

Shiga-toxin-producing *E. coli* infection and hemolytic uremic syndrome in France, 1996-2002



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Introduction

- A nationwide surveillance system of HUS in children < 15 years was implemented in France in 1996
 - to assess the incidence of HUS,
 - to describe the clinical characteristics of patients,
 - to determine the proportion of cases associated with STEC infection
- Risk factors for sporadic HUS were investigated in a national case control study on sporadic cases reported in 2000-2001

Methods

Surveillance of HUS

- Universal voluntary reporting of pediatric HUS cases since 1996
- Reported by the pediatric nephrology unit in the public hospitals
- Data collected: age, sex, illness (onset of symptoms, treatment, complications) and main potential risk factors (consumption of unpasteurised dairy products or ground beef, contact with cases of HUS or diarrhea)
- Serum samples collected on admission and 15 days later tested for antibodies (IgA, IgM) against lipopolysaccharide (LPS) of 26 STEC serogroups at the National Reference Center for *E coli*

Case definition

HUS: children < 15 years old with:

- microangiopathic hemolytic anemia:
 - hemoglobin < 10g/100ml and schizocytosis 2%
- and renal involvement:
 - serum creatinine level > 60 mol/L if age < 2 years, > 70μmol/L if age ≥ 2 yrs
- +/- hematuria > 20 000/ml (or ≥ ++) +/- proteinuria > 1g/L

Evidence of STEC infection:

- detection of serum antibodies to *E.coli* LPS
- or STEC isolation
- or gene sequences encoding ST production

Case control study

- Sporadic cases with prodromal diarrhea identified through the surveillance system in 2000-2001
- 2 controls, matched for age group and sex, with no diarrhea within 7 days before or after the onset of diarrhea of the case, selected by the case's general-practitioner
- Interviews conducted by telephone using a standardized questionnaire
- Information collected on sex, age, clinical illness, and exposures (foods, water, animals, farms, day-care or school attendance, contact with a patient with diarrhea, travel) in the 7 days before the date of onset of the prodromal diarrhea of the case.

Analysis

- Univariate analysis: Mantel-Haenszel matched odds ratio (MOR) with exact 95 confidence intervals (95%CI). Epiinfo 6.0
- Multivariate analysis: conditional logistic regression.Stata 6.0.
- Stratification by season (May-September/October-April) and age group (<= 1 year, > 1 year)

Results

Surveillance

Epidemiological, clinical and serological features

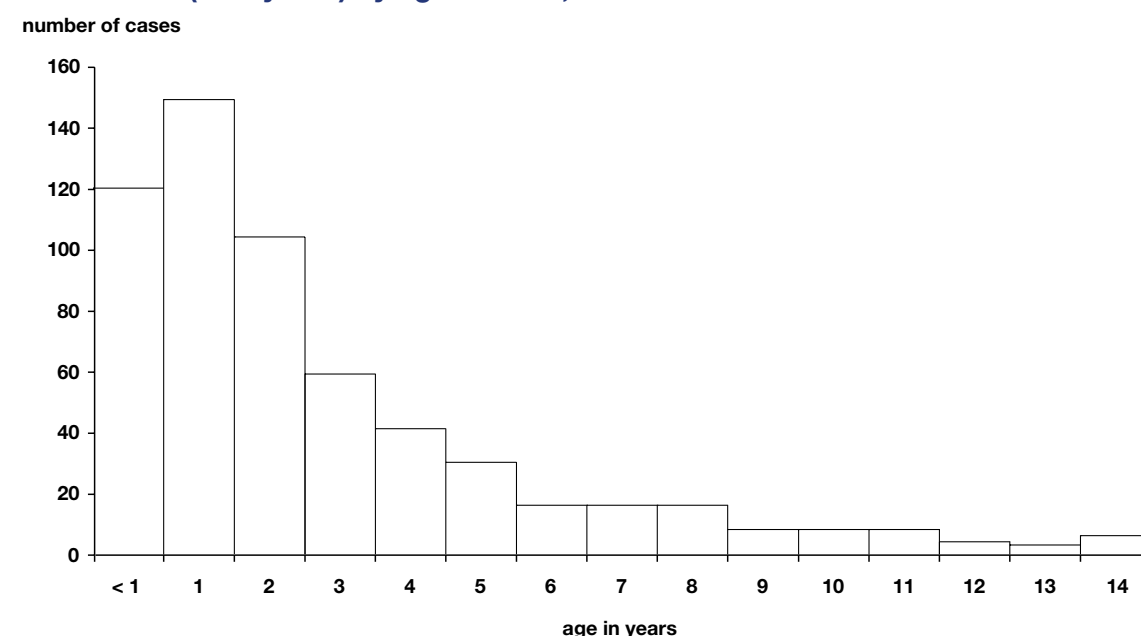
- 591 cases from January 1996 to December 2002
- Mean annual incidence: 0,7/10⁵ children < 15 ans,
- Incidence stable since 1996

Annual number of cases and incidence rate of HUS (<15 years) France, 1996-2002

Year	Number of cases	Incidence rate / 10 ⁵ children < 15 years / year
1996	88	0.77
1997	99	0.87
1998	79	0.69
1999	99	0.87
2000	81	0.70
2001	75	0.65
2002	70	0.61
1996-2002	591	0.74

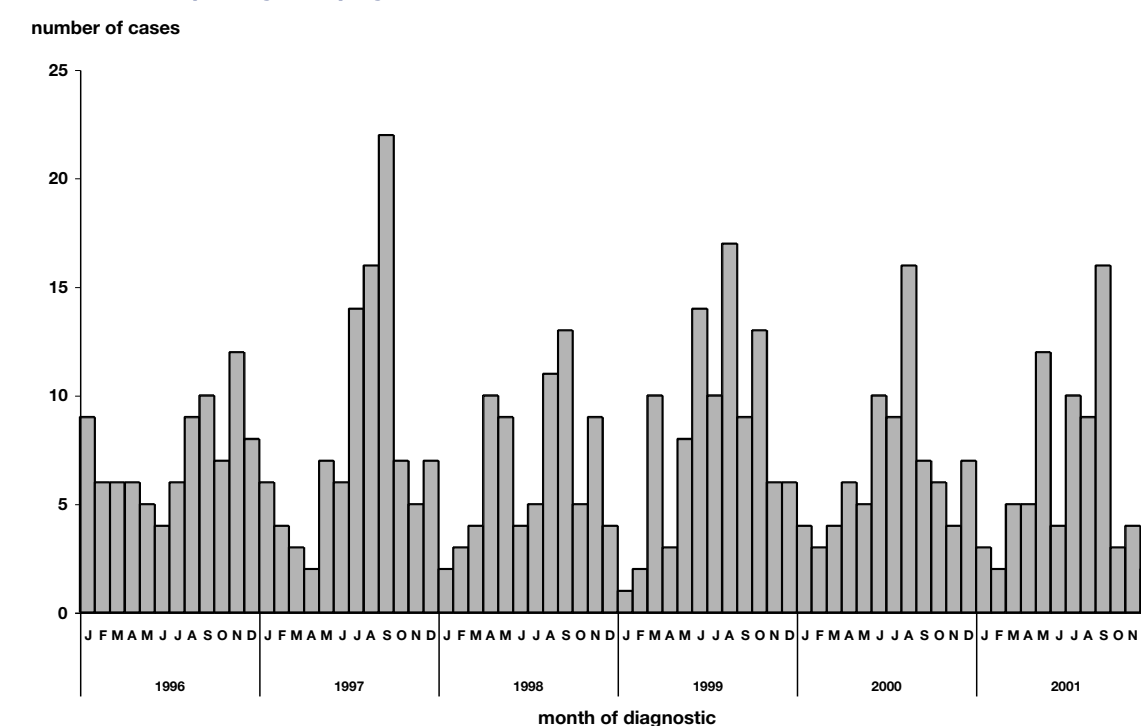
- Median age: 25 months [range: 17 days-15 years]
- Highest incidence rate among children < 2 years: 2.6/10⁵
- 52% female
- Prodromal diarrhea: 94% ; bloody: 57%
- 7 deaths, case fatality rate: 1.2%

Distribution of HUS cases (< 15 years) by age. France, 1996 - 2002



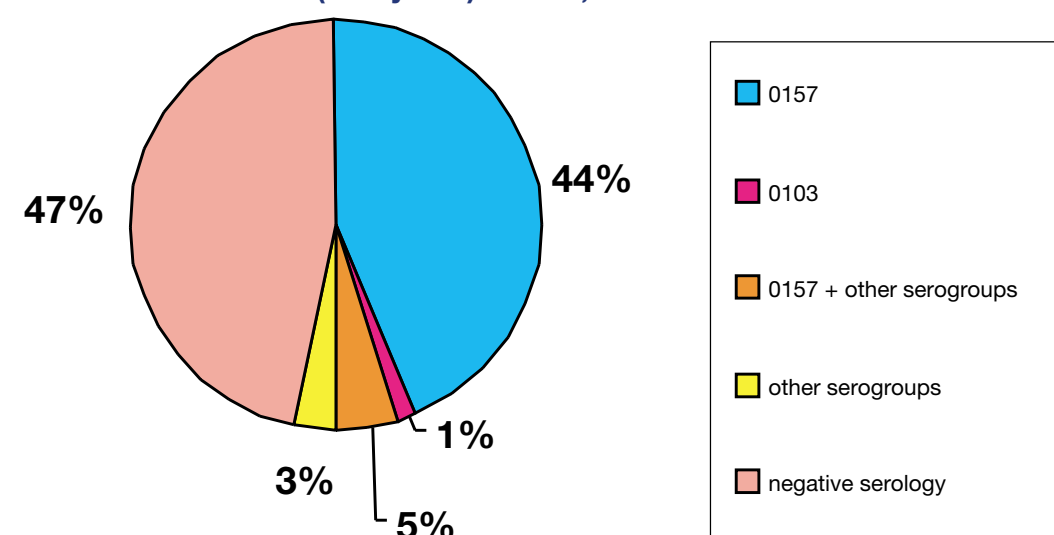
- 49% of cases in warm season (June to September)
- One outbreak of *E coli* 0157 infection detected in 2000: 10 cases of diarrhea (1HUS) attributed to the consumption of merguez (sausage)

Distribution of HUS cases (< 15 years) by month France, 1996 - 2002



- Antibodies against LPS
 - tested in 515 (87% of cases)
 - positive in 283 (55% of those tested)
 - 0157 in 232 (82% of those who tested LPS positive)

E coli serogroups associated with HUS (< 15 years) France, 1996 - 2002



Case control study

- 105 sporadic cases included in 2000-2001
- 61 with confirmed STEC infection
- 196 matched controls
- HUS associated with:
 - consumption of undercooked minced beef,
 - contact with household member with diarrhea,
 - contact with day care or school mate with diarrhea

Conditional logistic regression analysis HUS < 15 years. France, 2000-2001

Exposure	Adjusted OR	CI 95%	p
Undercooked minced beef	5,47	1,4-21,8	0,01
Contact with Household member with diarrhea	3,74	1,1-12,4	0,03
Contact with day care or school mate with diarrhea	5,73	1,0-32,5	0,04

Conclusion

- HUS incidence rate in France has been stable since 1996 and below 1/10⁵
- STEC infection was serologically confirmed for 55% of HUS cases
- high prevalence of 0157 serogroup observed among the serologically confirmed STEC infection
- HUS also associated with infections by non-0157 STEC
- annual incidence of HUS in children, age distribution, and summer seasonality observed in France are comparable with reports from other European countries
- Consumption of undercooked minced beef and contact with household members or day-care mate with diarrhea are the main risk factors for HUS in children in France
- These findings are consistent with other studies undertaken in other industrialized countries and indicate opportunities for prevention
- Prevention strategies aimed at ensuring the safety of minced beef production and preparation and at educating child carers on enteric precautions may reduce the risk of STEC infection and HUS in France