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.

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.
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.

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 île-de-France, and hospital centers in Val-de-Marne:53 approximately 7000 cases reviewed, with no duplicates;
  - approximately 360,000 pathology reports:
  - specialists in private practice in Val-de-Marne: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).
(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.

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.
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.

### References:


---

### 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).

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)

Number of cases

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.

A Cryptosporidium epidemic

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

Cryptosporidium, cryptosporidia: sporozoal 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.
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.

Reference:
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 (SO₂), particulate matter, metals (lead, mercury, cadmium), and dioxins. Emissions of these pollutants have been measured since 1991.

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 SO₂). 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 SO2 emissions 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).

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

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

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.

References:

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, Lymnaea 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).

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:

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
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:

● **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 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.

In 1998 InVS conducted a seroepidemiologic survey among a representative sample of the national population to estimate the seroprevalence profile of antitoxin 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 antitoxin 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.
Nosocomial infection reporting is an alert system intended to supplement the national surveillance networks administered by the alert network for the control some of them. Documenting them enables the continuous improvement of recommendations directed at healthcare personnel.

Epidemiologic investigations and specific studies involving all of the participants in the fight against nosocomial infections, reinforces our capacity 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 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.

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 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.
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 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.

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.

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

<table>
<thead>
<tr>
<th>Month</th>
<th>Genotypes</th>
</tr>
</thead>
<tbody>
<tr>
<td>April</td>
<td>1b</td>
</tr>
<tr>
<td>May</td>
<td>1b</td>
</tr>
<tr>
<td>June</td>
<td>1a</td>
</tr>
<tr>
<td>July</td>
<td>2</td>
</tr>
<tr>
<td>August</td>
<td>2</td>
</tr>
<tr>
<td>Sept</td>
<td>2</td>
</tr>
<tr>
<td>Oct</td>
<td>2</td>
</tr>
<tr>
<td>Nov</td>
<td>2</td>
</tr>
<tr>
<td>Dec</td>
<td>2</td>
</tr>
<tr>
<td>Jan</td>
<td></td>
</tr>
<tr>
<td>Feb</td>
<td></td>
</tr>
</tbody>
</table>

**References:**


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.

**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.
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.

### Table 8: Results from 211 facilities

| 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

| 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 |
| Including *M. tuberculosis* | 16 |
| including other mycobacteria | 9 |
| including unspecified mycobacteria | 5 |

*lung disease on D7, probably present at bronchoscopy
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-Goélo (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:
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. 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.
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:

• 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).
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:

- 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).
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**

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

\( N_p \) = Number of lifetime deaths from lung cancer  
\( N_m \) = Number of lifetime deaths from pleural mesothelioma