

# Q fever in Logroño: an attack scenario

Georgios Pappas<sup>a</sup>, José R. Blanco<sup>b</sup> y José A. Oteo<sup>b</sup>

<sup>a</sup>Institute of Continuing Medical Education of Ioannina, Greece. <sup>b</sup>Área de Enfermedades Infecciosas y Medicina Preventiva. Complejo Hospitalario San Millán-San Pedro de La Rioja. Logroño, España.

**Bioterrorism has emerged as an important infectious disease and public health challenge in the 21st century, and issues of preparedness and response are now prominent. The development of attack scenarios for assessing this problem contributes to the organization of response systems and identifies aspects that may need to be improved. The authors present an attack scenario involving Q fever in a specific area, the city of Logroño, Spain. The evolution of the outbreak is described and the attempts at diagnosis and implementation of public health measures are outlined. Knowledge of the pathogen in the specific scenario and the ability to directly diagnose the disease it causes may be of help to facilitate a fast response that will contain public unrest and the eventual outcome in terms of morbidity and mortality.**

**Key words:** Q fever. *Coxiella burnetti*. Bioterrorism. Attack scenario.

## Q fever in Logroño: an attack scenario

La aparición del bioterrorismo supone uno de los principales retos en el ámbito de las enfermedades infecciosas y de la salud pública en el siglo XXI. El desarrollo de escenarios para la evaluación de este problema contribuye a la organización de sistemas de respuesta y de mejora de la misma en caso de atentado, siendo necesario mejoras adicionales. Los autores presentan un escenario de ataque con fiebre Q en una zona concreta: la ciudad de Logroño, en España. Se describe la evolución del brote y se presentan los intentos de diagnóstico y de puesta en marcha de medidas de salud pública. El conocimiento sobre el patógeno en el escenario concreto y la posibilidad de hacer un diagnóstico directo del mismo pueden ser de ayuda para una respuesta rápida que permitan limitar la alarma social y mejoren los resultados clínicos, en términos de morbilidad y mortalidad.

**Palabras clave:** Fiebre Q. *Coxiella burnetti*. Bioterrorismo. Escenario de ataque.

Correspondencia: Dr. G. Pappas.  
Velissariou, 15-19. 45221 Ioannina, Greece.  
Correo electrónico: gpele@otenet.gr

Manuscrito recibido el 30-3-2006; aceptado el 26-6-2006.

## Introduction

Bioterrorism has emerged as one of the most significant public health problems of the 21<sup>st</sup> century.<sup>1</sup> Preparedness for the premeditated release of biological agents has intensified in recent years, as is expressed by intensive research in countermeasures<sup>2</sup>, educational programs to enhance the awareness of medical and paramedical personnel<sup>3</sup>, and the development of attack scenarios or crisis simulations to highlight responses in need of refinement<sup>4,5</sup>. These scenarios should take into account parameters related to the specific area targeted, which may dramatically alter the local priorities of response intensification. We present such a scenario, utilizing a simulation mode that has been presented elsewhere for a specific place<sup>6</sup>.

## Place

Logroño is the capital of La Rioja, one of the smallest provinces of Spain, located in the middle of Northern Spain. La Rioja has 300,000 inhabitants, almost half of them living in Logroño. The city is located 336 km. north of Madrid, 468 km. west of Barcelona, and 152 km south of Bilbao. Numerous trains from all the major Spanish cities reach Logroño, and two flights from Madrid and one from Barcelona are scheduled daily, although the evening one is frequently cancelled. La Rioja is a quiet province, and is not usually implicated in political problems, which are more prevalent in the North. It is an idyllic environment and the extensive wine industry, the region's most important economic motor, make it a popular tourist destination.

## Time

The weather in Logroño in early June is usually hot, although light winds prevail on some days. The San Bernabes festival, in honor of a local saint, takes place on 11 June and various venues in Logroño celebrate the event, which attracts a large audience.

## Day 0

On 11 June 2007, a day that is not particularly hot, with a light *cierzo* (northern breeze), locals and guests are enjoying themselves, as the weather is ideal for the outdoor festivities taking place. Many notice a helicopter overhead carrying an advertising banner, but it does not make a particular impact. The festival is a success, drawing many Spanish and international tourists who especially enjoy sampling the La Rioja wine. For the next few days, noth-

ing particular happens. No one is aware that the advertising helicopter was used to distribute a significant amount of aerosolised *Coxiella burnetii*, a bacterium mainly recognized as a cause of a mild atypical pneumonia, but also an agent listed and tested in many countries in the past as a potential biological weapon<sup>7</sup>. By the night of Day 0, the people responsible for this act have already caught a flight to Madrid and then abroad. For the following week nothing unusual happens. On days 7-10, 15 individuals experience the symptoms of an influenza-like illness; nevertheless, only one of them seeks medical advice and is diagnosed as suffering from a mild viral illness that is expected to resolve without any specific medical treatment.

### Day 11

Complejo Hospitalario San Millán-San Pedro de La Rioja is the hospital in Logroño, and the main hospital of La Rioja. It is a 50-year-old, 684-bed, tertiary care hospital that hosts a 12-bed Intensive Care Unit (ICU). The hospital Emergency Department (ED) works on a 24/7 basis, admitting the majority of emergencies occurring in La Rioja. A smaller, 83-bed hospital is located in Calahorra, 50 km east of Logroño. On Day 11, the ED notices that an unusually large number of patients have sought medical advice for influenza-like symptoms, including fever, myalgia and dry cough. Of the 40 patients presenting with these symptoms, only two elderly people are admitted, one in the Internal Medicine Unit, and one in the Pulmonary Medicine Unit, and both are empirically administered amoxicillin-clavulanate. No specific serologic tests for bacteria are performed in the few blood samples drawn from these patients, although by the night of Day 11, the physicians on duty agree that a minor outbreak of viral disease may be evolving and samples should possibly have been kept, or should be kept if similar numbers of patients present at the ED during the following day. The two patients admitted are both of urban origin, and do not recall exposure to any risk factors specific for infectious syndromes. A family member of one of the hospitalized patients experiences similar symptoms, but this is considered further proof of an upper respiratory disease of viral etiology. Both hospitalized patients have an unremarkable laboratory profile, apart from mild increases in serum aminotransferases. Blood samples for bacterial serological tests and cultures are taken from these patients, but no specific orders for emergency processing of the samples are issued.

### Day 12

By noon of day 12, an additional 30 patients have come to the ED with similar symptoms. The obvious evolving outbreak has alerted the physicians on duty, and after a brief telephone discussion among the heads of the Internal Medicine, Pulmonary Medicine, and Infectious Diseases Department, it is agreed that all patients should be exhaustively assessed at the ED, including a review of the medical history for specific risk factors, blood samples to be used for serology, culture, centrifugation and storage (apart from the typical blood count and biochemistry profile) and chest x-rays. The physicians on duty are not advised to prescribe any particular treatment regimen and are asked to act on their judgment, either admitting patients with underlying risk factors for severity, or dis-

charging patients with medical advice depending on the severity of their clinical condition. If empirical antibiotic coverage is warranted, the department heads suggest administration of levofloxacin. Hand washing and the use of surgical masks is advised for hospitalized patients and the staff caring for them, but no recommendations for further respiratory isolation procedures is issued. Arrangements for common ward hospitalization of the admitted patients are only made after three of these patients initially stay in wards with other patients. The microbiology laboratory is asked to perform a panel of serologic tests, including, among others, Q fever testing. The National Infectious Disease Reference Center in Madrid is contacted to arrange for samples to be sent later that day for detection of West Nile virus, tularemia, and, although out of season, influenza. The Research Laboratory for Special Pathogens (dependent on the Infectious Disease Department) also performs a panel for some pathogens (tularemia and Q fever).

By the end of Day 12, 150 patients have been assessed in the ED, and seven have been admitted, including one third-semester pregnant woman and one patient with lung cancer undergoing chemotherapy. The head of the La Rioja Health System has been informed about the situation, and a meeting is held in the Hospital in the afternoon. Communication with the Calahorra Hospital reveals that similar cases have not been noted. An epidemiological analysis of the patients presenting this day is not enlightening to the attending physicians: almost all the patients are of urban origin, do not recall any specific common exposure to a particular risk factor, and their residences are scattered within the city limits. A number of physicians from the private sector report that they too have seen a large number of similar patients, all from the city of Logroño. Pooled laboratory data from all Day-12 patients indicate an atypical pneumonia-like outbreak. A major concern is whether this is a disease transmitted by respiratory particles, but conclusions cannot be drawn since, even for intrafamilial case clusters, the presentation of symptoms appears to be simultaneous, no similar syndromes/index cases were noted during the past week, and the route of exposure is still not clear. Although the definition of a possible bioterrorist attack includes the otherwise unexplained, unexpectedly high number of simultaneous cases, premeditated release is only discussed briefly, as being simply impossible. Q fever is high on the differential diagnosis list. It is a known disease in this area, and the clinical presentation and severity rates are similar to the syndrome observed; nevertheless, the means of exposure is not obvious and most of the patients are of urban origin. Legionellosis, for example, would be more severe, present with a higher percentage of hospitalizations, and patients would recall a similar indoor environment where they had presumably been exposed. Tularemia would also be more severe. A respiratory viral pathogen is also high on the differential diagnosis, and someone suggests the threat of avian influenza; yet no signs of a local epizootic outbreak were recorded in the previous days, and most patients were not exposed to animals. Since the host hospital is one of the most highly recognized tick-borne and arthropod-related infectious disease center, traditionally including Q fever, a rapid diagnostic investigation for *C. burnetii* is decided (Research

Laboratory for Special Pathogens). By dawn of Day 13, polymerase chain reaction (PCR) testing was found to be positive for *C. burnetii* in the vast majority of samples tested and a diagnosis is established.

### Day 13

Early in the morning, the regional scientists have a diagnosis. The absence of the City Mayor and two hospital department heads, who have also developed symptoms, mars a new meeting held as soon as the PCR results are out. The diagnosis can be considered definite, emerging from the Reference Center, yet samples are also urgently sent to the Rickettsiosis Centre in Marseille for confirmation. Two major pathways have to be paved: Investigation into the possibility of premeditated release, and organization of the health system response. Premeditated release is contemplated more seriously, yet everyone considers it impossible. Tracing back through the incubation period to the time of exposure, the festivities of San Bernabes appear to be the event where exposure took place, and all the patients questioned report that they were at least in town on that day. A minority of patients report that family members who were out of town that day have not developed symptoms, nor have individuals on holiday out of La Rioja. Nonetheless, although a reasonable exposure event and a consistent epidemiological trend has been identified, there is no obvious answer to who initiated the attack or why. La Rioja is characteristically quiet region, especially when compared to its northern neighbors. The Basque separatists cannot be considered suspect, since there is no relevant history of such a massive attack, and no suspicion of possessing biological weapons has ever been attributed to them. Religious and national minorities are underrepresented in La Rioja and have never been at the epicenter of the region's relations and policy. Still, the press and television broadcasts will be screened for the presence of comments that might be considered offensive to specific minorities. The possibility of premeditated release, although still inadequately entertained, prompts the authorities to inform the Central Government. The Minister of Health is also informed, and a mutual agreement is made to continue the investigation and to provide further communications and decisions later in the afternoon. International Organizations, such as the World Health Organization (WHO), the European Union, and the North Atlantic Treaty Organization (NATO) will be informed about the situation, if the Central Government ensures that it is a premeditated event. Since Spain is divided into autonomous regions with their own regional governments and political structures, including a regional health system, the question of who is in charge at this stage is easily answered: the local authorities. However, if a premeditated release is officially considered, then the event exceeds local limits, since the attack, depending on its source, has major international implications, and should be handled by national bodies and the NATO. At the present meeting, someone mentions the helicopter flying overhead on 11 June and suggests that the police should seek further details about the flight and pilots, just in case.

The medical aspect of the meeting involves preparing an efficient response for an evolving outbreak of Q fever. The scientists reasonably fear that the peak of the outbreak

has not as yet been reached and thus have to prepare for a disproportionately high burden of cases. Furthermore, if the event is attributed to premeditated release, and taking into account that most patients are from the city of Logroño, then all the inhabitants of Logroño are theoretically at risk of developing the disease. Furthermore, all visitors to the city at that time should be actively identified and informed, many of them already having returned to their home countries. Partly because of the known low mortality rates associated with the pathogen, it is decided that this action should be carried out by the Central Government as soon as the event is officially characterized as one derived from premeditated release.

Since all the city inhabitants are presumably at risk of having been exposed and developing the disease, prophylactic administration of antibiotics is an issue. Either all patients should receive a prophylactic regimen of doxycycline, or antibiotic administration should be reserved only for those developing symptoms, as well as special populations at risk (pregnant woman, immunocompromised persons, patients with valvular heart disease). The latter option prevails. The most important issue at the moment is preparing the San Millán hospital for a huge burden of patients. The Calahorra hospital could help with this burden, but because of its small capacity, the ability of this hospital to handle patients would be rapidly overcome if massive admissions were needed. Navarra, 90 km north of Logroño, Zaragoza, 180 km east, and Bilbao, 150 km north, have hospital bed capacities greater than 1000 each. Thus, it is decided that the regional health authorities should be informed of the evolving outbreak in order to prepare for similar cases, should they emerge there as well, and to increase the capacity for handling patients over the following days. All medical personnel leaves are cancelled. It is decided that all medical personnel should receive prophylaxis with doxycycline. The available antibiotic stock is evaluated and considered initially adequate, but one of the scientists suggests that the Regional Health Authorities should put constraints on all stocks of doxycycline and other strong antibiotics from local pharmacies. No such decision is made, however, for the present time. An emergency meeting of all medical and paramedical personnel, with the aim of updating their knowledge of the disease, the evolving situation, and the expected burden of work is arranged for the following hours. Arrangements are made to distribute information in the form of leaflets, and all private practitioners are contacted, updated on the situation, and advised on treatment decisions with the main target being maximal avoidance of hospital referral. One final issue, which is of paramount importance, is the amount of information that the public should receive. It is agreed that a joint press conference by General and Regional Health authorities should be held as soon as possible, informing the public that an outbreak of Q fever is currently evolving in the region, and informing them of the relatively benign nature of the disease, the populations at risk, and the non-transmissible nature of the pathogen. It is decided that no special mention of bioterrorism will be made, although the police chief suggests the opposite because it would help in the task of collecting civilian information about a possible attack. The National Minister of Health is informed about the ongoing plan and agrees. As Day 13 dawns, it is evident that the

number of symptomatic patients has multiplied, and, furthermore, a significant percentage of doctors and nurses are absent because of illness. After the emergency meeting for personnel updating, a minority of nurses refuses to participate in patient management on the legal basis of exposure to danger, while a minority of the non-specialist doctors recruited refuse to participate, claiming ignorance. The ED is overcrowded, and new admissions reach 10 by noon, two of them in the ICU. As soon as the press conference is held, the number of patients presenting at the ICU rapidly multiplies, including patients from areas outside the suspected exposed zone, thus confounding the epidemiologic conclusions. Practically all pregnant women of the area seek hospital advice, and elderly people present in force, being afraid of their immune status and overall health. Hospitalized patients who had previously been in proximity with outbreak patients complain and threaten to sue the hospital authorities for endangering their health. Moreover, national media are switching their interest towards La Rioja, and a series of experts and "experts" appear on television and discuss the pathogen. Although it is acknowledged that the local experts on the disease are among the world's finest, some discuss bioterrorism and others discuss the need for prophylactic antibiotics for all the population targeted. The news travels fast and strong antibiotics are soon sold out in all the Logroño pharmacies. The Regional Authorities together with the National Authorities decide to officially declare that the outbreaks may be a result of premeditated release, and International organizations are informed on the events. The shortage of antibiotics and medical and paramedical personnel is handled rapidly. Antibiotic stocks and infectious disease specialists are called in from other regions of the country and arrive by plane to Logroño. There are some problems with distributing antibiotics to the populations at risk because of the initial shortage and the time-consuming need for confirmation of risk status. The diagnostic capacity of the microbiology laboratory is soon surpassed, and it is decided that samples from all patients should be held for further diagnostic purposes. For the present time, however, all patients presenting with related symptoms are diagnosed with Q fever and treated accordingly, without microbiological confirmation. By the end of Day 13, the exhausted medical department staff has evaluated more than 2000 patients, and 100 new hospital admissions have been made, sometimes because of sheer pressure by the patient, and despite the absence of indications. The ICU is reaching its limit of capacity, but the Bilbao and Navarra hospitals are ready to help in the management of patients with severe infection. Police inquiries are proceeding slowly, mainly because of the vast pool of inconsistent information from panicked civilians. National epidemiology and infectious disease experts arrive to the city to aid in the investigation, and all agree that, even though it was considered highly improbable previously, the outbreak was probably due to premeditated release. Still, the Regional and National Authorities do not issue an official confirmation. NATO experts on bioterrorism ask to travel to Logroño, but the National Authorities decide against it, although Spanish Army Units move towards Logroño to assist by setting up a military hospital. The World Health Organization issues a statement expressing its trust in the National and Re-

gional Health Authorities. Minor complaints are made from the Japanese ambassador, since a group of Japanese tourists who returned home are falling ill. The dispute is finally solved through the Prime Minister. During the night of Day 13, isolated episodes against various minorities take place all round Spain.

#### Day 14

As Day 14 dawns, the first fatality is recorded, an elderly patient with chronic obstructive pulmonary disease who developed severe Q fever pneumonia. The military hospital has been structured and is operational, while experts from various other regions of the country, arriving to compensate for the large percentage of ailing local personnel, turn a nearby hotel into a hospital. More than 3000 patients seek medical advice at these centers, and 200 patients are admitted. Antibiotic distribution to susceptible populations is developing, albeit not uneventfully, since everybody is rushing and the people in line are impatient. Pharmacies are closed after practically being raided by desperate seekers of antibiotic prophylaxis. NATO, European Centers for Disease Control (ECDC), and WHO experts are expected to arrive to Logroño the following day. The police investigation has reached a dead end. All those involved in the helicopter flight of June 11 are missing, and contradicting information is gathered on the identities of these people. Environmental sampling is ongoing, to determine the extent of the exposure area and persistence of the pathogen in the environment. Fear of a significant effect on agriculture is counterbalanced by the fact that the exposure area seems to be limited to the strictly urban area of Logroño.

The National Government President and His Majesty the King of Spain are also expected to arrive in Logroño the following day, in order to better moderate the response. Numerous politicians, of varying ranks and parties express their opinions about practically everything. Law firms send representatives to Logroño to investigate delays and sue... anybody. Journalists arrive from every part of the world, in general presenting the situation as tragic when, actually, it is only dramatic. The rumor spread by a representative of an obscure Australian television channel about the existence of a vaccine for Q fever causes additional fury among a minority of locals.

#### Day 15

The numbers on Day 15 hold steady: more than 3000 citizens experience symptoms, 200 patients are admitted and two more patients die, while minor conflicts keep going on about every possible aspect of the outbreak. The visit of His Majesty the King and the National Government President enhance the development of a sense of unity among the citizens of Logroño. Although many cannot be convincingly persuaded that the response was as rapid as possible, the majority acknowledge that a coordinated response has developed. At this point it is estimated that, although theoretically only 10,000-15,000 of the inhabitants of Logroño should receive antibiotic prophylaxis, more than 80,000 have done so, even acquiring antibiotic regimens via the Internet. Subsequently, it will be estimated that 60 patients had been hospitalized due to adverse reactions to the antibiotics used.

### Days 16-19

By this time, the response has been fully organized and minor problems arise, all resolved rapidly. A total of 15,000 new cases and 500 admissions are recorded these days, but no more fatalities occur. Most new cases are mild, and antibiotic administration by pre-set distribution points allows for early disease control. Loss of medical and paramedical staff due to illness has been adequately replaced with recruitment of staff from other Spanish regions. The police investigation leads nowhere. Environmental sampling and disinfection procedures for certain buildings is initiated. By Day 19, the daily morbidity rates are rapidly declining, and Day 22 records no new cases.

In total, 25,000 symptomatic cases, 80,000 regimens of solicited and unsolicited prophylactic regimens, 1000 admissions of which 40 are to the ICU, and 3 deaths are recorded. It is estimated that more than 1000 patients will develop chronic Q fever, and a surveillance program is scheduled to identify these patients and treat them accordingly, although it is extremely costly. It is also estimated that almost 1000 patients will need psychiatric support in the near future. Environmental pollution, mainly of buildings, will remain an understudied issue, and an estimated one percent of Logroño's population will relocate in the following year.

### Lessons learned

The following points can be easily drawn from this scenario.

1. The targeted area of the attack and its political, social, and health-related characteristics is paramount in deciding the outcome of the attack. In this case, early recognition was facilitated by the familiarity with the pathogen of the scientists requested to respond and by the ability for an extremely rapid diagnosis. Had the attack been initiated against another Spanish city, a delay of at least 24 hours would occur, which is a significant period in the setting of an acute outbreak, and thus morbidity and mortality rates might have doubled<sup>6</sup>.

2. Existence of a certain response plan greatly facilitates minimization of morbidity, mortality, and social disruption. This plan could be as primary as a simple definition of hierarchy in decision-making, but, as is already

outlined, delays and disagreements can geometrically affect the morbidity and mortality toll, and may enhance the natural tendency of the public to panic. A paramount issue in this setting is the response of the press, which is largely related to the individual characteristics of the mass media in each country and varies according to the time. Should the media get involved in a ratings war aimed at presenting the Apocalypse instead of an outbreak, the public would have little to do but follow, no matter how fast and definite the authorities' response is. In the present scenario, even a rapid, coordinated attempt to inform the public without evoking panic was not successful enough: most civilians self-medicated despite expressing no symptoms, and social and political extremists used the event to promote personal agendas.

3. Trying to find the guilty party is futile in bioterrorism, especially when pathogens that are widely present in the environment, such as *C. burnetii*, are used. Prevention is an issue here. In the USA, daily air sampling is performed in a number of metropolitan centers, yet, even if such an approach were implemented in Continental Europe, cities the size of Logroño would most likely be excluded from this measure.

4. In conclusion, preparedness can never be absolute, and it should take different forms in the various regions, depending on individual regional characteristics. Should such an event develop, coordination and a rapid response are paramount, although even then, certain adverse social consequences may not be avoided.

### References

1. Henderson DA. The looming threat of bioterrorism. *Science*. 1999;283:1279-82.
2. Relman DA. Bioterrorism—preparing to fight the next war. *N Engl J Med*. 2006;354:113-5.
3. Cosgrove S, Perl TM, Song X, Sisson SD. Ability of physicians to diagnose and manage illness due to category A bioterrorism agents. *Arch Intern Med*. 2005;165:2002-6.
4. O'Toole T. Smallpox: An attack scenario. *Emerg Infect Dis*. 1999;5:540-6.
5. Smith BT, Inglesby TV, Brimmer E, Borio L, Franco C, Gronvall GK, et al. Navigating the storm: report and recommendations from the Atlantic Storm exercise. *Biosecure Bioterror*. 2005;3:256-67.
6. Pappas G, Akritidis N, Tsianos EV. Attack scenarios with rickettsial species—Implications for response and management. *Ann NY Acad Sci*. 2005;1063:451-8.
7. Madariaga MG, Rezai K, Trenholme GM, Weinstein RA. Q fever: a biological weapon in your backyard. *Lancet Infect Dis*. 2003;3:709-21.