

DOSE-RESPONSE FROM FOODBORNE DISEASE OUTBREAK DATA

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Introduction

In France, outbreak diseases are to be notified (1). In this context, a network has been organized at a national level : for each of the 99 French districts, the veterinary services (DDSV – Direction Départementale des Services Vétérinaires), the public health services (DDASS – Direction Départementale des Affaires Sanitaires et Sociales) and the district public laboratory are associated in order to investigate the outbreaks. Investigations are centralised by the national institute for public health surveillance (InVs - Institut de Veille Sanitaire) and the food directorate of the Ministry of Agriculture (DGAI - Direction Générale de l'Alimentation) in relation with the national reference centres concerned.

This network generates an important volume of data which take into account exposed people, foods and pathogens incriminated making it possible the evaluation of the dose-response relationship. Unfortunately, these data may not be sufficient or not be formatted in the right way to derive dose-response relationship. For these reasons we investigated which data currently collected are interesting and which additional data need to be collected. We also wanted to have a direct contact with the field in order to determine the pertinence, the quality and the limits of the data we would collect. Our main objective was to set a methodology making possible the long term collection of data adapted to the evaluation of the dose-response relationship.

Material and Methods

During the usual investigation of an outbreak, the QMA team (Qualité Microbiologique des Aliments) is in charge of performing analysis of the samples collected by the veterinary services of Paris and 2 other districts closed to Paris (Hauts-de-Seine and Seine-Saint-Denis).

From November 2003 to June 2004, an eight month pre-study has been conducted in Paris. Numerous contacts have been established with veterinary and public health services. The pre-study was initially based on *Salmonella* because, in France, this pathogen is the most frequently isolated from foods implicated in outbreaks (2). Moreover *Salmonella* represents, for many countries, one of the pathogens with a great impact on public health (number of cases, hospitalisations and deaths) (3). However, this methodology could also be applied to other pathogens such as *Campylobacter*, Shiga-toxins producing *E. coli*, *S. aureus*, *Shigella*, etc...

We presented at first the project to the veterinary inspectors and medical staff in charge of the investigations. To the medical services, we proposed an additional questionnaire in order to get data concerning risk factors and then to better characterize exposed people (severity of the symptoms, hospitalisation, former exposition to the pathogen, nutritional state, quantity of

incriminated food ingested, general state, medical treatment, sensibility of the person, etc...). With the veterinary services, we defined a procedure allowing us being in the field during the investigation. In this context, as soon as the veterinary services are aware of a case, they contact the laboratory (on a voluntary basis). Immediately, we reach them everywhere in Paris in less than 1 hour.

During the usual investigation of the veterinary services, we had time to collect additional data which can be used for the evaluation of the dose-response relationship (temperature parameters, better understanding of the conditions responsible for the outbreak, etc...). Then, after inspection, the collected samples (set-aside meal, remainings of the foods, etc...) are sent to the laboratory and the QMA team searches the incriminated pathogen. Depending on the quantity of sample available, an enumeration is performed on one or more samples. The isolated strain of *Salmonella* is then serotyped by the laboratory.

At the end of this pre-study, a debriefing was organized with the veterinary services. To have a better knowledge in the field, we decided to participate to all investigations for which veterinary services contact us even if the symptomatology was not representative of a *Salmonella* infection.

Results

The pre-study allowed us to participate to the investigation of 9 outbreaks (33 % of the outbreaks notified in Paris for this period).

On these 9 investigations, some of them allowed us to get additional data (history of time-temperature, quantity of food consumed, characterization of exposed people,...) but not enough to assess the dose-response relationship. For most of them the pathogen was not identified or not enough sample was available to enumerate the pathogen incriminated (no data concerning the dose).

For Paris, one *Salmonella* outbreak investigation allowed us to get enough data to appreciate the dose ingested and the effect for the exposed people. It was a family outbreak where 3 children and their father were ill (all of them consumed the cheese St-Nectaire). At first, detection and enumeration were performed on the remaining of the cheese. Secondly, the veterinary services recalled 2 entire cheeses of St-Nectaire of approximately 1,5 kg each and detection / enumeration were performed on many samples (the cheese consumed by the family was from the same lot and the same retail shop than the entire cheese). We also had data on the quantity of cheese ingested by each exposed people, the history of time-temperature (retail, home and storage

after consumption by the family), and the characterization of exposed persons. This outbreak was interesting since it was due to *S. Dublin* and, even if all the exposed people were ill, we estimated a low ingested dose showing the importance of taking into account the virulence of the strain when studying the dose-response (4, 5). Moreover, 7 agars have been tested (XLD, other selective or chromogenic agars) and only 2 of them allowed us to obtain characteristic colonies. This showed us the great importance of the methodology used for detection or enumeration of the pathogen for a dose-response study.

At the same time, we also developed some contacts with other veterinary services (especially with District 93). We had recently the opportunity to investigate an other interesting *Salmonella* outbreak in a other family. *S. enteritidis* was implicated (approximately 15 ill persons). We had precise data on exposed people (severity of the symptoms, hospitalisation, former exposition to *Salmonella*, nutritional state, quantity of incriminated food ingested, general state, medical treatment, sensibility of the exposed persons, etc...). We can determine the dose of *Salmonella* ingested (high) taking into account a very good homogeneity of the level of contamination in the cake. This outbreak is still under investigation.

Then, in Paris, we had a third interesting outbreak due to *S. aureus* enterotoxin (type E) in Salers cheese. Again we had precise data on the characterization of exposed people and quantity of cheese ingested. This outbreak is also interesting due to the fact that the quantity of E toxin ingested seemed to be very low (under the limit of quantification during the analysis). Strains will be tested, in the future, for their capacity to produce this E toxin.

Discussion - Conclusion

This pre-study shows us that, in the context of the French surveillance of outbreaks, it is possible to collect pertinent and good quality data in order to assess the dose-response relationship. This work requires the laboratory to be extremely available to collect the additional data. It is important to be present each time the veterinary or public health services contact the laboratory even if it is known that all the data will not be available to evaluate the dose ingested and the response of exposed people.

Being the laboratory associated to the veterinary and public health services is important because it allows to establish consistent contacts with actors of the investigation. Moreover, in terms of methodology it is important to minimize the stress before enumeration (impact of the temperature and storage on the number of cells enumerated). Being in the field is also very important if it is sought to appreciate the quality and the pertinence of the data collected.

Only some of the outbreaks are interesting to evaluate the dose-response relationship. Thus, we think that family outbreaks are more interesting than others. Actually, we frequently have remainings of the meal, data on history of time-temperature, additional data on exposed persons and the analysed samples represent really what have been eaten. Concerning investigations in food catering such as schools (legislation with set aside meals) (6), the analysed samples and the ingested food can have different history (set aside meal are not always stored just before the meal, stress due to the cold storage can be of great importance for the determination of the ingested dose).

In the context of this pre-study, the tested methodology is adapted to *Salmonella* but it must be clear that this methodology is also applicable to other pathogens for which dose-response should be developed.

At this time, the project will be continued taking into account more outbreaks and trying to better characterize strains, food samples and exposed people. Contacts with veterinary and sanitary services from other districts will be developed (presentation of the project, expertise, training, ...).

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References

- (1) TIAC : déclaration, investigation, conduite à tenir. *Journal officiel de la République française* n°1487, juin. 1988.
- (2) S. Haeghebaert, F. Le Querrec, P. Bouvet, A. Gallay, E. Espié, V. Vaillant. Les toxi-infections alimentaires collectives en France en 2001. *B. E. H.*, 2002. N° 50/2002: p. 249-253.
- (3) Morbidité et mortalité dues aux maladies infectieuses d'origine alimentaire en France. 188 p. *Rapport Institut de Veille Sanitaire – collaboration Afssa*. Mars 2004.
- (4) P. Teunis, K. Takumi, and K. Shinagawa. Dose Response for infection by *Escherichia coli* O157:H7 from outbreak data. *Risk Analysis*, Vol. 24, n° 2, April 2004, p 401-407.
- (5) Joshua Fierer and Donald G. Guiney. Diverse virulence traits underlying different clinical outcomes of *Salmonella* infection. *The journal of Clinical Investigation*, April 2001, Vol. 107, Number 7.
- (6) Arrêté du 29 septembre 1997 fixant les conditions d'hygiène applicables dans les établissements de restauration collective à caractère social. *Journal officiel de la République française* du 23/10/1997.