Noma in Spain: a review of reported cases throughout the twentieth and twenty-first centuries

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Summary

Noma has existed throughout history in moments of dire conditions. We aimed to compile the evidence on noma occurrence in Spain since the 19th century.

Articles were identified as part of a larger ongoing systematic literature review. Search terms included noma, *cancrum oris*, necrotizing gingivitis, necrotizing stomatitis and their equivalent terms. Case series and case reports with no date restriction in main languages such as English and Spanish among others were included.

Nine articles reporting 26 noma patients were identified, corresponding to two distinct periods. During the post-civil war years, the disease was reported among paediatric patients in conditions of extreme deprivation, often following conditions like epidemic typhus, typhoid fever, measles, diphtheria or kala-azar among others. From the mid-1940s, the arrival of penicillin significantly improved the disease outcome. In the twenty-first century, cases reported corresponded to either young adults with necrotising stomatitis or immunocompromised adults who progressed to more advanced stages of the disease.

The history of noma in Spain highlights its profound association with the social vulnerabilities of the population, serving as a stark reminder of the health inequities that allow noma to persist today in vast regions of the world.

Keywords:
Noma. *Cancrum oris*. Spain. NTDs.

El noma en España: una revisión de casos publicados a lo largo de los siglos XX y XXI

Resumen

Introducción: El noma ha existido a lo largo de la historia en momentos de escasez. Nuestro objetivo fue recopilar la evidencia sobre la aparición del noma en España desde el siglo XIX.

Material y métodos: Los artículos se identificaron como parte de una revisión sistemática más amplia actualmente en curso. Los términos de búsqueda incluyeron noma, *cancrum oris*, gingivitis necrotizante, estomatitis necrotizante y sus términos equivalentes. Se incluyeron series de casos y reportes de casos sin restricción de fecha en los principales idiomas, como inglés y español, entre otros.

Resultados: Se identificaron nueve artículos que informaban sobre un total de 26 pacientes con noma, correspondientes a dos periodos diferenciados. Durante los años de la posguerra civil, la enfermedad se describió en pacientes pediátricos que vivían en condiciones de pobreza, a menudo tras padecer afecciones como tifus exantemático, fiebre tifoidea, sarampión, difteria o kala-azar, entre otras. A partir de mediados de la década de 1940, la llegada de la penicilina mejoró significativamente el pronóstico de la enfermedad. En el siglo XXI, los casos notificados correspondieron bien a adultos jóvenes con estomatitis necrotizante o bien a adultos inmunocomprometidos que progresaron a estadios más avanzados de la enfermedad.

Conclusiones: La historia del noma en España resalta su profunda asociación con las vulnerabilidades sociales de la población, sirviendo como un crudo recordatorio de las inequidades en salud que permiten que el noma persista hoy en día en vastas regiones del mundo.

Palabras clave:
Noma. *Cancrum oris*. España. ETDs.

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Introduction

Noma, or *cancrum oris*, is a rapidly progressing necrotising orofacial infection that primarily affects children living in conditions of extreme deprivation. The disease typically begins as a necrotising gingivitis (noma stage 1) and, if left untreated, rapidly progresses to necrotising stomatitis accompanied by oedema (stage 2), followed by necrosis of the facial soft and hard tissues (stage 3) and cicatrisation of the perforation (stage 4). Without treatment, mortality is estimated at up to 90%[1]. Survivors (stage 5) are left with severe facial disfigurement, often resulting in functional and psychosocial sequelae that require extensive reconstructive surgery and specialised support rarely available in resource-constraint settings. The recommended treatment depends on the stage, with oral amoxicillin and metronidazole for stage 1, and a combination of intravenous amoxicillin-clavulanic, metronidazole and gentamicin for stages 2 and 3, accompanied by nutritional support and wound debridement[1].

Nowadays, noma cases are mainly reported in the African continent, mostly in West Africa where non-governmental organisations have conducted surveillance and awareness-raising activities for several decades. However, the lack of reporting in other low-income countries is likely a result of neglect rather than true absence[2]. In high-income countries, sporadic cases are occasionally reported in a different population, mainly immunocompromised adults, usually individuals with untreated HIV infection[3].

However, noma was relatively common in Europe during the 19th century, with extensive body of literature from the Netherlands, Germany, France, Great Britain and the United States. In 1828, Adolph Richter *published Der Wasserkrebs der Kinder*[4], the first book dedicated to noma and the only such work until the publication in 2001 of *Noma the face of poverty*[5]. By the end of the 19th century, economic progress allowed the progressive disappearance of noma from the Western world. As Klaas Marck noted: "Noma disappeared from Europe not with the arrival of antibiotics, but when even the poorest families had enough to feed their children"[5]. Noma re-emerged in Europe during famine and war periods, particularly during World War II in Nazi extermination camps[6].

This work aimed at identifying and summarising the scientific evidence of the occurrence of noma in Spain since the 19th century.

Material and methods

Articles reporting noma cases in Spain were identified as part of a larger ongoing systematic literature review. Details on the methodology are available in the protocol registered in PROSPERO under number CRD42023408304[7]. In brief, literature searches were conducted in Scopus, PubMed/MEDLINE, Web of Science Core Collection, Unika and African Index Medicus. Search terms included noma, *cancrum oris*, necrotising gingivitis, necrotising stomatitis and their equivalent terms. The inclusion criteria were: (i) patients of any age diagnosed with noma at any stage, (ii) case reports or case series as study design, (iii) written in English, French, Spanish, Portuguese, Italian or German. No restriction for publication date was applied.

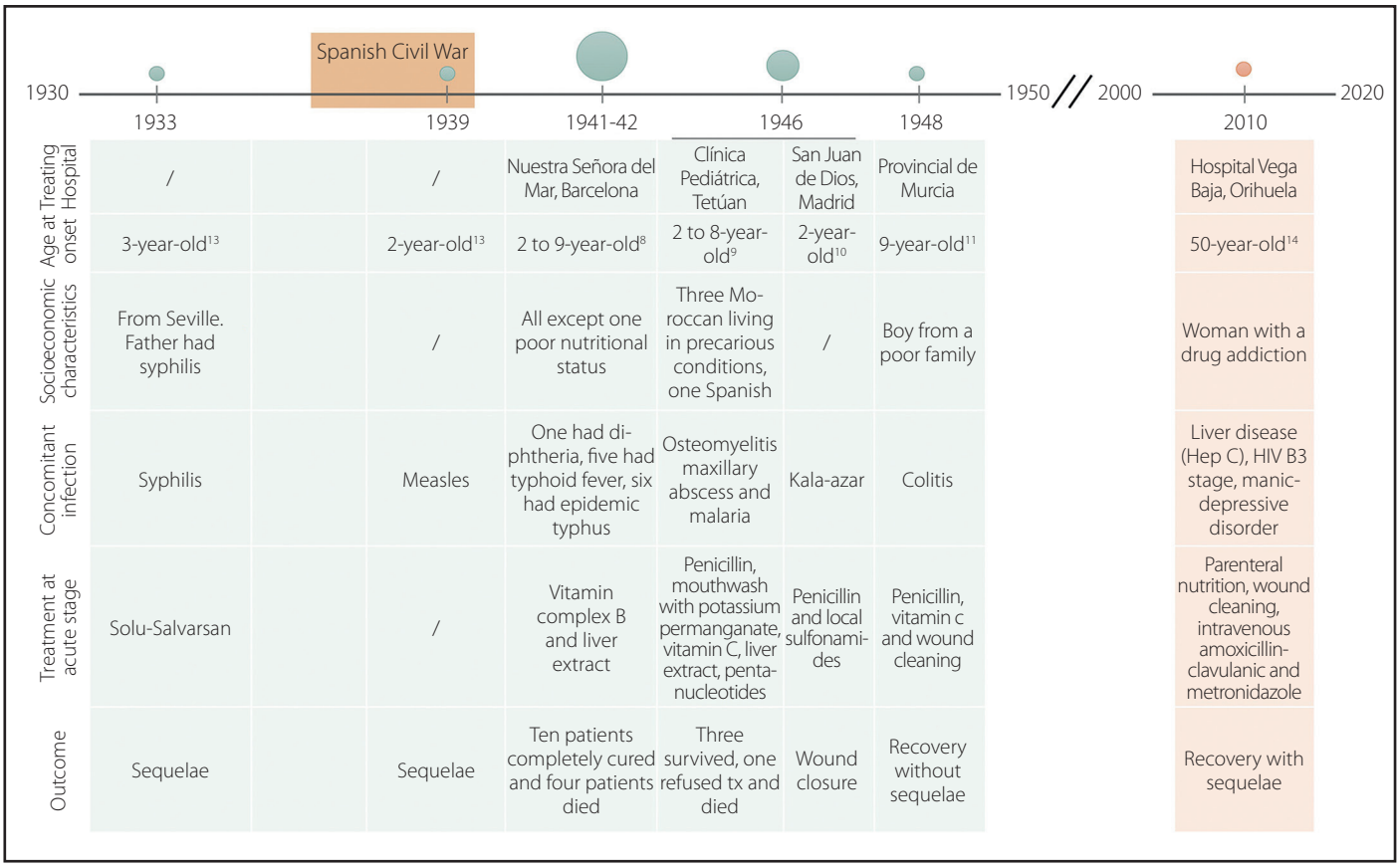
A three-step screening process was applied to select all suitable studies using the Covidence platform. Initially, all identified studies were screened for duplicates. Subsequently, two researchers independently screened titles and abstracts. Any discrepancies were resolved by a third reviewer. Finally, the full text of all potentially eligible papers was reviewed for inclusion using the same independent double-screening approach.

Results

Nine articles reporting a total of 26 cases of noma at different stages in Spain were identified through the literature search. No article published in the 19th century was found. Four articles published before the 1950s reported paediatric noma patients occurring during the Spanish post-civil war period[8-11]. Two additional articles reported surgical treatment for noma survivors over the following two decades[12,13] (Figure 1). In the twenty-first century, one case report described a woman presenting with stage 4 noma in 2010[14], while two subsequent reports described necrotising stomatitis in a total of three adults[15,16].

In chronological order, the earliest reported cases of noma in Spain were described in 1944 in a series of 14 patients treated at the Hospital Municipal Nuestra Señora del Mar in Barcelona, a hospital specialising in infectious diseases since its establishment in 1914 in response to a typhoid fever epidemic. The authors noted a marked increase in cases during the early 1940s. Although the hospital had treated a similar number of patients per year, only two noma cases were recorded between 1932 and 1940, compared with fourteen cases recorded between November 1941 and July 1942. No additional noma cases were identified after this brief period until the manuscript was written in 1944. The authors attributed this epidemiological shift to the improvements in hygiene and nutrition after the early post-civil war years[8]. Among the fourteen cases described, most patients developed necrotising stomatitis while being hospitalised for other conditions, mainly typhoid fever and epidemic typhus

Figure 1. Summary of articles reporting noma cases at stage 2 and above over a timeline. Dot size relative to the amount of cases reported on the given year.



	1933	1939	1941-42	1946		1948	2010
Age at Treating Hospital	/	/	Nuestra Señora del Mar, Barcelona	Clínica Pediátrica, Tetúan	San Juan de Dios, Madrid	Provincial de Murcia	Hospital Vega Baja, Orihuela
Age at onset	3-year-old[13]	2-year-old[13]	2 to 9-year-old[8]	2 to 8-year-old[9]	2-year-old[10]	9-year-old[11]	50-year-old[14]
Socioeconomic characteristics	From Seville. Father had syphilis	/	All except one poor nutritional status	Three Moroccan living in precarious conditions, one Spanish	/	Boy from a poor family	Woman with a drug addiction
Concomitant infection	Syphilis	Measles	One had diphtheria, five had typhoid fever, six had epidemic typhus	Osteomyelitis maxillary abscess and malaria	Kala-azar	Colitis	Liver disease (Hep C), HIV B3 stage, manic-depressive disorder
Treatment at acute stage	Solu-Salvarsan	/	Vitamin complex B and liver extract	Penicillin, mouthwash with potassium permanganate, vitamin C, liver extract, pentanucleotides	Penicillin and local sulfonamides	Penicillin, vitamin c and wound cleaning	Parenteral nutrition, wound cleaning, intravenous amoxicillin-clavulanic and metronidazole
Outcome	Sequelae	Sequelae	Ten patients completely cured and four patients died	Three survived, one refused tx and died	Wound closure	Recovery without sequelae	Recovery with sequelae

(louse-borne typhus). Upon the appearance of an intraoral necrotic ulcer, patients were treated with "Ilobán", a vitamin B complex and liver extract compound. All patients developed oedema, and four presented with bluish or purplish plaque at the centre of the oedematous cheek. Four patients died: a patient who was admitted at stage 2 with a necrotic plaque and died within a few hours, a patient who died within nine days despite the infection having been arrested at stage 2, and two patients admitted at stage 2 who progressed to stage 3 and died[8].

In 1946, a case report described a two-year-old girl with kala-azar who presented at a hospital in Madrid with an extensive full-thickness gangrene of the chin originated in the lower lip and gum and a second gangrenous plaque in the palate. She was treated with penicillin and with sulphonamide powder on the eschar. Despite treatment the gangrenous plaque sloughed off after 40 hours leaving a perforation that after three days had almost closed[10].

In 1947, four acute noma patients were reported at the Paediatric Clinic in Tetuan, in the Spanish Protectorate in Morocco. Three were of Moroccan origin and were successfully treated with penicillin, while the Spanish patient died within two days of admission after the parents refused hospitalisation and treatment[9].

In 1948, Guillamón and Llanos reported having treated several patients ranging from 6 years of age to adolescence. The case described in detail corresponds to a nine-year-old boy from Murcia who was malnourished and lived in poor hygienic conditions. He presented to the Hospital Provincial de Murcia with inflammation of the lower lip and right cheek, and a purplish spot with a central serosanguineous vesicle and a foul-smelling greyish ulceration on the inner surface of the cheek and loose tooth. He was successfully treated with intramuscular penicillin, vitamin C and wound cleaning with rivanol. The boy had suffered diarrhoea for about two weeks and had experienced lower jaw pain accompanied by fever for a week[11].

In 1953, Nuñez operated on a 23-year-old woman from Seville who had developed noma in 1933 in association with syphilis and had been treated at that time with Solu-Salvarsán[13], the first effective chemotherapeutic agent used primarily for the treatment of syphilis.

In 1962, a 25-year-old woman in Granada received surgical treatment for noma sequelae. She had developed noma at the age of two while suffering from measles. During the operation, her cheek was reconstructed using a Gillet tube adapted over a cervicofacial flap[12].

Following these twentieth-century reports of noma cases, only three additional reports were identified in the twenty-first century mostly associated with recreational drug and alcohol use. In 2010 Pacheco-Tenza *et al.* reported the case of a 50-year-old woman from Alicante presenting with noma stage 4. She had a history of habitual drug use, hepatitis C infection, untreated HIV infection, cachexia and a manic-depressive disorder. She presented with a 2 cm cheek perforation that had progressed over two weeks. She was treated with parenteral nutrition, wound cleaning, intravenous amoxicillin-clavulanic and metronidazole. One year later, the woman underwent reconstructive surgery[14].

In 2009, a case of necrotising gingivitis was reported in Barcelona in a 19-year-old man, occurring three days after recreational MDMA use and after the drug had been stored adjacent to the site of periodontal necrosis. He was successfully treated with surgical debridement, 0.2% chlorhexidine, oral amoxicillin clavulanic acid and metronidazole[14]. Finally, two cases of necrotising stomatitis were reported in Granada in 2015: one associated with work-related stress and the other following a weekend of excessive alcohol and tobacco consumption combined with lack of rest[16].

Discussion

We identified two differentiated periods of noma reports in Spain during the twentieth and twenty-first century, while no articles were identified reporting noma in the 19th century. The first period was concentrated in the post-war and corresponded to paediatric patients living in conditions of extreme deprivation. The second, by contrast, corresponds to recent decades and involves either young adults with necrotising stomatitis or immunocompromised adults who progressed to more advanced stages of the disease.

Interestingly, the 21 noma cases reported during the twentieth century occurred within the relatively short period between 1933 and 1948, with 20 concentrated in a single decade, between 1939 and 1948. Several factors may explain this restricted timeframe. First, this period coincided with the early post-war years, characterised by food shortage, hunger and epidemics of infectious diseases, key risk factors for noma. In line with this, Mas de Xaxars and Bardají mentioned an increase in noma cases after the Spanish Civil War, and in their practice observed a peak of cases treated at Hospital Municipal Nuestra Señora del Mar (Barcelona) between 1941 and 1942. However, they noted that this high number should not be considered representative, as their hospital specialised in infectious diseases[8]. Royo noted that in Tetuán (Moroccan Spanish protectorate) the disease was "present with relative frequency". Conversely, Guillamón and Llanos deemed it "relatively infrequent"[11] and De Dulanto and Armijo-Moreno two decades later described it as "exceptional" within their practice as surgical dermatologists[12].

Although a higher incidence of noma during that decade is plausible given the aforementioned epidemiological and social factors, the observed concentration of reports during this period might reflect publication bias. Spain entered the academic world later than its European neighbours. This, combined with the unrest of the Civil War (1936-39) may partially explain the lack of reports prior to the 1940s, especially during the 19th century, where noma was described as relatively common in other European countries[5]. It is also possible that the cluster of cases reported in the late 1940s was influenced by enthusiasm around the arrival of the first antibiotics, which prompted physicians to document the successes of these new drugs. The first doses of penicillin arrived in Spain in 1944. Indeed, both Alvarez in 1946 and Royo in 1947 titled their manuscripts from Madrid and Tetuán, respectively, "Noma and Penicillin"[9,10]. Further research in medical history is needed to determine whether this concentration of cases reflects a true incidence peak or, at least in part, is the result of reporting bias.

Noma cases reported in the twentieth century affected a markedly different population from those reported in the twenty-first century. This epidemiological shift observed reflects changes in living conditions. Diseases mentioned by the authors as common antecedents of noma, including measles[10,11], scarlet fever, oral sepsis[10], kala-azar or typhoid fever[11], are no longer prevalent in Spain, nor are the hygienic and nutritional deficiencies described across the twentieth-century manuscripts. Today, necrotising gingivitis is rare enough in Spain to be reported as individual academic case reports[15,16]. However, the HIV epidemic introduced a new population at risk. In high income countries, advanced noma is now mainly reported in immunocompromised adults, particularly those with untreated HIV infection. Although universal access to treatment through the Spanish health system protects most patients, vulnerable individuals who discontinue care, such as the patient reported in Alicante in 2010, may remain at risk.

Regarding treatment, all acute noma cases reported after 1944 received penicillin. Treatment before its arrival, according to the articles reviewed, included serum and arsenics, which were

not effective, and gold salts which were reported successful[11]. The success of gold salts might be explained by a spontaneous cure, which occurs in about 10% of patients, or by patients receiving it at an early stage, as seen in cases with necrotising stomatitis and a proportion of them with oedema in Barcelona in 1941-2 who -in ten out of 14 cases- were successfully treated with nutrition restoration and treatment of the concomitant infectious diseases[8]. The vitamin B complex with liver extract used by Mas de Xaxars[8] may have worked mainly by improving the patient's nutritional deficiencies, which made them more vulnerable to the disease, rather than through a direct antimicrobial effect. Sulphonamides, which were available a few years before penicillin, were used for noma in other countries[6], among the articles reviewed only Alvarez reported using it in its powder form over the wound[10]. Cases reported in the twenty-first century received treatment according to current WHO recommendations[1], except that they also received debridement[15,16], and no gentamicin was given to the noma patient at stage 4[14].

The cases described here should not be considered a comprehensive account of the noma cases occurring in Spain since the 19th century. The better a country registers its burden of disease, the fewer number of noma patients there are[5]. In addition to the publication biases discussed above, several other limitations may have hindered the identification of noma cases and should be considered when interpreting our findings. First, many patients may have died before reaching a health facility. Second, only a small proportion of cases are documented in the scientific literature. Third, our literature search strategy may have missed relevant publications. In this regard, it was not possible to retrieve an article by Orbaneja for which the only information available is that they reported on noma and penicillin[10], and another by Hernández-Ros who reported several cases treated with gold salts[11]. Likewise, the list of terms used in the searches might not have been scientifically comprehensive. Indeed, the authors in the twentieth century mentioned that multiple terms were used at the time to describe noma: gangrenous stomatitis[8,12], water cancer, estomacace, "carbunco de las mejillas", scurvy cancer, *cancrum oris*, *Wasserkrebs* or *charbon de la joue*.

In conclusion, the history of noma in Spain illustrates its profound association with social vulnerabilities of the population, with fluctuations in occurrence and re-emergence during periods of severe deprivation. This review serves as a stark reminder of the health inequities that persist today, and continue to place a substantial proportion of the world's population at risk of noma. It also underscores that no geographical area is permanently protected from noma unless basic standards of nutrition, hygiene, and healthcare are guaranteed.

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