

TULARAEMIA OUTBREAK IN CASTILLA Y LEÓN, SPAIN, 2007: AN UPDATE

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An outbreak of tularaemia occurred in Castilla y León in northwestern Spain between June and December 2007, as previously reported by Martín et al. [1]. The scope of the present article is to describe in more detail, and update the results of, the outbreak investigation.

An increased incidence of cases diagnosed as “fever of unknown origin” was detected in late June 2007 by the Castilla y León Epidemiological Surveillance Network based on a series of notifications from a rural area in the province of Palencia and from Leon city. Subsequent epidemiological investigation confirmed a tularaemia outbreak.

Outbreak investigation

After the initial cases were confirmed as tularaemia, the regional Epidemiology Service launched an active search for cases, both prospective and retrospective. Primary and specialised healthcare professionals were informed about the situation and asked to notify all suspected cases and to take clinical specimens for laboratory investigation.

Most collected samples were sent to the National Reference Laboratory in Madrid, where cases were confirmed by means of serological techniques (microagglutination and tube agglutination), culture or PCR.

All cases were first interviewed face-to-face by clinicians and then over the phone by epidemiologists. The questionnaire collected information about the patient, clinical symptoms and potential exposures associated with the risk of infection. Follow-up information on the conclusion of the treatment and disappearance of the symptoms were available for 73.5% of the cases.

The cases, as reported by clinicians, were classified by epidemiologists by means of the case definition and confirmation criteria agreed jointly with the National Epidemiological Surveillance Network and the European Centre for Disease Prevention and Control [2].

The clinical symptoms compatible with one of the different forms of tularaemia included:

- Ulceroglandular (cutaneous ulcer with regional lymphadenopathy),
- Glandular (regional lymphadenopathy with no ulcer),
- Oculoglandular (conjunctivitis with preauricular lymphadenopathy),
- Oropharyngeal (stomatitis or pharyngitis or tonsillitis and cervical lymphadenopathy),
- Intestinal (intestinal pain, vomiting, and diarrhoea),
- Pneumonic (primary pneumonic disease),
- Typhoidal (febrile illness without early localising signs and symptoms).

The laboratory criteria for diagnosis included:

- Isolation of *Francisella tularensis* from a clinical specimen,
- Detection of *F. tularensis* genome by PCR,
- Demonstration of a specific antibody response in paired serum samples.

Classification of confirmed case: a clinically compatible case confirmed by laboratory diagnosis.

Additional criteria for cases associated with the outbreak included: a person resident in Castilla y León who between mid-May and December 2007 met the above criteria.

Results

A total of 507 cases were laboratory-confirmed, of these 91.5% using serological techniques (microagglutination and tube agglutination), 5% by culture and 3.5% by PCR. *F. tularensis holarctica* was identified as the agent causing the outbreak.

The outbreak was focused in the northwest quadrant of Castilla y León (in five of the nine provinces) and has not spread to either neighbouring areas of Castilla y León or other Spanish regions.

Cases were reported with the onset of symptoms between week 20 (earliest 15 May) and week 52 (latest 31 December) of 2007.

Ninety percent of cases occurred from week 25 (starting 18 June) to week 43 (starting 22 October) of 2007, with a peak (59.5% of the cases) between weeks 26 and 33 (24 June – 18 August) (Figure 1).

The majority of cases (80.1%) were male. Patients aged 41 to 70 years accounted for 69.2% of cases, although all age groups were affected (Figure 2).

The most frequent clinical form reported was the typhoidal one (59.0%), followed by the ulceroglandular, glandular and pneumonic forms (14.6%, 12.6% and 7.9%, respectively) (Table 1).

The majority of cases (71.1%) were treated by general practitioners, 25.0% were hospitalised, while the remaining 3.9% attended specialist out-patient facilities.

Ciprofloxacin (750 mg every 12 hours) and doxycycline (100 mg every 12 hours) for 10 to 14 days were the most frequently used antibiotics, although other fluoroquinolones and tetracyclines were also administered.

Patients' responses to the prescribed antibiotic treatment were favourable in most cases, with only a few complications and no fatal cases reported. The most frequently observed complications were:

asthenia (8 cases), suppurative adenopathies (7 cases), persistent arthralgias (6 cases), persistent adenopathies (4 cases) and allergic reaction to prescribed treatment (2 cases).

Information on possible exposures revealed that 34.9% of cases were farm workers or people whose jobs involve contact with gardens or natural environments (e.g. gardeners, rangers or reserves and lakes maintenance staff). Contact with rodents (24.3%) or domestic animals such as dogs or cats (19.7%), handling crayfish (13.2%) or frequent walks through the countryside (11.8%) were reported in a significant number of cases. Other possible infection routes reported were recent arthropod bites (10.9%), contact with livestock (9.5%) or with manure, straw or alfalfa hay (4.9%), or having handled and/or skinned hares (6.5%). Patients could indicate more than one possible exposure and these are neither exclusive nor exhaustive (Table 2).

Discussion

The first known tularaemia outbreak in Castilla y León, with 534 reported cases, took place in 1997 [4,5,7]. Another, smaller one,

FIGURE 1

Confirmed cases of tularaemia by week of onset of symptoms, outbreak in Castilla y León, Spain, 2007 (n=507)

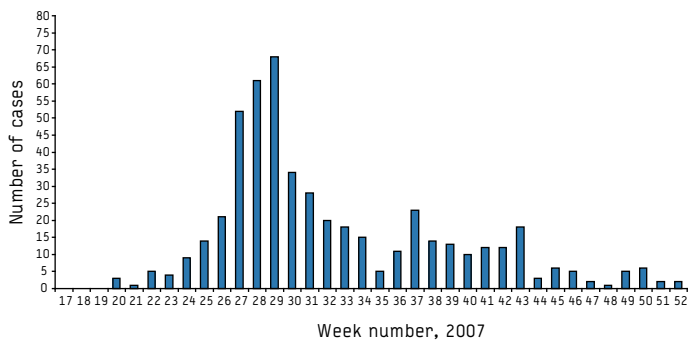


FIGURE 2

Age distribution of confirmed cases of tularaemia, outbreak in Castilla y León, Spain, 2007 (n=507)

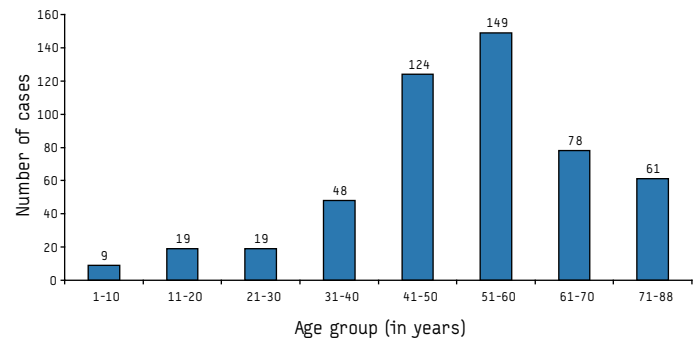


TABLE 1

Clinical form of tularaemia reported in confirmed cases identified in the outbreak in Castilla y León, Spain, 2007 (n=507)

Clinical form	Number of cases	Proportion of all cases (%)
Typhoidal (febrile illness with no early localisation of signs or symptoms)	299	59.0
Ulceroglandular (cutaneous ulcer with regional lymphadenopathy)	74	14.6
Glandular (regional lymphadenopathy with no ulcer)	64	12.6
Pneumonic (primary pleuropulmonary disease)	40	7.9
Oropharyngeal (stomatitis or pharyngitis or tonsillitis with cervical lymphadenopathy)	14	2.8
Intestinal (abdominal pain, vomiting and diarrhoea)	10	2.0
Oculoglandular (conjunctivitis with regional lymphadenopathy)	6	1.2
Total	507	100.0

TABLE 2

Possible exposures associated with the risk of tularaemia infection reported by cases in the outbreak in Castilla y León, Spain, 2007 (n=507)

Exposures	Number of cases	Proportion of all cases (%)
Farm work or jobs related to gardens or natural environments	177	34.9
Contact with rodents	123	24.3
Contact with other animals such as dogs or cats	100	19.7
Having handled crayfish	67	13.2
Walks through the countryside	60	11.8
Recent arthropod bites	55	10.8
Contact with livestock	48	9.5
Exposure to untreated water	41	8.1
Having handled and/or skinned hares	33	6.5
Manure, straw or alfalfa hay	25	4.9
Raw to medium cooked meat consumption	1	0.2

Note: Cases could indicate more than one possible exposure, hence the percentages do not add to 100%

with 13 cases, occurred in 2004 [6]. Several sporadic cases were also notified in the interim. The prevailing modes of transmission for these earlier outbreaks were contact with leporids in 1997 [4,5,7] and crayfish in 2004 [6].

In the 2007 outbreak, the most frequent clinical presentation of the disease, the typhoidal form, together with the potential risk factors indicated by cases suggest two different means of transmission responsible for the outbreak: mainly by inhaling the bacteria, a pattern seen in just over half the cases (pneumonic and probably many of the typhoid forms), and, secondly, through direct contact, with local manifestations of the disease (ulceroglandular and ganglionar forms).

At the time of the outbreak, harvesting and related farm works were being conducted, which may have caused aerosols capable of transporting the bacterium. Unusual climatic and environmental circumstances (mild winter and dry spring) might have contributed to this outbreak, together with the significant diversity of illness reservoirs and infection sources that usually take part in transmission (leporids, sheep, rodents, canids and haematophagus vectors). All these factors have probably aided the proliferation of *Francisella tularensis*, a bacterium that can survive for long periods in water, mud and animal carcasses.

Different studies are being conducted in order to improve our knowledge of this outbreak and its causes: a) a spatial analysis to evaluate the possible correlation with either environmental or animal factors; b) a case-control study to identify the potential risk factors associated with infection sources and modes of transmission; and c) a seroprevalence study of *F. tularensis* in asymptomatic people in the case-control study area. A collection of cases' sera was created to allow further investigation.

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