

A brief history of Bornholm disease

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ABSTRACT

In the summer of 1930 on the Danish island of Bornholm, Dr Ejnar Sylvest and his wife, friends, and neighbours experienced symptoms of severe pain in one side of the chest, with pain resolving two weeks later and leaving no sequelae. Interested in the symptoms he had himself experienced, Sylvest described 23 similar cases on the island. He coined the terms 'epidemic myalgia' and 'Bornholm disease' and published several articles, disseminating knowledge of the process. This was soon followed by several other articles reporting similar epidemic outbreaks throughout Europe and America.

Interest in the topic increased after Dalldorf and Sickles discovered the virus responsible, coxsackie B virus, in Coxsackie, New York, in 1949.

Epidemic outbreaks of Bornholm disease in Spain were certainly not uncommon, despite which they went largely disregarded, with the exception of two reports by Pedro Pons and Farreras Valentí (in *Medicina Clínica*, 1948) and by Ortiz Molina (in *Revista Clínica Española*, 1951; the journal was under the directorship of Dr Jiménez Díaz at the time). In fact, there is no official epidemiological or healthcare system data on Bornholm disease in Spain.

We provide a first-hand account of what may have been an epidemic outbreak of Bornholm disease in the summer of 2014, affecting at least four people in La Butiplaya, a housing complex in Cala de Mijas, in the Spanish province of Málaga.

KEYWORDS

Epidemic myalgia, Bornholm disease, coxsackie B virus, Ejnar Sylvest

Introduction

From the waters of the Baltic Sea, facing the coasts of Germany, Poland, Denmark, and Sweden, emerges the picturesque Danish island of Bornholm, slightly larger in size than Ibiza in the Balearic archipelago (588 vs 572 km²). The island's small houses, round churches, and sheer cliffs, combined with its mild summer weather, make Bornholm a popular tourist destination, particularly among the Swedish. Gustaf Munch-Petersen (Copenhagen, 18 February 1912–Battle of the Ebro, 2 April 1938), one of Denmark's greatest poets, lived on this beautiful island. The poet is credited with the anti-fascist slogan "No pasarán" (they shall not pass), chanted

by the Republicans during the Spanish Civil War. Munch-Petersen joined the International Brigades at the age of 24 and was killed in the Battle of the Ebro.

Due to its strategically advantageous position for controlling maritime transport, Bornholm was occupied by the German forces during World War II and heavily bombed by the Soviet air force near the end of the war. The island, a popular location for political meetings (Figure 1), was also a summer destination for the young, restless, Danish general practitioner Ejnar Sylvest and his wife. In the summer of 1930, Sylvest, his wife, neighbours, and some local fishermen experienced intense chest pain, which seemed pleuritic in nature and was associated



Figure 1. The island of Bornholm, ©GraphicMaps.com

with few systemic manifestations. Sylvest named the condition epidemic myalgia, or Bornholm disease, due to its epidemic character, identifying 23 cases in a relatively enclosed area. He described the clinical manifestations of Bornholm disease in a preliminary study published that same year.¹ Encouraged by Thorvald Madsen (1870-1957), the eminent Danish bacteriologist who developed the first pertussis vaccine, Sylvest wrote his 155-page doctoral thesis “Epidemic myalgia: Bornholm disease”,² which was instrumental in raising awareness of the disease. Our discussion of the disease will take a systematic approach.

Ejnar Sylvest

Little is known about the life of Ejnar Sylvest (full name Ejnar Oluf Sørensen Sylvest), aside from the data provided by the Dansk Biografisk Leksikon, a biographical dictionary of eminent Danish figures.³ Sylvest was born in Hillerød and died in Copenhagen (11 November 1880-28 June 1972). He graduated in medicine from the University of Copenhagen. Sylvest had extensive knowledge of bacteriology and became a general practitioner in the city. His sense of public spirit

led him to join the social-democratic party from 1937 to 1950 and to become a member of the Danish Medical Association, where he served as president and organised a national vaccination campaign against diphtheria. In the summer of 1930, Sylvest and his wife experienced “the devil’s grip”. Sylvest was able to identify 23 further cases with similar symptoms. He coined the terms ‘epidemic myalgia’ and ‘Bornholm disease’, publishing several studies and reviewing previous cases in Scandinavia that seemed to be compatible with the condition. Sylvest’s observations led to the condition becoming a frequent, easily diagnosed disease.

Epidemic myalgia or Bornholm disease

According to Sylvest’s description, epidemic myalgia is characterised by the following features:

1. It occurs in the warm summer months.
2. It may occur at any age but mainly affects children.
3. Symptoms are acute.
4. Pain is the main manifestation and is usually severe.
5. Pain location varies but usually affects one side of the chest, and less frequently the upper abdomen.
6. The disease does not result in significant systemic alterations, with the rare exception of headache, sweating, and mild fevers.
7. Symptoms usually last two or three days. Symptoms may be unpredictable, with occasional exacerbations, and rarely last as long as a month.
8. Symptoms are always benign and leave no sequelae.
9. This epidemic disease is simple to diagnose. Similar cases usually appear at the same time, particularly within the same family. Incubation usually takes three to four days.²

Sylvest performed a literature review, finding previous cases of Scandinavian epidemics associated with symptoms similar to those of Bornholm disease. The earliest cases were reported by Daae and Homann in Norway in 1872, and diagnosed with ‘epidemic muscular rheumatism’ or ‘Bamble disease’ (several of the patients had attended a wedding in Bamble).⁴ Vogelsang⁵ corroborates the fact that these symptoms were first seen in Norway. Also in Scandinavia, John Finsen described an outbreak of ‘epidemic pleurodynia’ in Iceland between 1856 and 1873, which he published in 1874. The publication of Sylvest’s monograph in 1933 by Oxford University Press led to the popularisation of epidemics compatible with Bornholm disease. Harder

reviewed the American cases of epidemic pleurisy (another term for the same disease), finding reports of 11 epidemics occurring in summer in New York, Boston, and Durham, with a total of 282 patients affected since the initial outbreak in Virginia in 1888.⁶ A patient from Virginia referred to these symptoms as “the devil’s grip”. Dabney⁷ drew a clear distinction between dengue and this new epidemic based on his description of the disease in a family in 1888.

Reilly also described outbreaks in New York in 1899 and 1921, and in Torrey, Pennsylvania, in 1924; Richter and Levine described an outbreak in Massachusetts in 1933.⁸

Two years after Sylvest’s monograph was published, numerous studies in Scandinavia, particularly in Denmark, began to report new cases of the epidemic, reaching 10 000 cases.² The epidemic was also observed in England, Germany, and Portugal. We should highlight the 23 cases reported by Ludo Van Bogaert and Raymond Bogaert, which took place in a hospital setting in Antwerp (Antwerp Hospital) between May and September 1942.⁹ The patients affected included Raymond Bogaert and another physician at the hospital. The number of cases of Bornholm disease is assumed to be much higher; however, due to the benign nature of the symptoms, many cases may have not been seen at the hospital.

Raymond Bogaert experienced unilateral back pain (trapezius muscle); hard points were detected in the belly of the muscle upon palpation. Pain disappeared three days later, reappeared at day five, and resolved at one week. His maid experienced similar symptoms, although pain fluctuated more and lasted longer. The cases of a 24-year-old physician, his two flatmates, two nurses, and a man and his two children reveal the nearly familial character of this epidemic. The authors of the article observed that some cases had a neuritic component. CSF analysis results were normal. Muscle biopsy revealed oedema, with no specific findings in a microscopy study.

William N. Pickles also contributed to the understanding of Bornholm disease with his description of the cases of a family and their neighbours in Yorkshire. These patients had extremely severe, acute-onset chest pain of probable pleural origin, which interfered with breathing and was triggered by cough and deep breath. Symptoms resolved six days after onset. This study was published in 1933.¹⁰ In 1954, Pickles reviewed his study, commenting that the term ‘Bornholm disease’ was inappropriate, since

the island had nothing to do with the disease; the same was true of Malta, where another epidemic outbreak had been reported. He travelled to Denmark to meet Sylvest and was fascinated by the Danish general practitioner’s intelligence (by that time, Pickles was already president of the Royal College of General Practitioners). Pickles published his review in the renowned *New England Journal of Medicine*, proposing the name Sylvest disease, in honour of the Danish physician, whom he regarded as an exemplary general practitioner. It was in this study that Pickles reported the pathogenic mechanism of Sylvest disease: coxsackie B virus.¹¹

Coxsackie B virus

Coxsackie is a rural town in the state of New York. In 1948, two children experienced limb weakness and were initially diagnosed with poliomyelitis. Dalldorf and Sickles made suspensions using faeces from these children and inoculated them to nursing mice, which caused the animals to die. They subsequently concluded that the virus causing this disease was different from the one causing poliomyelitis and called it coxsackievirus.¹²

Coxsackievirus is a small virus (picornavirus) with an RNA-containing capsid. Coxsackievirus infects the intestinal tract (enterovirus) much in the same way as poliovirus (which causes epidemics in the summer and usually affects members of the same family) and enteric cytopathic human orphan (ECHO) virus. From the intestinal tract, these viruses can infect other internal organs. There are over 30 different serotypes of coxsackievirus. Coxsackie A virus (including at least 23 serotypes) is present in the mouth whereas coxsackie B virus (six serotypes) displays affinity for the striated muscle tissue of the heart. High concentration of coxsackie B virus in an area seems to reduce the presence of poliovirus. Coxsackie B virus was first reported in ten children with encephalomyocarditis in a maternity home in Johannesburg in 1956.^{13,14} Coxsackie B virus usually infects the heart, pancreas, and liver, causing pleurodynia, myocarditis, pericarditis, and hepatitis, in addition to Bornholm disease. Both coxsackie A and B viruses may cause ‘non-specific febrile disease’, upper respiratory tract disease, orchitis, nephritis, and aseptic meningitis. At present, there is thought to be an association between diabetes in adulthood, recent coxsackie B virus infections, and hand-foot-mouth disease.¹⁴

Bornholm disease in Spain

Although Bornholm disease apparently spread across Europe, including some epidemic outbreaks in Portugal, very few cases have been reported in Spain. Poor infrastructure, a lack of knowledge of the condition, and the benign course of the associated symptoms may explain why Bornholm disease largely went undetected in Spain; the condition may, however, have been very prevalent, as we will suggest in a later section.

Two small case series were reported in 1948 and 1951 in Madrid and Barcelona by two renowned Spanish schools of medical thought, which were competing for supremacy in the field. The cases were published by Farreras Valentí and Pedro Pons, of the Barcelona school, in *Medicina Clínica*, and Ortiz Molina, a follower of the Madrid school of Jiménez Díaz, in *Revista Clínica Española*.

Farreras Valentí (Barcelona, 4 April 1916-17 May 1968) was an assistant professor to Pedro Pons, Chair of Medicine in Barcelona, and subsequently became Chair of Medicine in Cádiz and Salamanca and president of the Spanish Society of Internal Medicine. His treatise *Farreras-Rozman: medicina interna* has been republished 18 times since its initial publication in 1949.

In 1948, Farreras published a review article on epidemic myalgia or Bornholm disease, reporting no new cases of the disease. This was the first monograph on the condition to be published in Spain. Although the role of coxsackievirus in Bornholm disease was yet to be discovered, Farreras stated that the “causal agent is thought to be a filterable virus present in rhinopharyngeal secretions”.¹⁵

Three years later, Pedro Pons and Farreras Valentí¹⁶ described the cases of four patients with Bornholm disease (ages 29, 27, 39, and 18), one of whom displayed symptoms of meningitis following a benign course, similar to the symptoms observed in seven young Swiss patients with Bornholm disease, described by Gsell.¹⁷ The novelty of this study resided in the fact that it presented coxsackievirus as the causative agent of the disease; three years earlier, the virus had been reported to be a variant of poliovirus (pseudopolio).

Pedro Pons (Barcelona, 1898-1971), Chair of Medical Pathology at the Barcelona Faculty of Medicine, published the *Tratado de patología y clínica médica*, an 8-volume treatise on pathology and clinical medicine.

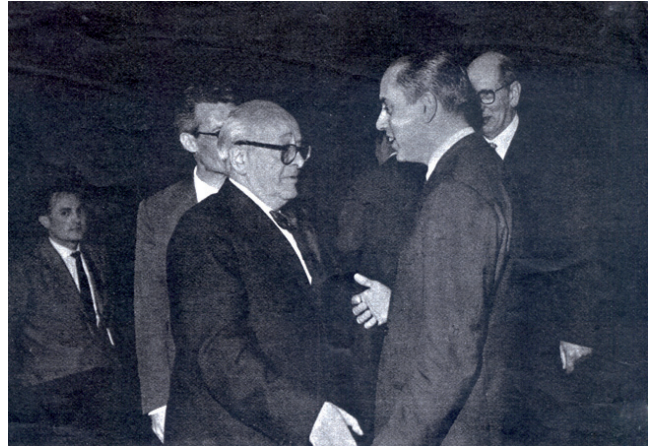


Figure 2. Jiménez Díaz and Farreras Valentí.



Figure 3. La Butiplaya, in Cala de Mijas.

Almost simultaneously, Ortiz Molina published the cases of three patients who lived in the same house in *Revista Clínica Española*, a medical journal directed by Jiménez Díaz.¹⁸ The first of these patients, aged 34, had arrived from Geneva three days previously. The second patient, aged 33, had neck pain, whereas the third had neck pain with painful points in the sternocleidomastoid muscle.

Carlos Jiménez Díaz (Madrid, 1898-1967) was born the same year as Pedro Pons and followed a similar academic career (Figure 2). At the age of 22, he made unsuccessful bids for the Chairs of Pathology in Barcelona and

Valladolid; the Barcelona position was awarded to Catalan physician Pablo Ferrer Piera, a friend of Lerroux. Jiménez Díaz was awarded a grant from the Board for Study Extensions to complete his studies in Germany. He was later appointed Chair of Medical Pathology in Seville at the age of 24 and in Madrid at the age of 26. He described lathyrism and founded *Revista Clínica Española* in 1940 and founded the Nuestra Señora de la Concepción clinic in 1955.

These three short studies are the only articles on the disease to have been published in Spain. No further cases have been published in the Spanish medical literature since 1951.

A possible, recent epidemic outbreak of Bornholm disease in Spain

A singular epidemic outbreak took place in mid-August 2014 on the hot south coast of Andalusia. In the province of Málaga, between the towns of Fuengirola and Marbella, Cala de Mijas (known for almost a century as La Butiplaya) rests upon the ruins of an ancient Roman villa (Figure 3). This area has numerous houses, mainly duplexes, in close proximity to the sea. During the summer months Cala de Mijas attracts many tourists, most of whom come from other parts of Spain, and its population reaches 5000 inhabitants. During the winter, however, Cala de Mijas has a population of barely 500, mostly from Britain. Cala de Mijas is a quiet, family-friendly residential area within a busy tourist region.

In the summer of 2014, several tourists in Cala de Mijas experienced acute-onset symptoms of pain with typical features. At least two men and two women were affected. The first case was a 66-year-old man who developed sudden-onset pain on the left side of the chest, which intensified over the course of the following days; the pain had no known cause and was preceded by flu-like symptoms (irritation of the pharynx, general discomfort, mild fever). Pain intensified with movement and deep breath, suggesting pleural involvement. During the first week, pain affected the left scapula. The intercostal spaces were painful upon palpation. Results from a chest radiography and an ECG study performed at day five were normal. Pain was not relieved by painkillers (ibuprofen, metamizole). Likewise, physiotherapy failed to deliver any significant improvements. Pain fluctuated in intensity, improving over the course of two weeks until complete symptom resolution.

The second case was that of a 35-year-old doctor, daughter of the first patient. Symptoms started three days after the father's; the pain had the same characteristics, although it was milder and irradiated to the upper abdomen. Pain lasted a week, after which the patient fully recovered.

The third patient was a 36-year-old gynaecologist, the husband of the second patient. He experienced extremely severe, disabling pain lasting a week.

The fourth case is that of a 57-year-old woman, a neighbour of the family described previously, who experienced progressive pain affecting the neck and right side of the rib cage. A chest radiography revealed no abnormalities. The patient was bedridden for three days and was asymptomatic at day five.

At this point, it should be disclosed that the first three cases correspond to the author of this study, one of his daughters, and his son-in-law. The author had the opportunity to discuss the symptoms with the physiotherapists at a well-regarded physiotherapy clinic in Cala de Mijas. The director of the clinic was also puzzled by these symptoms, which he had observed in six adult tourists, most of whom were German. Pain resolved partially or completely in all cases, although improvements were not always attributable to physiotherapy.

None of these cases were tested for viral infection. However, the symptom characteristics (epidemic, occurring in summer, benign, pain location) point to Bornholm disease.

This is the extent of what is known about Bornholm disease in Spain. The benign course of the disease makes a more in-depth study impossible. Likewise, there are no official epidemiological or healthcare system data on presence of Bornholm disease in Spain. The only data available to date are the cases published in *Revista Clínica Española* and *Medicina Clínica* over 60 years ago and the more recent cases described in the present study. Although the Spanish National Centre of Virology (Majadahonda, Madrid) has never studied the presence of coxsackievirus in patients with the condition, there is an active group of Spanish virologists specialising in enteroviruses who have made important original contributions on this topic.¹⁹

Conflicts of interest

The authors have no conflicts of interest to declare.

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