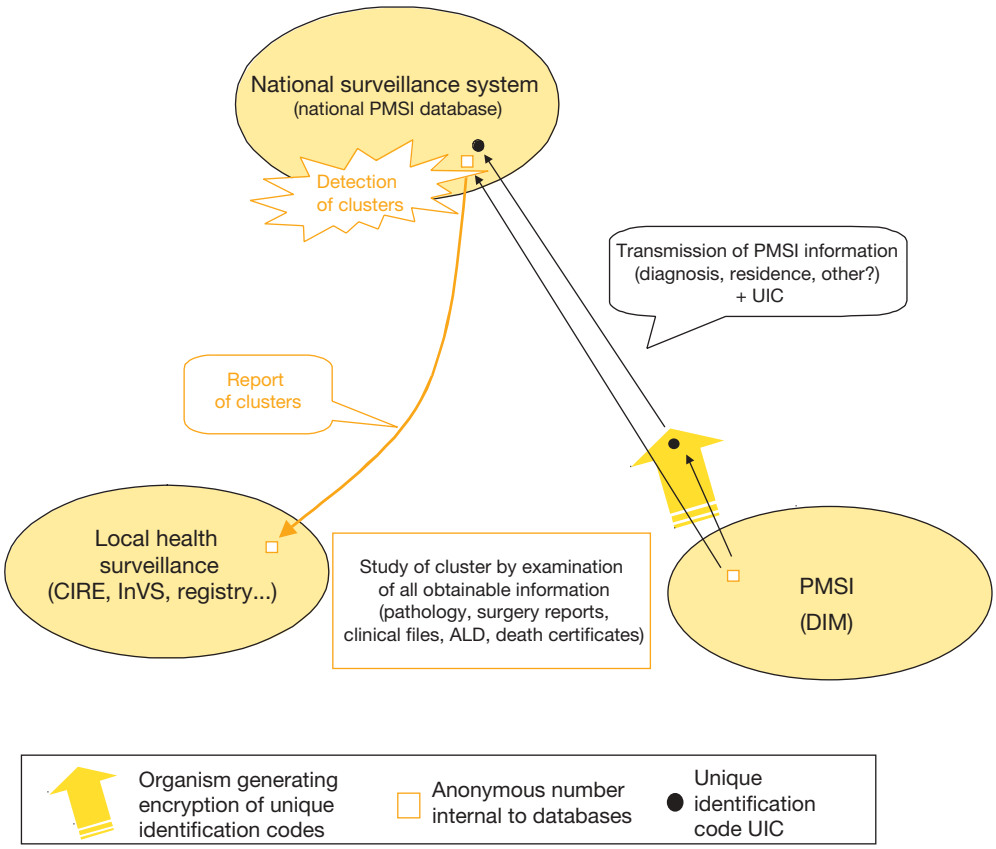
1 – ensure the exhaustive and permanent recording of all incident cancer cases in France. This will make it possible to obtain a baseline for current cancer epidemiology at the national, regional, and even district levels, and to analyze the variations over time and space of incidence, and the trends and deviations relative to the reference levels, so that we may assess the need for specific studies;
2 – respond to alert situations triggered by the onset of a potential case cluster, identified by the national surveillance system, or at the request of the population, or by exposure to an observed risk (for example, a possible radiologic accident);
3 – contribute to epidemiologic studies (cohorts or case-control studies), for example, by looking for thyroid cancers within cohorts of exposed subjects (environmental, occupational, or medical radiologic exposure).

This surveillance system will rely first on data sources available at the national level, albeit not

intended for epidemiologic use: PMSI and the chronic disease lists from health insurance fund records (ALD 30). The cancer registries, which are thought to provide the reference data in the districts they cover, will be used to help calibrate the data from each of these sources. At the same time, the collection of pathologic, histologic, and cytologic data must be structured to make it appropriate for epidemiologic surveillance. The objective is to construct a network that covers all cytopathology laboratories, public and private. The information needed to monitor incidence will be defined and standardized jointly, with the procedures used to make them anonymous. We plan to develop this structure progressively over a five-year period and to generate a unique identification code for the same patient, to facilitate the use of separate, supplementary sources of information (PMSI, cytopathology laboratories).

The final national surveillance system to be constructed and administered by InVS will thus be a multisource system (PMSI, ALD30, cytopathology laboratories, and, if possible, death certificates) containing exhaustive, anonymous, and crossed data that provide supplementary information about the incident cases. It will cover all cancer sites for which the usefulness of national surveillance has been demonstrated.

Figure 24: Organization of two-level epidemiologic surveillance system



Reference:

Leenhardt L, Grosclaude P, Chérié-Challine L, pour la Commission. Recommandations pour la mise en place d'un dispositif de surveillance épidémiologique nationale des cancers thyroïdiens. Synthèse du Rapport. Rapport InVS, octobre 2002

Cosmop: cohort for the surveillance of mortality by occupation

Unlike the English-speaking countries, which have long conducted permanent mortality surveillance by occupation, the only studies available in France explore social inequalities in health through socio-occupational categories. The CnamTS statistics supply data on mortality from occupational accidents and occupational diseases among hourly workers, but do not consider cases that are not reported, not recognized, or not indemnified. They thus cannot be used to assess the role of occupational causes in mortality in France, either globally or for specific occupations. Furthermore, it is probable that the very substantial underestimation of the consequences of occupational exposures contributes powerfully to delaying the provision of information and implementation of prevention, both essential for reducing this premature mortality. It is in this context that the InVS occupational health department developed the Cosmop project.

The principal objective of this surveillance program is to describe systematically and regularly mortality by cause of death, occupation, and activity sector for a representative sample of the French population and to monitor its changes over time. In the absence of occupational exposure data for the general population, the study of mortality by occupation is an interesting approach towards assessing the impact of occupational activity on workers' health status.

The aim of this program is to build a reference database of mortality rates by cause of death and by occupation. It should help to identify the occupations and sectors at particular risk, orient prevention programs, and generate hypotheses and targeted studies in the case of unexplained excess mortality in different groups. In the long run, this monitoring should make it possible to assess the impact of changes in work processes and organization, the effect of prevention policies, and the contribution of occupational risks to the development of social inequalities in mortality.

INSEE's permanent demographic sample (EDP)

EDP is a sample of the French population composed from the 1968 census data and regularly enriched with new subjects. It currently contains approximately 1 million persons randomly selected according to their date of birth (4 days during the year); INSEE follows these people over time, collecting for each of them social, demographic, and occupational information from different census schedules and from vital and civil status forms.

Feasibility study: early results

The feasibility study for the Cosmop project explored the use of EDP data (sidebar) for a systematic analysis of mortality by occupation. The protocol concerning this use, finalized at the end of 2001 in collaboration with INSEE, was approved by the Committee on health research and information in December 2001 and then by the CNIL in March 2002. The EDP file, received by InVS in June 2002, contains socio-demographic and occupational information from four censuses (1968, 1975, 1982, and 1990) for each subject as well as the vital and civil status forms completed since 1968. The sample comprises 322,050 men and 332,396 women born before 1974. In this group, 67,574 men and 59,439 women died between 1968 and 1997: 97% of the causes of these deaths were obtained from the Center for death statistics and epidemiology (Inserm CepiDc).

The first exploration of the file revealed some of the pitfalls in matching vital status with this repertory. Those born before 1891 (1% of the men and 3% of the women in the sample) and those born abroad (18% of the men and 16% of the women in the sample) are included inconsistently or not at all. Moreover, most

National repertory for the identification of persons (RNIPP)

The RNIPP is a file kept by INSEE containing information about the civil status of all persons born in metropolitan France and in the overseas districts since 1890. This repertory is kept up to date in accordance with the civil status registries through the civil status forms completed and transmitted to INSEE by each local records office. Persons are added several months after their birth, when they receive a repertory inscription number (NIR). For those persons born outside France or in the overseas territories, the National Old-Age Insurance Fund attributes this number on behalf of INSEE.

of those born abroad also died abroad, and their deaths are not recorded. This mortality is therefore substantially underestimated. Moreover, deaths were collected for only half of the EDP individuals after 1990 (two of the four birthdays). The analysis must therefore be restricted initially to those individuals born in France after 1891 and to the 1968-1990 study period.

Preliminary exploration of the EDP occupational data shows that occupation is missing for 10% of the men and women aged 16 years or older at each of the four censuses. More generally, career data is complete for approximately 80% of the men and women present in 1968. Some inconsistencies were identified for a very small proportion of subjects. Now that we have defined the plan of analysis, we are in the process of regrouping occupations and diseases as necessary.

These data indicate that use of the EDP will substantially restrict the study population, especially since the analysis concerns in any case only those who were employed during the study period. Other population samples concerning workers more specifically can be envisaged, in particular, the annual social data reports (DADS) transmitted each year by employers to URSSAF, which cover nearly 80% of the salaried jobs in France.

New anonymized system of mandatory reporting: implementation

The law dated 1 July 1998 and the decrees of 1999 and 2001 applying it enshrine the principle of the anonymity of persons with diseases subject to mandatory reporting and reinforce its protection. To implement these regulatory requirements, InVS and the DGS have agreed upon a strategy with the assistance of the DCSSI (Central Information System Security Office of the Secretary-General of National Defense). In February 2002, the DGS assigned the implementation of this strategy to InVS, which led the project during the past year with an interinstitutional steering committee including experts in information system security (DCSSI) and representatives of the agencies involved (DGS, DAGPB-Sintel, HFD, DHOS) and of concerned associations (Act Up, Human Rights League).

The system of mandatory reporting for specific diseases was completely re-engineered in 2002. The difficulty of the process lay in the need to take into account the demands of all participants, that is: reinforcing the protection of anonymity and respect for individual rights, not imposing an unacceptable work load on the reporting physicians and laboratories, and obtaining high-quality data for epidemiologic surveillance. The CNIL approved the new system at the end of 2002.

This new system for handling diseases subject to mandatory reporting (MRO) is based on four principles:

– involvement of laboratories as well as physicians in mandatory reporting;
– protection of patients' anonymity through double anonymization of the data;
– reinforcement of the data protection rules for reporters, the DDASS, and InVS;
– provision by physicians of individual information to patients about mandatory reporting, its purposes, and their right to access and correct the data about them.

The reporting networks between the various participants were redefined during this process: the reporting physicians and laboratories, the

public health physicians (MISP), the DDASS, and the InVS epidemiologists. Double anonymization of individual data occurs at two levels:
– first at the local level, by the laboratory, physician, or public health inspector, depending on the disease. This first anonymization consists in an irreversible informatic coding of elements of identification (initial of surname, complete first name, date of birth and sex) through software furnished by InVS;
– later, the initial code is recoded when the individual's data are entered into the InVS national files.

Implementation of this new system required a European call for tenders for the development of software to perform this double anonymization. Reporting forms were created for the new mandatory reporting diseases and for the rare old ones for which no form already existed (HIV infection, acute hepatitis B, orthopoxviruses, including smallpox, rabies, etc.), and all the others were reviewed. The rules protecting the confidentiality of individual data on paper and computers were also reviewed for reporting physicians and laboratories, public health physicians from the DDASS, and InVS personnel involved in this data management.
On the occasion of the implementation of this new system, which will guarantee the anonymity of patients and thus enable the collection of sensitive data necessary for the surveillance of acute HBV and HIV infection, InVS and the DGS developed an assortment of information tools to sensitize the healthcare professionals concerned to the issues involved in mandatory reporting and health surveillance. The deployment of the anonymization software and the diffusion of these information tools should enable the new system to go into effect at the beginning of 2003.

The 26 diseases subject to mandatory reporting (MRO)
– Botulism
– Brucellosis
– Anthrax
– Cholera
– Diphtheria
– African hemorrhagic fevers
– Yellow fever
– Typhoid fever and paratyphoid fevers
– Acute symptomatic infection with hepatitis B virus
– HIV infection, any stage
– Invasive meningococcal infection
– Legionellosis
– Listeriosis
– Orthopoxviruses, including smallpox
– Autochthonous malaria
– Imported malaria in the overseas districts
– Bubonic plague
– Poliomyelitis
– Rabies
– Lead poisoning in children
– Suspected Creutzfeldt-Jakob disease and other subacute spongiform encephalopathies transmissible to humans
– Tetanus
– Grouped or clustered food poisoning
– Tuberculosis
– Tularemia
– Exanthematous typhus

Virologic HIV surveillance combined with mandatory reporting

Combined with the system for mandatory reporting of HIV, its virologic surveillance is being studied among volunteers, under the coordination of InVS and the HIV CNR. This study should make it possible to estimate the incidence of HIV infection and to improve the orientation of prevention activities by providing information on the populations recently infected by HIV in France.

This virologic surveillance concerns those older than 13 years with confirmed HIV infection (the reporting of which is now mandatory) who agree, after information from their physician, to participate in this study. This surveillance takes place in the same conditions of anonymity as the mandatory reporting of the infection itself (same anonymity code).

The aim of this study is to assess whether or not the HIV infection is recent (less than 6 months) through a new "detuned assay" and to identify new HIV variants (group O, HIV2) by serotyping. These two examinations do not require an additional blood sample; they are conducted from blotting paper with the first blood sample used for the HIV diagnosis.

The new detuned assay, developed by the HIV CNR, can distinguish recent infections from older ones. Specifically, this test is less sensitive than the newest generation screening (ELISA) currently used to diagnose HIV infection. Thus, the combination of a positive serology with a new-generation ELISA test and a negative result with a detuned assay on the same sample makes it possible to conclude that the infection occurred less than 6 months earlier.

The results of the detuned test and the serotyping will be analyzed with the epidemiologic data collected by mandatory reporting to improve our understanding and analysis of the course of HIV infection, especially in the recently infected population. It will also enable us to follow the development of HIV variants over time.

The use of this detuned assay as well as the non-reporting of its result to the patient has provoked numerous debates with patient associations and is now controversial among physicians.

The result of the test cannot be given to the patient because it was developed as an epidemiologic tool to be used on a population scale and has therefore been validated statistically only from this perspective (sufficient specificity). Its positive predictive value is insufficient for use as a diagnostic test at the individual level, that is, the probability of being infected for less than 6 months when the test indicates recent infection is not adequate from an individual perspective.

The new anonymized mandatory reporting system for HIV/AIDS and the deaths attributable to them combined with virologic surveillance represents major progress in the surveillance of the HIV epidemic in France. The virologic surveillance in particular should make it possible, by moving closer to the point of contamination, to improve prevention strategies and to do so more rapidly.

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HIV/AIDS surveillance: EuroHIV

As coordinator of EuroHIV, InVS is a WHO and UNAIDS collaborating center for HIV/AIDS surveillance. The data from this surveillance, updated on 30 June 2002, show important disparities between Western and Eastern Europe.

The situation in Western Europe (European Union countries, Norway, and Switzerland)

Although the number of newly diagnosed HIV infections remains globally stable (figure 25), the trends differ according to transmission groups: while incidence continues to diminish among injecting drug users and remains stable among men having sex with men, it shows a continuous increase among persons infected through heterosexual contact (+64% between 1997 and 2001), primarily among immigrants from countries where HIV is widespread (mainly sub-Saharan Africa). The data for the first six months of 2002 seem to confirm these trends. Moreover, the recent increase in sexually transmitted diseases among homosexuals in several Western European countries suggests a return to risk behaviors in this group.

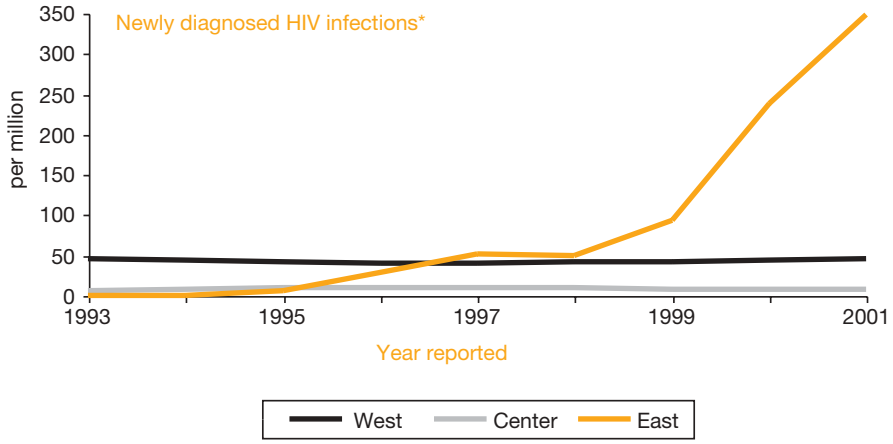
The major challenges currently facing Western Europe are therefore to prevent a slackening of safer sex practices and to improve access to screening and treatment for all infected persons, especially immigrants from sub-Saharan Africa.

The situation in Eastern Europe (countries of the former Soviet Union)

Since the collapse of the Soviet bloc the number of newly diagnosed HIV infections has exploded, climbing from 234 cases in 1994 to nearly 100,000 cases reported in 2001. This major epidemic (the number of infected subjects is estimated at one million), which touches all countries in the region including those in the Caucasus and central Asia, is concentrated among injecting drug users (89%, excluding those with no reported risk factors), in an unfavorable socioeconomic situation (increased prostitution, drug use, and economic depression). The primary risk in this region is the large-scale dissemination of HIV through heterosexual transmission. Currently, the number of cases attributed to heterosexual transmission remains low but has recently increased (53% in 2001 over 2000). Action to contain the progression of this epidemic is thus urgent.

The situation is all the more dramatic in Eastern Europe because the region will inevitably – and soon – be struck by a massive AIDS epidemic, and the local healthcare systems, on the point of collapse, cannot cope.

Figure 25: Newly diagnosed HIV infections (1993-2001), per million inhabitants in Western and Eastern Europe – data reported as of 30 June 2002



* West: excluding Spain, Italy, and France, which did not have national mandatory reporting of HIV seropositivity for the 1993-2001 period.

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Tuberculosis surveillance: EuroTB

As coordinator of EuroTB, InVS is a WHO collaborating center for tuberculosis surveillance. This surveillance showed major disparities between different areas of Europe in 2002.

The 51 countries of WHO's European region reported a total of 385,810 tuberculosis cases in 2000, with marked differences in reporting rates for three areas:

– 12 cases per 100,000 inhabitants in the west (the 15 European Union countries, Andorra, Iceland, Israel, Malta, Monaco, Norway, San Marino, and Switzerland);
– 90 per 100,000 inhabitants in the east (15 countries of the former Soviet Union);
– 41 per 100,000 inhabitants in Central Europe (the remaining 13 countries in WHO's European region).

The surveillance data indicate that tuberculosis control is on the whole effective **in most countries in Western and Central Europe.** In the west, the population of those born elsewhere constitutes a group at risk for tuberculosis (30% of all cases and more than 40% in 9 countries) and for resistance to anti-tuberculosis drugs (2.7% of cases compared with 0.5% among the French population, for example).

In Eastern Europe, the massive increase in reported rates (more than 57% since 1995) expresses an increase in the incidence of tuberculosis and, in some countries, better exhaustiveness and diagnosis due to expansion of the strategy recommended by WHO. The high levels of drug resistance (37% among cases already treated, 9 to 12% among cases with no treatment history) and the inadequate results of treatment observed in several countries show the reduced efficacy of anti-tuberculosis programs in the difficult economic situation there. These trends, which may be accentuated by the contemporaneous HIV epidemic, require urgent readjustment and reinforcement of the programs in Eastern Europe.

Listernet: a feasibility study

InVS and the Listeria CNR (Pasteur Institute, Paris) studied the feasibility of European surveillance of listeriosis (Listernet). This foodborne infection is an important public health problem because of its seriousness, its epidemic potential, and its economic impact. Contaminated products may cause epidemics in several countries, with cases dispersed and only limited numbers in each country; this makes it difficult to detect them on a national level and points to the utility of European surveillance – whence the Listernet project.

Seventeen European countries participated in the feasibility study: 14 countries of the European Union and 3 others (Iceland, Norway, and Switzerland). All of the participating countries, except Portugal, already have a surveillance system for listeriosis, based on mandatory or voluntary reporting in 14 countries and on a sentinel network in 2 others; 16 countries have a national reference Listeria laboratory. The most common methods used to characterize Listeria strains are serotyping (15 countries) and molecular typing (9 countries; 2 others are ready to develop this technique as part of a Europe-wide surveillance).

A panel of experts from ten of the participating countries critically analyzed the surveillance systems and methods and determined that harmonization of case definitions, national data, and laboratory methods is feasible.

Representatives of all participating countries recommended implementation of a European surveillance network and pooling of the harmonized national data, including results of molecular typing, to be performed routinely according to a standardized protocol. On the basis of these recommendations, six countries may begin to contribute in 2003, and seven other participants will begin partially and progressively adapt their surveillance system and their typing practices.

The creation of this surveillance network and this centralized database should make it possible to detect more rapidly and investigate more effectively listeriosis epidemics that until now have not been detected by national surveillance systems. Harmonization of the systems will also facilitate the assessment and comparison of national prevention policies.

Summaries of InVS scientific departments

Department of infectious diseases (DMI)

The department of infectious disease (DMI) is responsible for surveillance, alerts, and the provision of information for decision support, through activities that are both planned (surveillance, studies for decision support) and unplanned (that is, dealing with alerts and governmental referrals).
The difficulty therefore is combining the continuity of planned activities undertaken contractually with the ability to anticipate and react to multiple and increasing alert signals of either community or nosocomial origin.

The function of microbiological expertise, performed by the national reference centers, is an essential component of surveillance and must be harmoniously coordinated with epidemiologic activities. Emerging diseases cause a kind of alert different from the usual kind where the risks are known: they concern previous unknown infectious risks. They raise important problems of detection, investigation, and health response because the responsible agent, the clinical and epidemiologic aspects of the disease, and the methods of control are all unknown. The example of SARS, which first appeared in 2003, illustrates this difficulty: it represents the first test of this type of threat that InVS has faced since the national public health network was created in 1992.

Our surveillance activities are diverse and include systems established long ago (mandatory reporting, laboratory networks), systems set up over the past two years that are producing their first results (hepatitis C), and systems currently in either an experimental phase (Labville network) or beginning deployment (new mandatory reporting for HIV and hepatitis B). Some are administered directly by the department (mandatory reporting, laboratory networks, hepatitis C), while others are delegated under contract to a different public organism (for example, surveillance of Creutzfeldt-Jakob disease to Inserm U390, the Sentinel network to Inserm U444) or coordinated by a group of participants in partnership (for example, nosocomial infections by RAISIN, the alert network for the investigation and surveillance of nosocomial infection, and the surveillance network of regional pneumococci observatories).
The heterogeneity of methods, organization, management, and stage of development of these surveillance systems, each responding to specific objectives, is only too obvious. They nonetheless have in common the continuous provision of sufficiently exhaustive and representative data and the need for rigorous management (collection, validation, databases, detection tools, analysis, and feedback). Their management in secure databases is a major issue. InVS has seen some delay in this domain in recent years. Updating is underway for the diseases subject to mandatory reporting as part of the deployment of the new system with anonymization. This effort at modernization must also address the other surveillance systems so that, for example, regional epidemiology units can access national databases securely; perhaps even direct queries from outside the agencies would be possible.

The surveillance systems must also be evaluated regularly – their operations, performance, and the extent to which they meet their public health objectives. Now that the hepatitis C surveillance system, based on reference centers, has begun producing results after two years of operation, it will be evaluated in 2003. This assessment should show the system's utility and effectiveness and enable us to identify problems to take into account in the future. To the extent that both needs and priorities are evolving and resources are limited, it will be increasingly necessary to conduct such evaluations to identify the surveillance networks that must be modified or even closed. Surveillance at the European level also plays an increasingly important role, especially given the possibility of a European surveillance center. InVS, for example, transmits data to European networks and coordinates several of them (HIV infection, tuberculosis, listeriosis). The organization of our surveillance activities must better take into account this time-consuming constraint and work to ensure the optimal development of the European projects we coordinate.

Signals of infection alerts, already extremely varied (meningitis, foodborne infections, zoonoses, etc.), have expanded with the reporting of nosocomial infections and the equally various responses they may evoke from public health authorities (prophylaxis

for contacts, emergency vaccination program, recall of food products, disinfection of cooling towers, screening of exposed individuals, modification of a medical system, etc.). This requires previous experience and thorough knowledge of governmental and international decision processes and control mechanisms (DGS, AFSSAPS, Ministry of Agriculture, European agencies, WHO, and so on) and a responsiveness and ability to react immediately to analyze signals and launch specific investigations rapidly. Quality assurance procedures have been established and must be regularly revised. Alerts imply investigative approaches that cannot use standardized one-size-fits-all methods. Each situation requires a case-by-case response that is flexible, rigorous, "dialectic," and expert. Response to alerts also entails working in a network with many partners with complementary expertise so that authorities may receive useful responses as rapidly as possible and the risk may be controlled. Finally, the regional epidemiology units are conducting investigations more often (thereby decentralizing them), as they did in 2002 for Q fever in Chamonix and fascioliasis in Nord. This policy, which should continue, implies that the department will more often coordinate than conduct work in this domain. It must nonetheless continue the regular practice of field investigations to maintain its expertise in this fast-moving field.

Epidemiologic surveillance of infectious diseases and response to alerts must rely on high-level microbiological expertise (detection, identification, typing, comparison of strains, etc.). The national reference centers, coordinated and evaluated by InVS, provide these services in France. InVS and the 46 CNRs interact daily on matters covering the entire range of infectious diseases, including those that might be used as bioterror weapons. In 2003, SARS showed yet again that identification of the microbial agent and development of diagnostic tests are key points that require the rapid mobilization of high-level laboratories. In France, these are the influenza CNR, and in the Nord region, the Pasteur Institute. We must therefore maintain this excellent laboratory capacity within the CNR network and reinforce its coordination and interaction with epidemiologic surveillance functions. This requires consolidating the role of InVS in this system, in particular through the CNR Committee, which reports to the InVS Executive Director, and through an adequate and secure level of public funding so that the CNRs can meet the responsibilities assigned to them. InVS is currently working on a permanent resolution of the problem raised by the transportation of strictly regulated strains.

Complementing the department's surveillance and alert investigation activities are the multiple studies that provide the authorities with decision support. They too are based on a variety of methods (survey of population samples, analytic surveys, assessments of the impact of crisis measures, modeling, social sciences). Most often financed by InVS, they may also receive outside subsidies (for example, from ANRS). In 2002, we were able to provide officials with findings on morbidity and mortality associated with foodborne disease, prevalence of HIV and HCV infection among drug users in Marseilles, modes of transmission and incidence of hepatitis C among drug users in northeast France, risk factors for hemolytic uremic syndrome in children, characteristics of HIV infection in immigrants, and vaccine-related seroepidemiology; at the same time we began other studies on delays in HIV screening, population prevalence of and mortality associated with HBV and HCV, and risk factors for sporadic legionellosis.

The results of surveillance, alerts, and investigations must be compared with those from studies. This consistency enables the synthesis of information and analysis needed for recommendations, control, and prevention. Thus, for hepatitis C, the perspective made possible by results from the surveillance networks, investigations of nosocomial reports, and studies among intravenous drug users allowed us to identify inadequacies in the screening and prevention of nosocomial transmission and to document the failure of policies for HCV risk reduction in drug users (even though these policies have been effective for HIV). We were able to make appropriate recommendations. This approach has also proved important for tuberculosis among immigrants: surveillance indicates an increase in its incidence among immigrants in the Paris metropolitan region, and the investigation of an epidemic of more than 80 cases in a hostel for African immigrants showed the extreme vulnerability of this population to this risk. Appropriate response called for the public authorities and local governments to strengthen and modify their

anti-tuberculosis efforts. Finally, confirming and monitoring the implementation of recommendations is essential. For example, we noted during the investigation of a new legionellosis cluster in 2002 that the ministerial recommendations concerning the inventory and monitoring of systems classified as cooling towers following previous investigations had not always been implemented in the field. The perspective provided by tuberculosis surveillance data included in an expert evaluation of vaccine-related policies helped InVS to assess the epidemiologic benefits of the current BCG vaccination policy and propose changes supported by internal and external experts. The Ministry of Health ratified some of these proposals in 2002 (elimination of revaccination and routine tuberculin tests). Others, involving changes in the primary vaccination policy, will be studied as part of a referral to an Inserm expert advisory group in which InVS is participating.

The evaluation of the national vaccination program is based on surveillance of the diseases targeted by the program, regular follow-up of vaccination coverage at different ages, and serologic studies in the population to test the real level of immune protection and its changes with age. The department of research, studies, evaluation and statistics in the Ministry of Health (DREES) currently handles the assessment of vaccine schedule. The changes in the vaccination schedule in accordance with the new recommendations by the Vaccination Advisory Committee (CTV) will require regular adjustments of vaccine coverage surveys, similar to those InVS has already implemented for surveillance of target diseases. InVS coordinated a working group on the assessment and changes in the measurement of vaccine coverage. It included numerous partners (DREES, ORS, regional General Councils, Ministry of Education, the DGS) and made recommendations that were translated into action by the inclusion of a permanent vaccination module in the triennial survey cycle (kindergarten, sixth year and ninth year) conducted by the DREES and the Ministry of Education. InVS activity in the field of vaccine coverage relies on the data produced by DREES, which is published with some delay. The changes in the vaccination calendar and the need for more rapid and responsive data, asserted regularly by the Vaccination Committee and the DGS, indicate that adaptation of collection of vaccine coverage data to specific vaccination-related questions will be less than optimal. Consistency and effective reaction would improve if measurement and follow-up of vaccine coverage were integrated into INVS's surveillance activities in the future.

Finally it is important to summarize what we know about the 2003 SARS epidemic and take it into account for structuring alert response; in particular, links must be reinforced with reference hospital departments for the Biotox plan, university hospital center departments of infectious diseases, and hospital and CNR laboratories. This orientation is essential. Nonetheless many other issues related to disease control and prevention remain in numerous essential public health domains, particularly, chronic infections (HIV, HBV, HCV, tuberculosis), nosocomial infections, antibiotic resistance, vaccine-preventable diseases, and zoonoses. The mobilization and vigilance necessary for dealing with bioterrorism and emerging diseases must not divert us from these goals.

Department of environmental health (DSE)

Environmental health: a complex field

The relation between a population's health status and its environment is difficult to establish and raises important methodological problems. The relations between environmental determinants and diseases are expressed differently depending on a wide range of specific factors (low exposure levels, nonspecific diseases often appearing long after exposure, multifactorial exposure): the methodological tools to be used and how to improve them – both for epidemiologic surveillance activities and for risk assessment procedures – thus require constant consideration. Despite the methodological progress in this field, the tools are often too limited to allow a precise quantification of the health impact associated with environmental exposures. This awareness that scientific procedures do not provide an exhaustive knowledge of risk but rather point out the lacuna and try to pinpoint, insofar as possible, the uncertainties connected with environmental risk assessments reinforces already strong concern by the public about risks that it thinks concern it.
As a field, environmental health intervention suffers from a blatant absence of structure. In fact, mandates involving any aspect of health security or environmental risk have become extremely fragmented and unnecessarily complicate both organizational collaboration and the implementation of any type of consistent or comprehensive action plan.

Department of environmental health (DSE): objectives and approaches

Within the framework of InVS's responsibilities, DSE's objectives are to:

- contribute to the development, orientation, implementation, and evaluation of environmental health public policies, especially the identification and characterization of risk factors or situations;
- respond to requests from government bodies, in particular the Ministry of Health, to assess the health impact of chronic or accidental pollution for decision support purposes.

DSE uses several complementary approaches to meet these objectives. Accordingly, it:

– contributes to the establishment and reinforcement of surveillance systems for health risks (hazards, exposures, risks) related to environmental factors;

– participates in, provides methodological support for, and performs epidemiologic studies of local, national, and international scope, as well as quantitative risk evaluations when scientific knowledge and available data permit;

– develops recommendations (good practice guidelines) and methodological guides that are based on the knowledge, skills, and experience acquired while conducting expert evaluations, epidemiologic investigations, and risk assessments;

– contributes to the development and reinforcement of training activities in the field of ecological epidemiology and risk assessment and develops tools for science watch and information about environmental risks intended for decision makers and professionals.

The strategic areas for DSE development

After substantial work to define priorities in environmental health, DSE began a multiyear activity program in 2001 to apply its approaches to various specific topics. They were applied in many projects, in 2002, several described in detail in the highlights section. 2002 was also characterized by intense development within the department, which obtained new funding contracts. This development took place amidst radical institutional transformation. First, at the regional level, the regional epidemiologic units were reinforced: this improved our territorial coverage substantially. Second, the French agency for environment health and safety (AFSSE) was officially born in 2002. This pivotal year therefore provided the occasion to formalize the three strategic areas on which DSE, taking these changes into account, intends to focus its development.

1. **Rely on the network of regional epidemiology units to deal with environmental health alerts and work to develop methods for use in environmental health**.

Examples include the reports of case clusters in the general population (illustrated above by the Vincennes investigation). Reports of this type, which express increasing social concern about the environment, have multiplied in recent years. Their social and political context is often difficult and they are often highly publicized; their management is therefore extremely delicate, especially since the methodological limitations described above are exacerbated here by the reduction of the field of investigation – in time, space, and population size. During 2002, DSE set up an expert group – epidemiologists from InVS, the regional teams, and Inserm, as well as an oncologist, biostatisticians, and sociologists – to develop recommendations for handling these events.

2. **Develop its national programs for risk identification and surveillance by relying on its network of scientific and technical partners in environmental health.** Here again we can look at an example discussed above, concerning the system for chemical safety or toxicity monitoring. The DGS asked InVS and AFSSE to define their roles in relation to this system and to propose its reorganization. The system's object is to survey the toxic effects in humans related to exposure to chemical products or environmental pollution; its goal is to alert, prevent, and provide information on these chemical risks. This mission of toxicity monitoring fits perfectly into InVS's general mission of epidemiologic surveillance and investigation. We note in this regard that InVS's overall mission covers the entire field of toxicity monitoring (all toxic products in contact with the environment, workers, and consumers). InVS suggests that it play a primary role in structuring this field and leading it; beyond the existing network of toxicity monitoring centers, it concerns – and will concern – an ever-increasing number of healthcare providers and stakeholders. It offers to do this as a "facilitator," that is, leading a close partnership and continuously keeping up with the needs of:

– ministerial bodies, for decision support and evaluation;

– other agencies with related statutory responsibilities: first of all AFSSE (product alerts, toxicological evaluations of products seeking marketing approval), but also AFSSAPS (joint toxicity monitoring and adverse drug reaction reporting), AFSSA (food alerts and food allergy monitoring).

3. **Use social sciences in dealing with environmental health questions.** Vincennes and the health crisis related to the incinerator at Gilly-sur-Isère in late 2001 both illustrate the essential aspect of risk perception and risk communication in the analysis of environmental health questions. These areas are nonetheless underdeveloped at DSE and the regional teams, although every scientist facing such a situation is rapidly persuaded of the validity of including these dimensions from the beginning and throughout the process. Echoing the recommendations of the Scientific Council presented above, DSE initiated collaboration with social scientists while dealing with the issues for Gilly-sur-Isère but also through the "Cluster" working group. These specific collaborations are the prelude to a more detailed reflection on how best to employ the social sciences in handling environmental health questions. Based on an analysis of several typical situations (the contents of intervention requests and problems raised by the responses), we will make and implement concrete recommendations to improve the efficacy of the responses provided by the health security system.

To better express these strategic themes the department has decided upon a reorganization, which will become effective in January 2003. It is based on a division into three functional units:

– a "risk knowledge and surveillance" unit, which brings together the substantive or thematic programs (risks associated with air or water or soil, with a chemical product or a physical factor, environmental diseases, etc.)

– a "statistics and information systems unit" that covers the support activities of statistics and informatics, including database organization, computer security, relations with CNIL, etc.

– a "methods and investigations" unit that works on developing methodology and training in

epidemiology, risk assessment, and the social sciences and that provides support to the substantive programs and to investigations, in particular those conducted by and with the regional epidemiology units.

Department of chronic diseases and trauma (DMCT)

One of the major issues in the department of chronic diseases and trauma involves the creation of an exhaustive system of cancer registration that can respond to most of the questions posed by decision makers, physicians, and citizens.

InVS took important steps towards meeting this objective in 2002 with the major reinforcement of its partnership with the cancer registries. The InVS budget confirmed the funding plan for the cancer registries, conducted jointly with Inserm: their subsidies increased, reaching 1.2 million euros in 2002. Thus eight registries received grants in 2002 to fund an epidemiologist and data collection technicians. The registry network, thus consolidated, is increasingly effective as well as more closely anchored to the field of surveillance. Moreover, a meeting chaired by the executive directors of InVS and Inserm in November 2002 adopted a three-year scientific partnership program between InVS and the registries. It covers all of the relevant topics, from surveillance through screening evaluations.

The department has completed its major project to consider the best procedures for monitoring thyroid cancers. Twenty-four experts – epidemiologists, physicians, and pathologists – participated in this undertaking, which produced a large amount of original work. The orientations proposed by the working group have been discussed with the Ministry of Health, and the scenario chosen was launched before the year ended. Experimenting with a thyroid cancer surveillance system based on the pooling of data from different sources, linked by a unique identification code, will make it possible to test a new cancer surveillance system for the entire country.

Working with local district breast cancer screening centers, we succeeded in validating a new data traceback format for evaluation purposes. It is integrated in the software used by the screening centers; tests on the 2001 data make clear that it will facilitate the transmission of information on this screening, which is becoming widespread. Finally, early work on how this screening affects breast cancer mortality showed a positive impact in the districts that had conducted the most screenings. Other work currently underway will complete these early results.

Thus the programs that InVS developed in 2002 in the area of cancer provided the basis for the proposals we presented to the Cancer Policies Committee, chaired by M. Lucien Abenhaim, the Director General of Health. These proposals were adopted almost entirely in the 70 proposals of the cancer plan presented by M. Jean-François Mattei, the Minister of Health. InVS's role in cancer epidemiology and surveillance was affirmed there, with the perspectives for regional development of this surveillance. These proposals also confirmed the effort expended for the registries, with plans for reinforcing them that should provide France with a surveillance system that meets the expectations of decision makers and of all the stakeholders in the healthcare system.

A second department focus is being built around nutrition, diabetes, and cardiovascular diseases. The Ministry of Health, which has substantially assisted the organization of InVS surveillance programs, has developed national programs around these three themes.

Nutritional surveillance involves first and foremost a national population study of individual food intake (part of the national study of nutrition and health), which includes clinical and laboratory examinations. Conducted with AFSSA, this project has helped to bring these two agencies much closer together and to work out their

respective roles in nutritional surveillance. The results of the test survey conducted in July 2002 led to revision of the survey protocol and to planning for a new test survey in 2003. InVS and AFSSA will reinforce their financial support of this project to ensure the funds to complete performance of this tool, which both agencies consider essential for the assessment of nutritional policy and of risk factors for cardiovascular diseases in the population.

For diabetes, a partnership between ANCRED (the national association for the coordination of diabetes networks, which is heading the project), InVS, CnamTS, Inserm, and the AFD (the French association of diabetics), together with financial support from FAQSV and InVS, made it possible to survey 10,000 persons. The first published results concern data about healthcare use, furnished by CnamTS from its information system (SIAM, health insurance information system). This survey, which should be renewed every three years to measure changes over time, shows the importance of partnerships between numerous participants if this extremely cumbersome type of survey is to succed.

During its first year of operation, the cardiovascular disease surveillance program defined its program contents and launched the measures planned in the national program proposed by the Ministry. A project to survey sudden adult deaths began in collaboration with the ischemic heart disease registries and CepiDc. Moreover, InVS began to support cardiovascular disease registries and thus to consolidate this network so that it may soon participate actively in surveillance.

These three programs have demonstrated their synergy within InVS. Collaborations with other agencies call upon and substantially benefit from the expertise developed within each surveillance program. InVS is thus involved in drafting the guidelines published by INPES for the national nutritional health program and the ANAES working group on diabetes screening. An international dimension is also present: InVS participates actively in projects developed as part of the European health surveillance program. The tools and programs necessary for the surveillance of nutrition, diabetes, and cardiovascular diseases are under construction and will progressively yield the results expected to help evaluate relevant policies.

Finally a third area is being developed around the topic of traumas and injuries. The decision to maintain and reinforce the network for surveillance of everyday accidents, based on emergency room admissions, was a first step in this direction. This reinforcement will take place in 2003. The most complete and highest quality data from this network will furnish the backbone of a surveillance system for the accidents of daily life. We were able to include a section on these accidents in several population-based surveys during 2002: the 10-year health survey (INSEE), the health and social protection survey (CREDES), and the triennial cycle in schools (Ministry of Education-DREES). These surveys will round out the emergency room data and provide better knowledge of the incidence and seriousness of preventable accidents. These partnerships enable us to benefit from synergy between institutions (the State and public or voluntary establishments), from the know-how of other participants, and from existing surveys, without the need for InVS to set up its own specific population surveys.

Beyond these generalist approaches, the department has begun more precise work on this theme with a survey on drowning conducted jointly with the Ministry of the Interior. The purpose was to obtain reliable data to serve as the basis for preparing and evaluating annual prevention campaigns. After the success of the limited survey in 2002, it was decided to make it permanent and extend it throughout the country. This subject will provide the occasion to collaborate anew with INPES, which will take over the drowning prevention campaign from the Consumer Safety Committee.

Finally the program is highly involved in European work and participates actively in the European network of injury prevention, established as part of the European Union program of the same name. The aim is to position France and InVS as important partners in European injury surveillance.

The field of traffic-related injury surveillance is a possible area of expansion, for reduction of such injuries is a major government objective.

Overall, 2002 was another a year of building for the department, which implemented and consolidated both tools and partnerships for surveillance. Regular publication of results has already begun for the oldest programs (breast

cancer screening), and the newest programs have already issued several reports and publications. The department's strategy centers on the construction of partnerships that are specific to each topic in areas where multiple participants already exist. Existing programs must be reinforced to guarantee that they have reached a critical size and will remain functional at the same time as new surveillance programs are considered.

Department of occupational health (DST)

In 2002, the workload of the Department of occupational health rose substantially in number of referrals, requested expert opinions, and other unplanned activities. These requests came from the Ministry of Health, decentralized state agencies, and occupational physicians seeking methodological support to respond to questions from labor and management. For example, we analyzed the mortality of workers at the CEA Vaujours site at the request of the district DDASS (93), which was investigating the possibility of remediating this site. Similarly, at the end of the moratorium on the ban against reselling or otherwise transferring vehicles with asbestos-containing components, the Office of Labor Relations (DRT) sought to base its decision on a quantitative evaluation of the risks of mesothelioma and lung cancer among automobile mechanics. These two "emergencies" took two months of a DST epidemiologist's time, although the department had only seven epidemiologists at the end of 2002.

The AZF catastrophe in Toulouse on 21 September 2001 required that DST hire a locally-based epidemiologist. A cohort study of workers in the metropolitan area was planned jointly with the Toulouse CPAM health examination centers and the technical support and training center for health examination centers (CETAF). This study should make it possible to follow the social, occupational, and health effects – both in the intermediate- and long-term – of the catastrophe on the population of workers in the metropolitan Toulouse area. In addition, it will provide the opportunity for real-life experimentation and development of epidemiologic methods for the follow-up of a regional multisector workers' cohort. This is part of the Coset project, which will set up a cohort of workers representative of the French working population; it is one of the projects that forms the core of DST's program for epidemiologic surveillance of occupational risks.

The study of the feasibility of using data from the INSEE permanent demographic sample (EDP) to analyze causes of death systematically according to job history also officially began, with the arrival of an epidemiologist in July 2002; early results should appear in 2003. Moreover, as a member of the committee established by article L 1.176-2 of the Social Security Code, DST estimated the number of cases of some cancers attributable to occupational exposure in France. Because of the lack of sufficient data on the prevalence of various lifetime occupational exposures to occupational carcinogens in the French population, we had to base some of these estimates on data from the international literature. This involved most particularly mesotheliomas, lung cancers, leukemia, and cancers of the bladder and of the nose and sinuses. These estimates will be refined and updated regularly with the implementation of the Matgene job-exposure matrix, designed to be applicable to the French population. It will enable us to assess the extent of past occupational exposure to carcinogens. Moreover, a new collaboration with CANAM will allow us to document diseases related to occupa-

tional activity among self-employed (independent) workers.

DST promotes the development of epidemiologic surveillance activities in companies. One example is the implementation of a surveillance system for occupational risks at the RATP, which recently hired an epidemiologist to work closely with us to conduct the project. We worked with the Ministry of Education's medical department to identify the medical-administrative data recorded by the personnel department that could be used to document employees' health status and identify some occupations or sectors with particular problems. Unfortunately, for reasons related to the Ministry of Education, this project remains on hold. The analysis of cancer deaths among EDF-GDF employees as a function of their occupational exposures continues.

As part of its work in cancer research, the Association for Research on Cancer created a center for the epidemiology of occupational cancers; together with DST, it has mobilized various stakeholders in the occupational risk world to stimulate cross-sectional activities in the area of occupational exposure evaluation – necessary for both research and surveillance. The consequent identification of a network of partners and the pooling of their methods and data should facilitate the DST program on occupational exposure evaluation and in particular the completion of the Matgene matrix. DST must therefore hire professionals able to lead this program and must train young industrial hygienists in the methods specific to exposure evaluation from an epidemiologic (surveillance and research) perspective. This requires the effective implementation of a planned partnership with the Lyons university institute of occupational medicine.

From its creation, DST began searching for the solid alliances essential for structuring epidemiologic surveillance in the area of occupational risks. It has sought to collaborate with research organizations (Inserm, INRS, IRSN, universities, etc.) specializing in the domain and with those working in the field (occupational medicine, CHSCT, industrial hygienists, occupational medical Inspectors, occupational disease departments). This effort must continue. The goal is to mobilize occupational physicians to work as effectively as the network of 80 occupational physicians in the Loire Valley, who are participating in a program of musculoskeletal disease surveillance in industry, or the physicians working for the agricultural workers' insurance fund who are involved in surveillance of meat industry workers in Brittany. This can only be envisaged if these volunteer networks of occupational physicians can count on effective and permanent leadership. The Office of Labor Relations planned from DST's origins to second a medical inspector (Mirtmo) to DST for this purpose; unfortunately, this assignment could not be made in 2002, for reasons beyond InVS's control.

The effort to build a structure for the epidemiologic surveillance of workplace health must continue if we are to document the effect of occupational factors on the health status of the French population. The Matgene job-exposure matrix project and the Coset project to built and follow a multisector multirisk cohort in the general population must therefore take off rapidly. These two tools will enable the systematic surveillance of the population's health status in relation to its occupational activity, but only after the partnerships necessary for their implementation have become reality.

International department (DIT)

The DIT was created in July 2002. Rather than report our activities, necessarily limited at this stage, we describe here the steps leading to the department's creation and define its responsibilities.

Justification

International activity is included in the tasks assigned to InVS by the law of 1 July 1998, which stipulates that InVS may "*perform health surveillance functions for the European Union, international organizations, and third countries*" and "*participate in France's European and international activities, in particular in international public health networks.*"
InVS accordingly created an international health unit (IHU) as early as January 2000. Its mission was to provide technical assistance to partner countries and to participate in international health surveillance networks. Comprised of only two persons, this team had primarily a leadership and cross-sectional coordination role, without any real operational capacity.
To increase the visibility of InVS's international activity, the creation of a true international department was proposed in spring 2002.
To maintain a structural consistency with the other InVS departments, the department was also assigned a scientific theme, tropical epidemiology.
The Board of InVS approved this new organizational chart in July 2002.

Missions

DIT's missions cover the following four priority themes:
- technical assistance to partner countries,
- participation in international epidemic alert and response networks,
- surveillance of specific tropical diseases,
- health information about events abroad.

With the first two themes, the department is continuing and expanding the activities of the international health unit. These activities are conducted principally in partnership with the Ministry of Foreign Affairs (MAE) (technical assistance) and WHO (alert networks). The highlights section of this report describes several recent accomplishments in these two domains. The activities involve health surveillance and are thus consistent with InVS's national mission. This logic also governs the choice of priority areas: the Mediterranean region, in particular North Africa, Eastern and Central Europe, especially the countries soon to accede to the European Union, and the regions of the overseas districts and territories (Caribbean, South Pacific). The department's specific field within the area of tropical diseases remains to be defined and will, in any case, be developed progressively. As a first step, malaria surveillance was transferred to DIT from the infectious disease department in 2002. This topic covers everything to do with malaria, in metropolitan France (imported malaria, transfusion accidents, etc.) and in the overseas departments where it is endemic (French Guyana, Mayotte).
The health surveillance of events abroad began during the anthrax crisis in the United States in late 2001. It then became apparent that a procedure of this type could be extended to other diseases that might reach our country and to health problems in tourist areas and in countries with large expatriate communities. This approach, presented to the DGS at the end of 2002, must now be conceptualized and made operational.

Resources

2002 marked not only the transition between the IHU and the DIT but also major personnel changes. At the end of the year, the department head and a secretary had begun work, and two epidemiologists had been hired for the beginning of 2003.
This very limited personnel situation required placing some projects on *standby*, in particular, bilateral cooperation projects, in order to meet the priority need to built the department and define its missions.

Perspectives

2003 will therefore be the DIT's first year of real operation. The construction of the department remains the priority, especially as we have not yet reached critical size. The hiring of two additional epidemiologists in 2003, for a total of five technical personnel, should guarantee the continuity of our work. Eventually, a 10-person team should allow

us to meet the objectives defined above.
The operational priority for 2003 is handling the work related to malaria and, beyond that, defining the area of tropical diseases DIT will cover. An inventory and census of partners is planned, both for metropolitan France and for French Guyana, for malaria. Connections with the relevant regional epidemiology units (West Indies-Guyana and Reunion-Mayotte) will be established as part of these activities.
The technical assistance programs will be structured progressively and will stress regional consistency. A first step in this direction will be taken in 2003 with the development of partnerships with Algeria, Morocco, and Tunisia. The program in Morocco will thus continue, and collaboration will begin with the Algiers Public Health Institute for chronic disease surveillance.
The department's growth should give InVS a greater presence in international epidemic response missions. These emergency activities will be rounded out by continuing support to WHO in the construction of alert networks, and especially in our participation in the revision of the international health regulations.
Finally, the system for surveillance of important health events abroad should be operational by the end of 2003, after evaluation of the needs and expectations of our partners.

Department of training and documentation (DFD)

Created in 2002, the department of training and documentation is a site for convergence, conversation, and the diffusion of InVS's knowledge and practices. InVS and the regional epidemiology units, now including several hundred epidemiologists, need to build a common scientific culture. One of the principal objectives of DFD is to meet the need for internal scientific consistency. Beyond the traditional training in which InVS participates, several training programs were developed in 2002 and will become available in 2003. PROFET, a training program for field epidemiology, began in 2002; from 2004 onward, its beneficiaries will be natural candidates to reinforce the epidemiologic intervention teams in the InVS/CIRE network.
Also in 2002 InVS epidemiologists participated in extensive teaching activities at various sites (ENSP, university, Inserm, etc.), thereby spreading knowledge that we must continue to promote.
Finally, DFD participated in InVS's international cooperation efforts by its renewed support of field epidemiology training programs (course in Morocco).

Documentation and science watch, conducted in this unit, are also means of sharing knowledge and making information available in the different areas of InVS and regional team activities.
Team organization was an accomplishment of the year 2002, and our documentary collection grew to meet as effectively as possible the ever increasing expectations and needs of the InVS departments and regional epidemiology units, but also of those asking questions from outside the institution.
The department should grow in 2003 and develop other aspects of scientific documentation, such as prospective monitoring, with various partners.

Finally, the publication of Eurosurveillance, for a Europe-wide audience, fulfilled our mission of diffusion of scientific and epidemiologic knowledge in the area of infectious diseases. Reorganization of this publication, with its weekly and monthly components, is planned in 2003 to take advantage of technological developments in publication resources (the World Wide Web) and to take into account the additional European countries concerned.

Appendixes

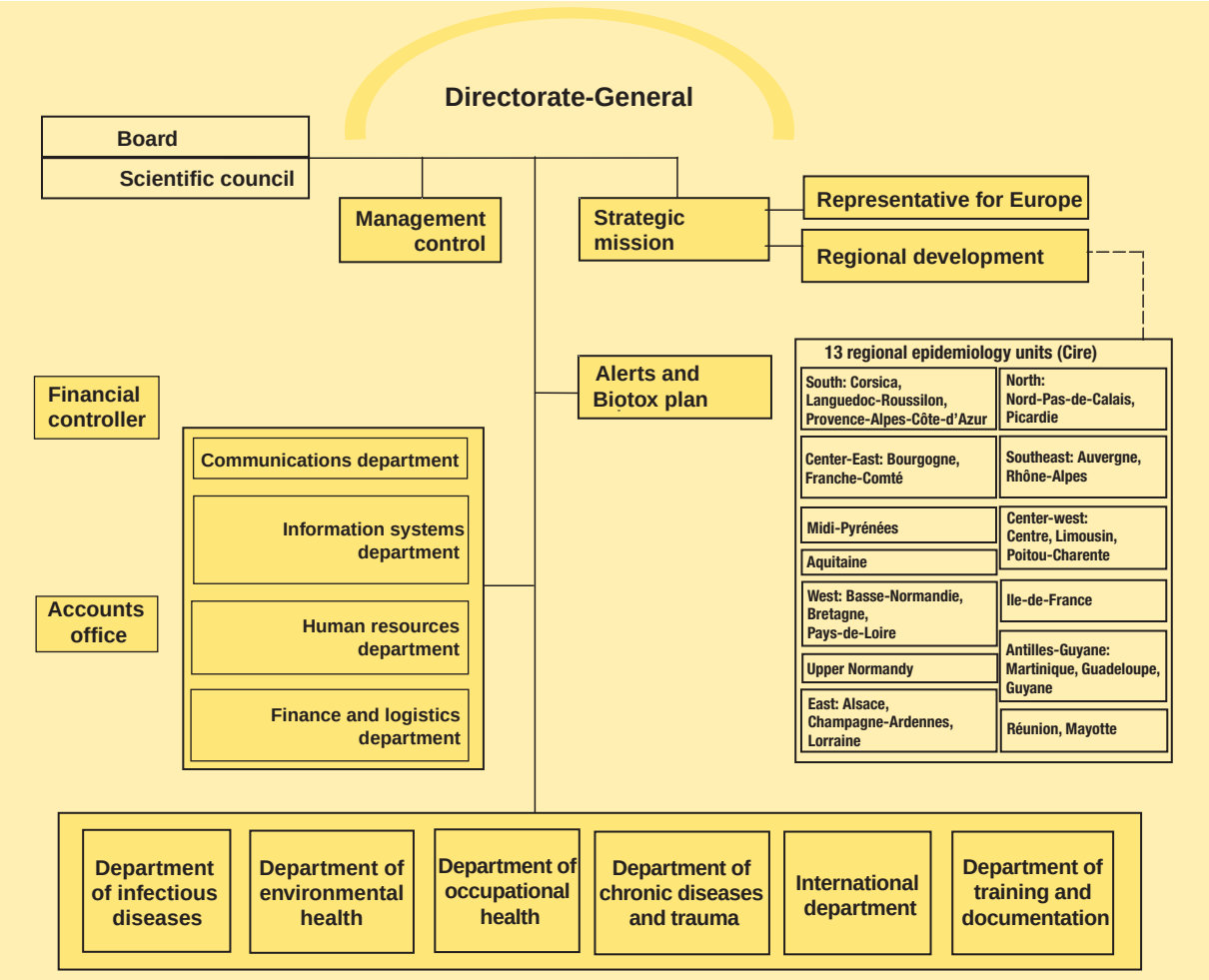
Organization and organizational chart for the InVS

The National Institute for Public Health Surveillance is headed by Pr Gilles BRÜCKER, executive director, aided by Martial Mettendorff, assistant director. It is organized in six scientific departments and four agency-wide service departments. The strategic team reports to the director's office. The institute has a Board of Trustees, chaired by Dr Gilles DUHAMEL and including 22 members, and a scientific council, chaired by Pr François Dabis, with 17 members.

In 2002, InVS had an annual budget of 22 million euros, with 200 employees, principally epidemiologists with underlying expertise in a variety of health and information sciences.

InVS regional activity is conducted through the 13 regional epidemiology units (CIRE), which are under the scientific supervision of InVS and physically located within regional health and welfare bureaus (DRASS): Dijon, Fort-de-France, Paris, Lyons, Marseilles, Lille, Nancy, Rennes, Toulouse, Bordeaux, Saint-Denis de la Réunion, Rouen, and Orléans.

InVS is developing a network to collaborate with its many partners who play a role in the surveillance of the health status of the French population (government departments, regional health observatories, disease registries, welfare agencies, hospitals, health professionals, etc.).



Scientific departments

The department of infectious diseases (DMI) includes 55 permanent staff members and is divided into five specific units:
– *HIV, HCV, and sexually transmitted diseases*
– *Enteric and foodborne infections and zoonoses*
– *vaccination-avoidable infections*
– *nosocomial infections and antibiotic resistance*
– *airborne infections (legionellosis, tuberculosis),* and *imported* and *tropical diseases.*

It also hosts three European programs: the European HIV-AIDS surveillance program, EuroHIV, the European tuberculosis surveillance program, EuroTB, and the experimental European listeriosis surveillance program, Listernet.

The department of environmental health (DSE) has 29 permanent staff members and is organized in three units:
– *the alert response unit*
– *the surveillance unit*, which includes all national and international epidemiologic surveillance programs (air and health; products, toxic substances and health; allergic and asthma diseases, etc.)
– *the risk assessment unit.*

All three units receive cross-sectional statistics and toxicology support.

The department of occupational health (DST) includes nine staff members and is responsible for epidemiologic surveillance of occupational risks: occupational cancers, in particular asbestos-associated mesothelioma and musculoskeletal diseases. It is setting up basic tools that will make it possible to assess mortality according to occupation and to exposures associated with occupational factors.

The department of chronic diseases and trauma (DMCT) includes 15 permanent staff, organized into five units:
– *The cancer unit: cancer surveillance and the evaluation of screening programs*
– *the nutritional epidemiology surveillance unit is a mixed unit staffed by personnel from InVS and from the institute for nutritional sciences and techniques (ISTNA)*
– *the everyday accidents surveillance unit (household, sports, and hobbies)*
– *the cardiovascular disease surveillance program*
– *the diabetes surveillance program.*

This department provides, jointly with Inserm, the technical secretariat for the national registries committee (epidemiologic organizations that "collect on a continuous and exhaustive basis data related to a specific disease: cancers, malformations, cardiovascular diseases, etc.").

The international department (DIT), with a staff of three, participates in international networks, including the international alert and emergency response network, and provides technical assistance to other countries in the areas of investigation and setting up surveillance systems.

The department of training and documentation (DFD) has a staff of 10 persons in two units:
– *the documentation unit,* which makes available to all InVS personnel and their corresponding networks the documents they need for their work
– *the training unit*, which runs a tutorial program in field epidemiology and the IDEA course, in association with the National School of Public Health. It also organizes InVS participation in numerous training programs, university-based and otherwise.

Moreover the DFD coordinates two European programs: EPIET (European training program in intervention epidemiology) and Eurosurveillance (bilingual newsletter of infectious disease surveillance in Europe).

Agency service departments

The communications department has ten staff members.
In collaboration with the Directorate-General, scientific departments, and agency service departments, it develops the external and internal communications policies for the Institute.
Its work is divided among three units:
– *the editing – publishing unit,* which sees to the production of the assorted media in which InVS content is diffused;
– *the unit in charge of the weekly epidemiologic bulletin* (BEH);
– *outside* (press relations, *Prevalence*, its quarterly journal, and its Internet site) *and internal* (*Resonance*, the in-house newsletter, as well as the intranet) communications units.

The finance, logistics, and economics department employs 21 persons. It is divided in two units, both reporting to the assistant director:
– *the budget, accounting, public purchasing and logistics unit,* which draws up the budget, monitors compliance with it, and develops a purchasing policy to ensure the quality of the competitive procedures. Logistics services are a part of this department: they are intended to contribute to improving working conditions for all InVS personnel by managing its property, moving, automotive vehicle fleet, etc.
– *the program management unit*, which works with the activity programs from their initial conception and ensures the legal aspects of their implementation and follow-up, in particular, all contracts and agreements.

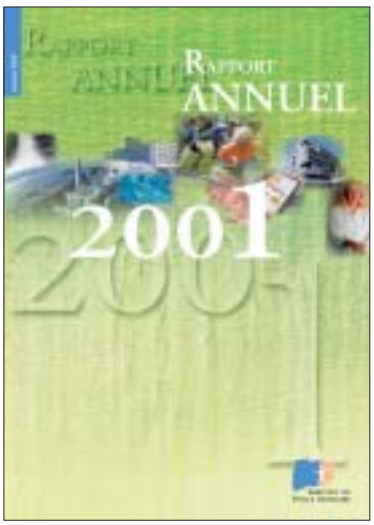
The information systems department includes 12 persons. It has two units:
– *the information technology unit* manages the computer and telephone systems, maintains them, and plans their future development.
– *the development unit* ensures the consistency of the information systems, develops surveillance applications, administers and develops the Internet and intranet sites as well as the databases necessary for health surveillance activities.

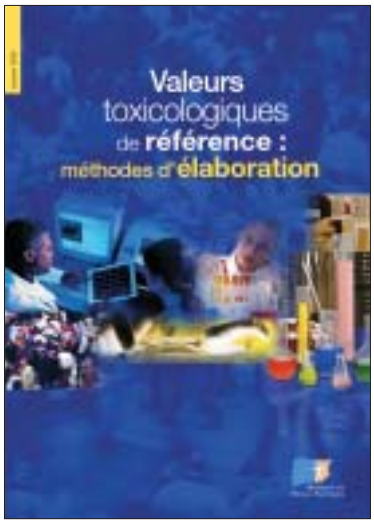
The human resources department has five employees. Through its policies in hiring, training, and continuing education, it helps to ensure that the institute has a skilled and competent staff; it is attentive to individual career path needs and sets up, with the communications department, the in-house communications policy that ensures the agency's cohesiveness. It guides management in its choices with regard to human resources policies (social policy, mobility, evaluations, etc.).

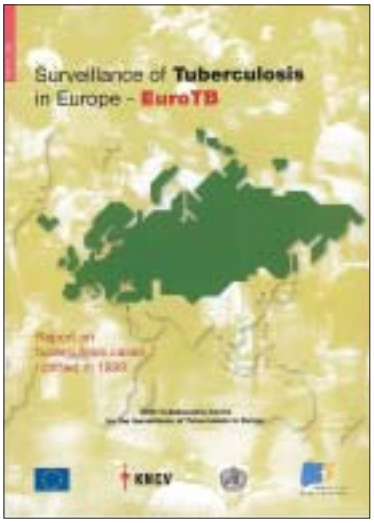
Strategic mission

This unit reports to the director, and its staff represent him in a wide variety of settings. This team implements regional development and coordinates European activities and the construction of the national public health network. It also conducts the follow-up and evaluation of initial departmental contracts, in association with the department, and prepares subsequent contracts. It is also charged, together with the information systems department, to develop the master plan for the information systems.

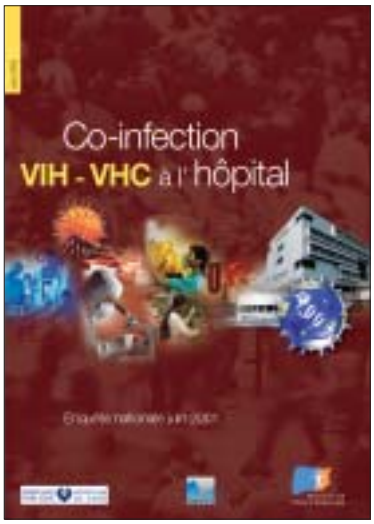
Publications 2002








Estimation
de l'impact sanitaire collectif


Co-infection
VIH - VHC à l'hôpital

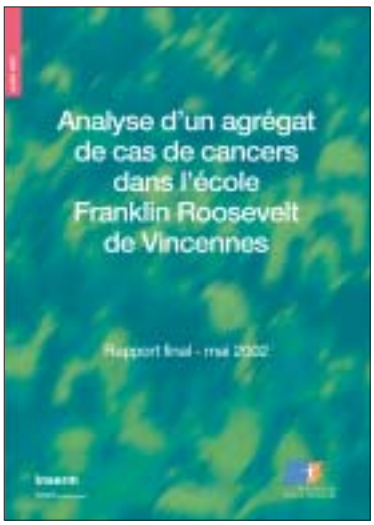

Programme de Surveillance
Air et Santé 9 villes


Programme de Surveillance
Air et Santé 9 villes


HIV / AIDS
Surveillance in Europe
Surveillance du
VIH / SIDA en Europe
EuroHIV


Rapport d'activité
2001
Programme
2002


Analyse d'un agrégat
de cas de cancers
dans l'école
Franklin Roosevelt
de Vincennes


Analyse d'un agrégat
de cas de cancers
dans l'école
Franklin Roosevelt
de Vincennes


Investigation
des évènements de santé

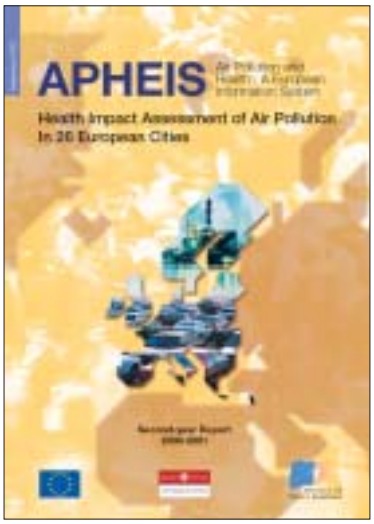

Rapport d'activité
2001
Programme
2002
CIRE

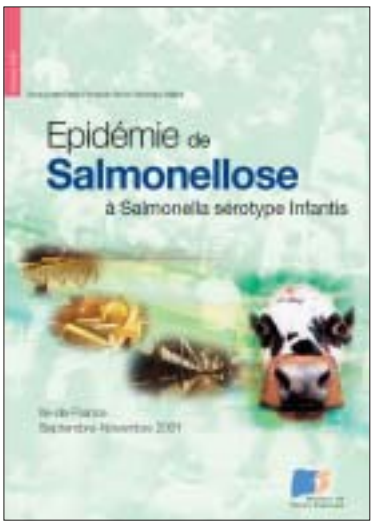

Contrat d'objectifs
et de moyens 2002-2003
Document de synthèse


Contrat d'objectifs
et de moyens 2002-2003
Entre l'Etat et l'Institut de veille sanitaire


Contrat d'objectifs
et de moyens 2002-2003
Annexes Programme


Dépistage
du
cancer du sein


APHEIS
Health Impact Assessment of Air Pollution
in 26 European Cities


Epidémie de
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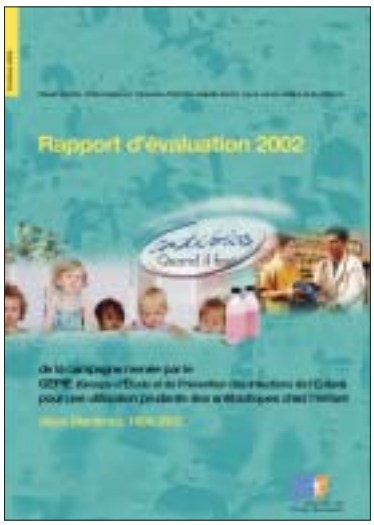
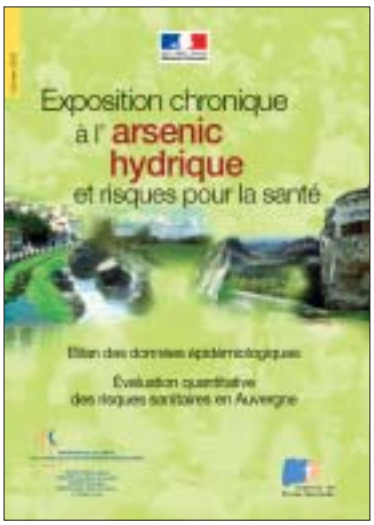
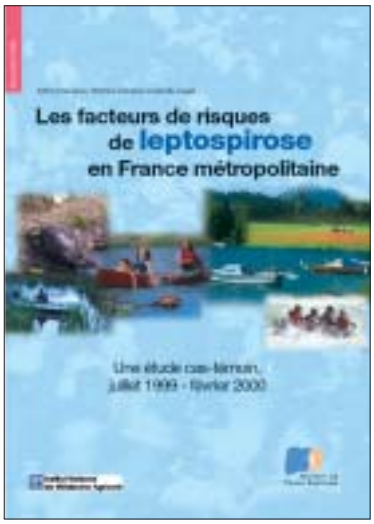

Rapport d'évaluation 2002


Exposition chronique
à l' arsenic
hydrique
et risques pour la santé
Bilan des données épidémiologiques
Évaluation quantitative
des risques sanitaires en Auvergne


SIDA,
VIH et IST
État des lieux
des données
en 2002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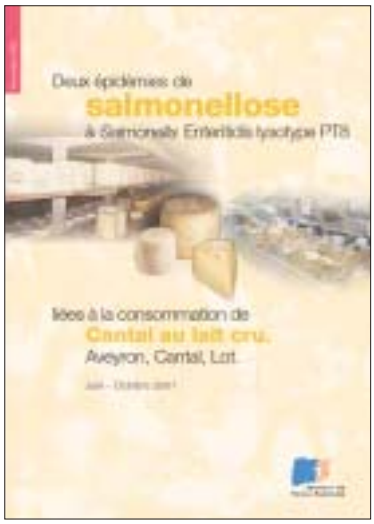
de leptospirose
en France métropolitaine
Une étude cas-témoin,
juillet 1999 - février 2000


Deux épidémies de
salmonellose
à Salmonella Enteritidis lysotype PT8
liées à la consommation de
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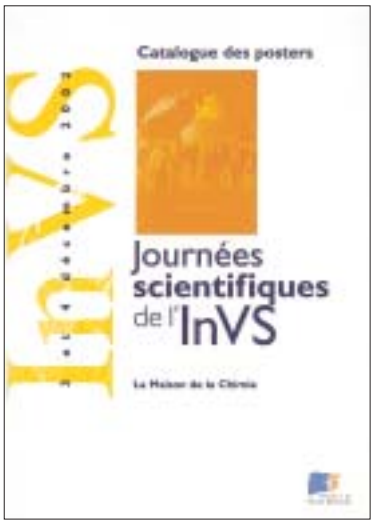
Bulletin d'information
Réseau de surveillance
de la maladie de Lyme
en Alsace


Catalogue des posters
Journées
scientifiques
de l'InVS
La Maison de la Chimie


Résumés des
présentations, posters
Journées
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de l'InVS
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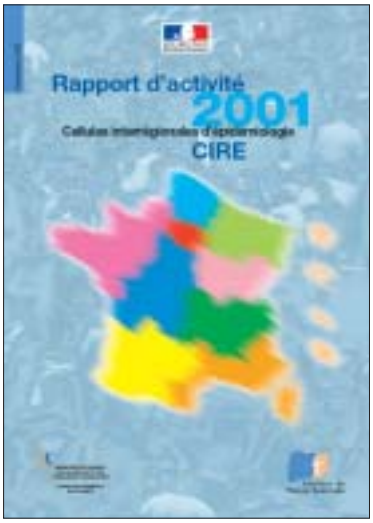
Rapport d'activité
2001
Cellules interrégionales d'épidémiologie
CIRE


HIV / AIDS
Surveillance in Europe
Surveillance du
VIH / SIDA en Europe
EuroHIV

Prevalence
newsletter of the National Institute for Public Health Surveillance

Eurosurveillance
(monthly journal)

Weekly Epidemiologic Bulletin (BEH)

Acronyms and abbreviations

-A-

AASQA	Approved air quality surveillance groups (Associations agréées de surveillance de la qualité de l'air)
ADEME	Environmental and energy agency (Agence de l'environnement et de la maîtrise de l'énergie)
AFSSA	French food safety agency (Agence française de sécurité sanitaire des aliments)
AFSSAPS	French drug agency (Agence française de sécurité sanitaire des produits de santé)
AFSSE	French agency for environmental safety and health (Agence française de sécurité sanitaire de l'environnement)
AIDS	Acquired immunodeficiency syndrome
ANAES	National agency for health accreditation and evaluation (Agence nationale d'accréditation et d'évaluation en santé)
ANRS	National agency for AIDS research (Agence nationale de recherche sur le sida)
APHEIS	Air pollution and health: European information system
APHENA	Air pollution and health: a combined European and North American approach
ARF	attributable risk fraction
AT-MP	workplace accidents and occupational diseases

-B-

BEH	Weekly Epidemiologic Bulletin (Bulletin épidémiologique hebdomadaire)

-C-

CAP	Poison center (Centre antipoison)
CDAG	Clinics offering free anonymous HIV screening (Consultation de dépistage anonyme et gratuit du VIH)
CDC	Centers for Disease Control
CEA	Atomic Energy Commissariat (Commisariat à l'énergie atomique)
CEPIDC	Center for death statistics and epidemiology (Centre d'épidémiologie des causes médicales de décès)
CIRE	Regional epidemiology units (Cellules interrégionales d'épidémiologie)
CNAMTS	National health insurance fund for salaried workers (Caisse nationale d'assurance maladie des travailleurs salariés)
CNIL	National commission for information technology and privacy (Commission nationale de l'informatique et des libertés)
CNR	National reference center (Centres nationaux de référence)
CNSS	National commission on health security (Comité national de sécurité sanitaire)
CPP	Occupational disease center (Consultation de pathologie professionnelle)
CSHPF	High Council of Public Hygiene in France (Conseil supérieur d'hygiène publique de France)
CSTB	Construction science and technique center (Centre scientifique et technique du bâtiment)
CTIN	Nosocomial infection committee (Comité technique des infections nosocomiales)
CTS	Carpal tunnel syndrome (Syndrome du canal carpien)
CTV	Vaccination advisory committee (Comité technique des vaccinations)

-D-

DAGPB-SINTEL	Department of information technologies, Ministry of Health (Sous-direction des systèmes informatiques et des télécommunications du ministère de la Santé)
DASES	Paris municipal health department (Direction de l'action sociale, de l'enfance et de la santé)
DAV	STD clinic network (Dispensaire antivénérien)
DCSSI	Central information system security office of the secretary-general of national defense (Direction centrale de sécurité des systèmes d'information du secrétariat général de la défense nationale)
DDASS	District health and welfare bureaus (Direction départementale des affaires sanitaires et sociales)
DES	Department of environmental health (Département, santé, environnement, InVS)
DFD	Department of training and documentation (Département formation-documentation de l'InVS)
DGCID	Directorate of international cooperation and development, Ministry of Foreign Affairs (Direction générale de la coopération internationale et du développement du MAE)
DGS	Directorate-general of Health, Ministry of Health (Direction générale de la santé)
DG SANCO	Health and consumer protection directorate-general, European Union (Direction générale santé et consommation – Union européenne)
DHOS	Hospitalization and healthcare organization, Ministry of Health (Direction de l'hospitalisation et de l'organisation des soins)
DIM	Medical informatics department (Département d'information médicale)
DIT	International department (Département international et tropical, InVS)
DMCT	Department of chronic diseases and trauma (Département des maladies chroniques et traumatismes de l'InVS)
DMI	Department of infectious diseases (Département des maladies infectieuses de l'InVS)
DRASS	Regional health and welfare bureaus (Direction régionale des affaires sanitaires et sociales)
DREES	Department of research studies, evaluation and statistics, Ministry of Health (Direction de la recherche, des études, de l'évaluation et des statistiques)

DRIRE	Regional offices of industry, research and the environment (Direction régionale de l'industrie, de la recherche et de l'environnement)
DRT	Office of labor relations (Direction des relations du travail)
DST	Department of occupational health (Département santé-travail de l'InVS)

-E-

EARSS	European antimicrobial resistance surveillance system
ECOEHIS	European countries environmental health indicators system
EDP	INSEE's permanent demographic sample (Echantillon démographique permanent de l'INSEE)
EPIET	European program for intervention epidemiology training
EU	European Union
EUROCHIP	European cancer health indicators project
EUVAC	European surveillance network for vaccine-preventable infectious diseases
EWGLI	European working group for legionella infections

-F-

FRANCIM	French network of 21 cancer registries

-G-

GOARN	Global outbreak alert and response network, organized by WHO

-I-

IARC	International agency for research on cancer (Centre international de recherche sur le cancer)
IDU	Injecting drug user (Usagers de drogues injectables)
INED	National institute of demographic studies (Institut national des études démographiques)
INPES	Prevention and health education institute
INRS	National institute for security research (Institut national de recherche et de sécurité)
INSEE	National statistics institute (Institut national de la statistique et des études économiques)
Inserm	National institute for health and medical research (Institut national de la santé et de la recherche médicale)
InVS	National institute for public health surveillance (Institut de veille sanitaire)
IRSN	Institute of radioprotection and nuclear safety (Institut de radioprotection et de sûreté nucléaire)

-L-

LCPP	Central Paris police laboratory

-M-

MAE	Ministry of Foreign Affairs (ministère des Affaires étrangères
MRO	Disease subject to mandatory reporting (Maladie à déclaration obligatoire)
MISP	Public health physician (Médecin inspecteur de santé publique)
MSA	Agricultural workers' insurance fund (Mutualité sociale agricole)

-O-

OQAI	Indoor air quality observatory (Observatoire de la qualité de l'air intérieur)
ORP	Regional pneumococci observatories (Observatoires régionaux du pneumocoque)
ORS	Regional health observatory (Observatoire régional de la santé)

-P-

PHEWE	Assessment and prevention of acute health effects of weather conditions in Europe
PINCHE	Policy interpretation network on children's health and environment
PMSI	Medical information systems program (Programme de médicalisation des systèmes d'information)
PROFET	Field Epidemiology Training Program
PRS	Regional health program (Programme régional de santé)
PSAS-9	Air and health surveillance program in 9 French cities

-R-

RAISIN	Alert network for the investigation and surveillance of nosocomial infections (Réseau d'alerte d'investigation et de surveillance des infections nosocomiales)
RATP	Paris metropolitan transit agency (Régie autonome des transports parisiens)
RMI	Welfare (revenu minimum d'insertion)
RNIPP	National repertory for the identification of persons (Répertoire national d'identification des personnes physiques)

-S-

SARS	Severe acute respiratory syndrome (Syndrome respiratoire aigu sévère)
SCHS	Town health bureau
SROS	Regional healthcare organization schemes (Schémas régionaux d'organisation des soins)
STD	Sexually transmissible disease
STEC	Shiga toxin producing *Escherichia coli*

-U-

UHC	University hospital center

-W-

WHO	World Health Organization

Glossary

Attack rate
Proportion of those becoming ill among the population exposed to an epidemic.

Bacteremia
Presence of bacteria in the blood, detected by a blood test, but involving an ephemeral phenomenon with no serious manifestations, and thus different from septicemia.

Carcinogenic
Capable of causing or promoting cancer development.

Carpal tunnel syndrome (CTS)
Symptoms (tingling and numbness, often nocturnal, of the first three or four fingers of the hand, diminished sensitivity or even muscle strength) resulting from compression of the median nerve in the carpal tunnel, the posterior or deep wall of which is defined by the carpal bones of the wrist (wrist bones) and the anterior wall by the transverse carpal ligament. CTS is one of the most common work-related musculoskeletal diseases. Electromyography is an examination performed by specialists, who record the electric current accompanying muscle activity and can confirm the CTS diagnosis.

Case-control study
Study comparing the frequency of a past exposure among a group of subjects affected by the disease under study ("cases") and a group of subjects who do not have the disease ("controls"), with the aim of assessing a possible association between the disease studied and exposure.

Cluster
Unusual aggregation, real or perceived, of health events that are grouped together in time and space.

Cohort
Group of persons who share a particular experience (employer, exposure, occupation, year of birth, etc.) and are followed up over time from the date of this experience (beginning of the experience = date of inclusion). The follow-up of the cohort is organized to collect information about one or several health events occurring at different points in time: for example, appearance of a disease with its diagnosis and date of onset.

Co-morbidity
Another disease presented by a patient, together with the disease under study.

Cytopathology
Branch of medicine that examines organs or tissues microscopically to study the lesions caused by diseases. Today it uses many techniques (including electronic microscopy, tissue culture, histochemistry, tissue enzymology, immunology, radioisotope labeling).

Epidemiologic surveillance
"Systematic epidemiologic follow-up and analysis of a health problem and its determinants on a population scale in order to control them through interventions at an individual or collective level and to identify unknown phenomena in terms of their effects or determinants."
This definition was chosen to differentiate epidemiologic surveillance from individual medical surveillance in the workplace and other forms of epidemiologic studies. In these conditions, surveillance must concentrate primarily on problems that have already been identified (through epidemiologic research) and on their expression in the population being monitored, in order to orient preventive or corrective activities.

Epidemiology
Scientific discipline that studies the different factors involved in the onset of diseases or health phenomena as well as their frequency, their mode of distribution, their time course and trends, and the implementation of the resources necessary for their prevention.
(Sources: Bonnes pratiques en épidémiologie.)

Escherichia coli
Previously called colibacillus, this germ belongs to the enterobacteria family and is usually found in the intestines of humans and animals. It can cause urinary infections, suppuration, infants' diarrhea, food poisoning, septicemia, etc. STEC are *Escherichia coli* that produce special poisons called Shiga toxins.

Excess risk
Additional risk due to a specific exposure and relative to the risk in a reference population (generally not exposed).

Health risk
In the area of health, risks are distinguished from hazards: a hazard is the intrinsic capacity of a given agent to cause an adverse effect on health, such as disease, death, malformation, organic or biological dysfunction, while risk is the probability that this effect will occur in a person or within a population exposed to this agent.

Hemolytic uremic syndrome
Combination of acute hemolytic anemia and renal lesions.

Incidence (rate)
Number of new cases of a disease (or of a health event, such as an accident or a risk) in a population during a given period of time, relative to the number of persons in this population (to be distinguished from prevalence).

Incubation
Term designating the latency period between infection by a microorganism and the appearance of the first symptoms characterizing the invasive phase.

Invasive
Term used to describe a morbid process that rapidly invades an organism. Invasive infectious diseases are characterized by the isolation of the pathogenic agent in a normally sterile site. Meningitis (isolated in the cerebrospinal fluid) and septicemia (isolated in the blood) are the primary types.

Ionizing radiation
All electromagnetic or particle radiation capable of producing ions directly or indirectly in passing through matter. They include X, alpha, beta, and gamma rays. They are used in medicine for radiography and radiation therapy and, more generally, in radiology.

Lethality
Death rate from a disease, or an epidemic.

Listeriosis
Infectious disease widespread among animals and transmissible to humans in food. In humans, it can cause meningitis and other central nervous system manifestations. It is especially dangerous for pregnant women, who can transmit it to the fetus.

Meningococcus
Bacteria responsible for meningitis and septicemia (meningococcemia: meningococcal infections).

Mesothelioma
Malignant tumor located principally in the pleura, often accompanied by effusion; its principal known cause is asbestos exposure.

Microbiology
Science that deals with microscopic and ultramicroscopic organisms. It includes bacteriology and virology (the study of bacteria and of viruses).

Musculoskeletal diseases
The entire group of periarticular conditions affecting the soft tissue (muscles, tendons, nerves, vessels, cartilages, bursa) of the limbs and back, caused by overuse of the locomotor system, essentially occupational (repetitive gestures, work involving force, extreme postures or vibrations, psychosocial and organizational factors associated with work).

Nosocomial (infection)
Term for an infection acquired during hospitalization. Infections acquired in hospitals (or clinics) by hospital personnel are also nosocomial infections.

Occupational disease
Disease listed in the tables annexed to the Social Security Code, which can give rise to specific workers' compensation under the conditions mentioned in the table.

Occupational-type disease
(English translation of term: Maladie à caractère professionnel)

Any disease related to workplace exposure that is not listed in the official French occupational disease tables. It does not give rise to specific compensation, but remains covered by national health insurance. Reports of occupational-type diseases contribute to the creation or modification of the occupational disease tables.

Pneumococci
Bacteria indigenous to the pharynx that can become pathogenic and cause diverse infections: otitis and meningitis, especially in children, pneumonia, especially in adults, septicemia, and bacteremia.

Prevalence (rate)
Total number of cases of disease (or a health event such as an accident or a risk) in a population during a given period of time (a year, for example) – without distinguishing between new and old cases – relative to the number of persons in this population (to be distinguished from incidence).

Primary prevention
All measures aimed at preventing the onset of a disease or poisoning. It is distinguished from secondary prevention, which consists of minimizing the disease effects and preventing its aggravation.

Quantitative health risk assessment
A structured methodological process that relies on the use of scientific evidence "to define the health effects of exposures of individuals or populations to hazardous materials and situations" (definition of the US National Research Council, 1983). It was designed to provide information for decision making in situations of scientific uncertainty, to overcome limitations on feasibility and interpretation that are inherent in epidemiologic studies in low-risk situations (associations that are difficult if not impossible to demonstrate in these studies). This type of study (also called a health impact assessment) most closely meets the need to provide information to an affected population about the overall risks engendered by environmental exposures. In 1983, the US Academy of Sciences defined the quantitative risk assessment procedure to include four steps: hazard identification, dose-response assessment (selecting the safe and unsafe values), exposure assessment, and risk characterization.

Registries
Epidemiologic organizations that "collect on a continuous and exhaustive basis nominative data related to one or more health events in a geographically defined population for purposes of epidemiologic and public health research by a team with the appropriate skills" (definition of the decree of 6 November 1995).

Risk factor
Variable statistically associated with the onset of a disease or a health phenomenon.
(Definition by A. Leclerc, L. Papoz, G. Breart, J. Lellouch. Dictionnaire d'épidémiologie. Ed. Frison Roche. Paris. 1990. 143 p.)

Screening
In public health, an activity intended to identify a subpopulation with an elevated probability of having a given disease (cancer or lead poisoning, for example). Screening relies on the existence and use of one or more acceptable, easy tests that make it possible to detect an asymptomatic problem that might not otherwise be noticed (mammography for breast cancer, blood lead level assays for lead poisoning).
Persons with a positive or uncertain test results must then undergo more thorough diagnostic examination for verification and, if the diagnosis is confirmed, they must undergo treatment.

Septicemia
Bloodborne dissemination of a pathogenic germ from an infection site. Septicemia involves generalized and serious events, which is what differentiates it from bacteremia.

Serogroup or serotype or serovar
Category in which bacteria or viruses are classified according to their reaction in the presence of serum containing specific antibodies. This serologic variety is one subdivision of species (for example: *Escherichia coli* serogroup O157, meningococcus serogroup C, *Salmonella enterica* serovar Typhimurium).

Strains
All of the bacteria deriving from the multiplication of a single bacterium; can be considered a sort of "bacterial line."

Syndrome
Combination of several symptoms, signs, or anomalies, constituting a recognizable clinical entity, either because of the frequency of this combination of signs and symptoms, or because it expresses a well-defined disease.

Tinnitus
Erroneous perception of an auditory sensation (buzzing, whistling, ringing or cracking).

Toxicity monitoring
Branch of health surveillance intended to monitor the toxic effects on humans of a product, substance or pollution, with the objective of conducting alert, prevention, training, and information activities.

Tuberculosis disease
Cases of *Mycobacterium tuberculosis* infection expressed by clinical or radiologic symptoms for which anti-tuberculosis treatment is administered and which must be reported to the government. The disease is distinguished from cases of tuberculosis infection, expressed only immunologically ("primary infection without patent site" or "simple visual inspection of tuberculin tests"), which are not subject to mandatory reporting, except (since 2003) for cases of latent tubercular infection in children younger than 15 years (to make it possible to find the source of contamination).

Zoonosis
Infectious disease transmissible in natural conditions from vertebrates to humans, and vice versa (for example: psittacosis, brucellosis).