YELLOW FEVER IN EUROPE DURING 19th CENTURY

MORILLON M., MAFART B., MATTON T Yellow fever in Europe in 19th Century. in Ecological Aspects of Past Settlement in Europe. P. Bennike, E.B. Bodzsar, C. Suzanne dir. European Anthropological Association, 2002 Biennal Yearbook. Eötvös University Press, Budapest. p 211-222.

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ABSTRACT

Known today as an exclusively tropical disease, yellow fever appeared in Europe in several outbreaks during the first half of the nineteenth century. Between 1800 and 1828, several ports in the south of Spain were affected. Each time, several thousands of deaths were registered.
We always possess several historical detailed reports containing a lot of clinical and epidemiological data. The features of the outbreaks (clinical symptoms, mortality, epidemiological aspects), allow us to eliminate the main other hypothesis: infectious jaundice. How could this tropical disease reach the coasts of Europe in a time where the ship trip required between 50 and 90 days? The settlement and persistence of this viral disease in Europe was link with the association of several ecological and entomological factors. If the persistence of eggs of *Aedes* in empty ships is well established, the possibility of virus transovarial transmission in the vector is more recently known. From the climatic, historic and demographic factors, we may propose explanations

for these outbreaks that devastated several towns in Europe. This analysis may allow us to imagine the consequences of both a climatic warming up and an importation of mosquitoes infected with some closely related viruses such as the dengue viruses.

INTRODUCTION

Today yellow fever is known as an exclusively tropical disease and the rare cases observed in Europe are imported cases. When they occur, their gravity can confound them for a while with terrifying viral haemorrhagic fevers (Lassa, Ebola, Marburg fevers). Importation of cases from African endemic areas to non-endemics countries periodically raises public concern and media interest. And yet, at the beginning of the 19th century, on several occasions this disease reached Europe, and especially Spain, by epidemics, responsible for several thousands of deaths. In this pre-Pasteurian era, the nature of the disease was not known and it would be necessary to await the beginning of the 20th century before its mode of transmission be explained. The definition itself of the disease, then called "yellow fever" as well as "plague" (Chastel, 1999), was vague and could constitute a difficulty for a retrospective analysis. The clinical observations had already been numerous at the time of colonization in Central America and Caribbean by 17th century and especially during military expeditions like that of St Domingo in 1802. The fact that a theoretically strictly tropical disease could decimate the population of cities in south-Europe seems difficult to explain today. Was it really yellow fever? How could have this disease been imported and how could it be transmitted in Europe? We shall try to answer these questions. It will be also interesting to analyse the economic, scientific and even political consequences of this phenomenon.

ACCOUNTS OF WITNESSES

Probably, the epidemics of the 19th century probably did not inaugurate the arrival of the disease in Europe. By the 18th century (Cadiz, 1765, according to Laveran, 1875) fatal epidemics occurred in Spanish ports. These could be the first appearance of the disease. However, during the very first years of the 19th century, the history begins with great epidemics of yellow fever in Europe that particularly devastated Spanish and Portuguese ports. There were at least 20 epidemics (fig 1, tab. 1), besides the countless sporadic cases concerning subjects living in ports such as Marseilles 1804 and 1807, the Island of Wight 1845, Southampton 1852, Brest, 1802 and 1865, Falmouth, 1862, London 1850 and Swansea 1865 (Dutroulleau, 1868, Grall et al., 1912). The history of these epidemics may only be known thanks to accounts of witnesses, generally doctors. Only most fatal and latest outbreaks within 19th century are very well described. The accounts of the epidemics of Cadiz and Seville in 1800 and Barcelona in 1821 (which reached us) report their gravity and explain their socio-economic and political impact as well as the scientific issues they raised about their causes and modes of transmission.

THE EPIDEMIC OF CADIZ AND SEVILLE OF 1800

The winter of 1799-1800 was described as mild and was followed by a rainy spring. There was then a very hot summer (87 F° on August 19th). At the end of July 1800 a corvette coming from Havana, entered the port of Cadiz after 9 days of quarantine (Berthe, 1802). During the following days the arrival, staff in contact with the ship or working at the port got sick (2 sentries on board, 3

sailors after the arrival of the ship, 1 guard of the port, 1 employee of the health's office, some customs officers and dock workers). On July 27th, a priest residing far away from the port returned to visit a patient and got sick. The initial outbreak area of the epidemic was thus in the port and 5 among the initial patients were directly linked to the ship. Between August 10th and 15th, during which an overwhelming heat prevailed in the city, the disease extended to the East part of the city, concerning mostly sailors and workmen from the port living in these districts bordering on the harbour zone. The authorities then noted the unusual character of this fever, which was accompanied by a strong odour of the patient, and they called it "a putrid fever". On August 15th, 200 patients were counted and the 28 monks who had come to look after them were to be added. The town of Seville was trading abundantly with Cadiz, not only by land but also especially by sea, generating an intense coastal traffic. In late August 1800, initial cases were observed in the sailors' district, where the families of these men were living mostly, commuting between Cadiz and Seville. On September 3rd, the municipality prohibited travels between these two ports. The disease, initially limited to the harbour's district, extended gradually to the whole city and then also to small cities and coastal villages (Oporto S.Maria, Isla, Chiclana, Puerto Real, San Lucar, Xerez of Frontera). It lasted until the early cold season. It was estimated that 51 000 people had died.

THE EPIDEMIC OF BARCELONA IN 1821

A brig, the 'Large Turk', coming from Havana arrived in Barcelona within the first fortnight of July 1821, during a particularly hot summer, after having achieved one period of quarantine in Malaga (Da-Olmi, 1828). The captain's family went on board, then died a few days later. Other ships as the "Josephine", a French ship not coming from America, had patients on board and workmen of the port were infected. On August 5th, 12 people had already died, on August 16th, 30 more died, on August 26th, 74 and on August 29th, 124 dead were numbered in the harbour district, mostly populated by modest people. The municipal authorities, after they had neglected this obvious epidemic, tried to organise the medical treatments, requisitioning the doctors, organising the burial of the corpses numbered in hundreds each day. They ensured the enforcement of the law and order and the food supply to the inhabitants which could not flee and who were blocked in a starving city by the sanitary cordon and measures of quarantine instituted around the city. On October 11th, it was decided to evacuate the city and the inhabitants were settled in rough and ready camps outside the city. The epidemic decreased during November and December, no further case was quoted, and the quarantine of the port was repealed at the end of the month. The number of dead was estimated to 4 500 among 80 000 inhabitants (5,6 %).

CURRENT KNOWLEDGE ABOUT YELLOW FEVER

The yellow fever prevails today exclusively in the tropical areas of the African and American continents. Its absence from the Asian continent is still an enigma. The disease concerns the human beings and the platyrrhinian primates from the New World. The pathogenic agent is a flavivirus, discovered and identified as the responsible agent in 1936 (Lloyd, Theiler Ricci). For a long time, the monkeys were considered as the reserve of the virus. But the persistence of the virus in the environment could not thus be explained, especially on the American continent where monkeys died from this disease. More recently, it has been proved than some mosquitoes, with a clear responsibility in the transmission of yellow fever, have also a reserve role. There is no possible transmission by direct contact from man to man. Transmission is carried out by mosquitoes of the Aedes group (*Stegomyia*) as demonstrated by Walter Reed in 1901. In order to survive, these tropical insects require heat (higher than 20°C) and moisture. They lay eggs in small natural collections of water (leaves of plants) and artificial ones (earthenware jars, barrels and nowadays, tyres and various wastes from civilisation). These eggs have as a characteristic, the ability to adhere to the walls of the containers and resist desiccation. Thus, containers, even empty ones, can preserve a population of mosquitoes until they receive some water again. The cycle can then start again: blossoming, larval moults and imago releasing the winged form. Even more recently, it is shown, that when an Aedes female is infected by yellow fever virus, it is able to transmit it to its eggs and thus to give rise to

infected insects. If, after the sting of a mosquito, a human being becomes infected, the first signs of the disease appear within 6 days on average. The clinical signs of the traditional form are evocative: dramatic beginning, including intense fever, headache, skin and mucous membrane congestion so called " red phase ", followed on the 3rd day by an apyrexia phase then a " yellow phase " with hepatic and renal attack and haemorrhages. In the first phase, the virus is staying in the blood and constitutes the source of contamination to another mosquitoes. Mortality is high (20 to 30%). Recovering patients and contaminated with an unapparent or paucisymptomatic form get a durable immunity, practically lifelong.

THE MEDICAL REACTION IN 19th CENTURY

Facing this emergent disease and recalling the devastations of the recently controlled plague of the old Europe, the doctors were in the foreground of the fight and diagnostic and prophylactic steps. The yellow fever that devastated the New-World colonies at the same period was very early evoked, even if this diagnosis was the issue of sharp controversies, as well about diagnostic matter as about contagiousness and thus of its way of transmission. Obviously, the exact nature of the pathogenic agent and its mode of transmission for epidemics of the 19th century can be only hypothetical, in the absence of a biological confirmation. Only the analysis of the medical literature of the time,

compared with modern knowledge, can make it possible to advance clinical and epidemiological arguments.

IDENTIFICATION OF THE YELLOW FEVER

Clinical descriptions were precise, as in Cadiz in 1819 (Devèze, 1820, Parizet, 1820) and in Barcelona (Bally, François and Parizet, 1823). Doctors described a quite stereotypical semiological set (fig 2). The beginning was described as variously dramatic and it associated asthenia, diffuse pains, and cephalalgias. Within this initial phase, whenever the beginning had been progressive and general signs slightly emphasised, it was then followed by a sustained fever associated with a congestive aspect of the face and then a cutaneous jaundice possibly lasting three to four days. Then the condition of the patient improved slowly until recovery. In the most acute forms, with which the most serious prognosis was related, patients presented within 24 h non-specific signs of serious infectious syndrome (high fever, intense cephalalgias, fast and major deterioration of the general condition). The intensity of initial symptoms increased and digestive troubles appeared: nausea, bilious vomiting. After the congestive phase of the face, the jaundice was evident (‘red’ then ‘yellow’ phases). The intense vomiting was accompanied with diarrhoea and mucoid stools. Then haemorrhagic signs appeared. Vomiting and stools became darker ; skin and mucous membranes haemorrhages (petechia, epistaxis, gums bleeding, haematuria, vaginal haemorrhages) were accompanied with signs of

shock such as a weakening pulse and with diffuse sweats without fever and marbling of members. The vomit had the colour of 'coffee grounds' (the "vomito negro") and emission of unceasing black stools with unconsciousness were signs announcing an imminent death. Autopsies were often carried out. The brain was not impaired while bleedings without breach of the vessels of the dura mater were described. All the internal organs possibly presented haemorrhagic lesions, particularly stomach and intestines. Moreover, the liver was often described as haemorrhagic and necrotic. These clinical and histological signs perfectly described by the doctors who had witnessed such pathetic scenes are, in modern syndromic classification, pathognomonic of an haemorrhagic fever (Touze et al., 2001) identical to yellow fever, particularly as it had been observed in Africa (Berenger Féraud, 1875) and in America (Laveran, 1875). Since 1800, the diagnosis of yellow fever has been based on a semiological and epidemiological analogy with the scourge then devastating Central America and southern North America (Berthe, 1801). This diagnosis was clearly reiterated in 1820 (Devèze, 1820) whereas some tried to describe a 'typhus amaryl' distinct from yellow fever. The etiologic discussion sharp with a political polemic background. However, in fulminant forms, autopsies did not reveal any anomaly. These autopsies were significant etiologic evidences at this early 19th century where two medical schools were opposed: the "vitalistics" one and the "solidists and humorists" (sic) one'. The former believed the disease was due to the deterioration of a vital principle and thus

the lack of specific lesions and the normality of some autopsies reinforced their opinion. The latter indicated that many autopsies were poorly carried out or one had not wanted to notice some lesions. Finally, it should be added that on several occasions, doctors having practised in the Caribbean during authentic yellow fever epidemics confirmed the nature of the disease.

Figure 2: “death of a young noble man”. These portraits represent the dramatic evolution of the face during the different steps of yellow fever during the Cadiz outbreak in 1820 (from Parizet, 1820).
A: Beginning of the fever; B: Erythematous period; C: Icteric period; D: Haemorrhagic and terminal period

EPIDEMIOLOGY

These epidemics have some common characteristics (table 1). The cities initially concerned were always ports trading with the Americas. The longest and most fatal epidemics occurred in areas of southern Europe where climate is the hottest. All epidemics started by the end of summer, often in particularly hot years and stopped at the beginning of winter. This is contrary to most Northern areas where only short duration epidemic outbreaks with a limited geographical spreading occurred. Since initial sources of epidemics always took place in very active commercial ports, the assumption of a sea imported infectious disease was prevailing among contemporaries and actually seems to be highly probable. The epidemics were fatal and involved as well poor as wealthy people (Rochoux, 1828). They always started in ports and often the responsible ship was identified: e.g. a sugar carrier coming from Cuba (Berthe, 1802) or from Brazil (Parizet, 1820, Lyons, 1995). The ships were all the more easily identified because there were patients on board during the journey. In cities where epidemics had already prevailed for previous years, as in Gibraltar, they became less and less fatal (table I). It was also noticed in Spain that people having stayed in American colonies or who recovered from this disease were protected (Parizet, 1820). To sum up, it seems that was an imported disease, occurring mainly in ports, not related to the population hygiene level and whose transmission depended on heat. These characteristics

clearly were those of a vectorial transmission disease. The epidemics were dramatic, fatal and appeared as fever cases with skin and renal lesions and haemorrhages. The subjects who recovered were immunised. Among all known infectious diseases, only yellow fever matches this description. We now have understand how this tropical disease could travel and be transmitted with such an effectiveness by the 19th century. Importation of infected adult mosquitoes is possible but not so probable: an imago can maximally survive for few weeks and the transatlantic journey was 50-90 days long. The possibility of infested crews before departure and having been stung by local mosquitoes on arrival cannot be supported: the 6 days incubation of this disease seems to be incompatible with the duration of journeys. If the virus could not arrive in Europe in the infected patients blood, one nevertheless can imagine that ships imported a complete ecosystem. The infected female insects, abundant in ports could lay their eggs in the innumerable rainwater collections present on board and especially in the freshwater stock barrels. Once these containers were drained or emptied, eggs, adhering to the walls, could await to receive some water again to start a new development cycle. This phenomenon is well known in current endemic areas where one recommends brushing the water stock containers walls. Once the mosquitoes had arrived and hatched, they could find terrestrial relays in the basins of the Andalusian patios and in the earthenware jars (tinajas) (Sawchuk, 1998) used to reserve water. In October and September, in this usually rainy area, the

natural lodgings were still multiplying. The cycle would be able to continue on board during the journey transmitting the virus from several generations of mosquitoes to the crewmembers. Indeed, several accounts reported the presence of patients on board (Berthe, 1802). But, the importance of these epidemics could be explained only by the appearance of secondary cases, especially when these lasted several months. The role of temperature, necessary for the persistence of several mosquitoes' generations seems to be obvious then and actually the epidemics of Andalusia lasted longer and ultimately, were most fatal. When winters were mild, it was even possible for this disease to persist from year to year. Some cities were regarded as chronically infected as it was testified by some reactions from French and British military authorities, then involved in the Spanish Independence War (Oman, 1996). One should also keep in the possibility of a "relay" by native Aedes species. Without formally dismissing this previous assumption, the adaptation of a pathogenic agent to a vector requires most of the time many years of co-evolution of the two species. The effectiveness of transmission to human beings seems to decrease through the years (Sawchuk, 1998), checked by a well-known epidemiological phenomenon so-called 'collective immunity' or 'herd immunity' that settled among survivors. Some noticed that subjects coming from northern Europe were less resistant than southern Europe natives and than those who stayed in the American colonies (Parizet, 1820). The contemporary scientists clashed between 'contagionists' (Parizet, 1820) and

'non-contagionists' (Rochoux, 1828). The former were certain that contacts with infected patients could be contaminating. Of course, the role of the vectors was not alluded to. The non-contagionists tried to find the causes of the disease among climatic conditions and the air quality. To disturb all and sundry, several observations had already been recorded during the epidemics of St Domingo where some daring doctors had laid down in the bed of recently died patients without contracting the disease. On the other hand, in Spain, the sentries at the entrance of the lazarets to whom having contacts with the patients was prohibited had been infected. The gatherings of population, particularly for burials, matched every time with an increase of cases.

CONSEQUENCES

The consequences of these outbreaks were far from the single medical problems and recovered scientific, demographic, economic, political and cultural fields.

- Scientific consequences: The quarrels in the medical control were going to last over one century without being possible to know if measures of quarantine could be effective. Medical recommendations adopted nowadays prohibit the transfer of patients, particularly towards not infected cities and insulation under mosquito's bed-nets. A campaign of insect control must concurrently be carried out (International Sanitary Rules).

- Demographic consequences: obviously such mortality has left traces; they are measurable in large cities. The population pyramid (ages distribution) of the Gibraltar city shows a very clear notch, corresponding to the overmortality for these epidemics periods.
- Economic consequences: Measures of quarantine and blockade imposed around the large harbour cities had a significant repercussion for those whose industry was based on international trading; that was case of Barcelona trading cotton for example.
- Political consequences: they are surely the most unexpected ones. The history of Spain during the first half of the 19th century is excessively disturbed due to the succession of independence wars against the Napoleonic troops and of the Civil War between the constitutionalists, favourable to a liberal reform and the absolutists, gathered around the King who had returned from exile. The King Louis XVIII French government, favourable to the absolutists and fearing an epidemic of republicanism, benefited from the epidemic of Barcelona in 1821 to mass a considerable army along the Pyrenean border on the pretext of a "sanitary cord". Once the epidemic was over and by decision of the Count de Chateaubriand, Foreign Minister, the French royal army entered Spain and returned its throne to Fernando VII after the conquest of the Trocadero Fort, key of Cadiz, starting point of the yellow fever epidemics.

- Cultural consequences: This significant mortality and the real or supposed reactions of devotion became literary ingredients that romantic authors could not ignore. Some grandiloquent drama had as a topic the yellow fever epidemics (e.g. Victor Hugo).

CURRENT LESSONS:

The analysis of the events one century after could be a rich lesson. Where the duration of the travels between the tropics and Europe has been reduce to a few hours and their number has considerably increased, we have observed only a few isolated cases of imported yellow fever. A better control of international airports and the lawful insect control of aircraft surely played their role. Vaccination, by reducing the urban human reserve in the cities of departure also took part to this evolution. But among these measures, some of them are sometimes imperfectly applied. However, the insect's vectors 'found' other means of travelling as it is testified by the intercontinental diffusion of *Aedes albopictus*, vector of dengue fever in South-east Asia and which recently settled in Central America. This insect has climatic requirements less strict than *Aedes aegypti*, vector of the yellow fever and it could adapt in some areas of southern Europe. Dengue fever is an arbovirus disease, and the pathogenic agent is close to the virus of yellow fever. *Aedes albopictus* is circulating around the world, benefiting from the traffic of used tyres and thus

is travelling hung on the retreads circulating from Asia towards European countries (Rhodain, 1996). This mode of circulation recalls the assumptions above mentioned to explain the circulation of the yellow fever virus by the 19th century. With these observations, concerns related to climatic changes are added today. Assuming a 2°C average increase of temperature, southern Europe would become a fair receptivity area for dengue fever, even for its haemorrhagic forms. Due to the current absence of an available vaccine, medical consequences could be considerable despite we are not as disarmed as our ancestors from the 19th century for fighting against the insects. The recently observed episodes related to the diffusion of the West Nile virus which is also an arbovirus, could be the first step to that (Epstein, 2001).

CONCLUSION:

The intensification of international trading and particular climatic conditions made it possible for the yellow fever to wreak devastation throughout 19th century Europe. Since our knowledge about infectious diseases has increased, the study of these past events provides however a cache of learning for today's scientists. Since they have adapted their spreading conditions to the modern trading, some tropical diseases close to yellow fever, could once again leave their own geographical limits.

Year	Months	Town or area	Number of deaths	Sources

1800	August	Cadiz, Sevilla, Gibraltar	51 000	Berthe, 1802, Devèze, 1821, Parizet,1820, Sawchuk, 1998
1804	August-December	Gibraltar, Malaga, Cordoue, Cadiz,	5 700	Sawchut, 1998
	Summer	Livourne	700	Grall et al, 1912
1810		Gibraltar	?	Sawchuk, 1998
1811		Murcie, Alicante	?	Oman
1813		Gibraltar	?	Sawchuk, 1998
1814		Gibraltar	?	Sawchuk, 1998
1819	September-December	Sevilla, Cadiz	?	Pariset, 1820
1821	August-December	Barcelona	4 500	Hoffman, 1964 Angolotti, 1980
1828		Gibraltar	?	Sawchuk, 1998
1845		Isles of Wight	?	Grall et al, 1912
1852		Southampton	?	Dutrouleau, 1868
1856		Oporto	?	Lyons, 1995
1857	August-November	Lisbon	5 500	Mêlier 1863, Lyons, 1995
1861	August-September	Saint-Nazaire	33	Mêlier 1863, Coleman
1865	September-October	Swansea	15	Gordon Smith, 1986

Table 1: localizations of yellow fever epidemics during the 19th century in Europe

This table was built from bibliographical data nowadays available. Thus, it is neither a complete collection nor a strictly accurate count of dead. However, the figures so gathered may give idea of the importance of this phenomenon.

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