

Leptospirosis in French Historical Medical Literature: Weil's Disease or Kelsch's Disease?

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Leptospirosis in French historical medical literature : Weil's disease or Kelsch's disease?

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4 Running head:

5	A. Kelsch and the description of the determinants of Leptospirosis
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24 Abstract

25 Early names for leptospirosis often indicate occupational or environmental exposure. 26 Leptospirosis is hard to identify in the tropical setting due to co-circulating diseases. This is not the case in the temperate setting, such as Europe, where the few differential diagnoses at the time 27 28 are malaria, typhoid and viral hepatitis. Leptospirosis presumably caused community epidemics 29 in Europe before 1900 and military epidemiologists carefully documented outbreaks in "constrained settings". Achille Kelsch (1841-1911) synthesized available military data and 30 31 epidemiological perspectives to define "Epidemic jaundice" as a nosological continuum, caused 32 by an infectious agent found in muds and water. He viewed Weil's disease as being only one form 33 of that now well-identified disease continuum. The causative pathogen and epidemiological 34 determinants were identified years later. The role of soils and muds as intermediate reservoirs, as 35 suggested by Kelsch, deserves further investigation.

Leptospirosis is a complex disease caused by a spirochete. The clinical entity ¹ and causative
infectious agent of leptospirosis were identified at the turn of the previous century, but these had
long been circulating and identified in a classic case of "disease emergence", descriptions being
rather an "unveiling" and the structuration of a disease entity.

Although infections and outbreaks were well-described, identifying a disease complex or
entity is challenging when many names are used. Many of those names, however, bore the notion
of behavior, occupation or seasonality: « Rat-catcher yellows »; « Cane-cutter's disease »; « Peapicker's disease »; « Harvest fever »; « rice/paddy field jaundice »; « Maladie des éboueurs »
(« sewage workers' disease ») or « Schlammfieber » (« slime fever ») ^{2,3}.

Leptospirosis is difficult to identify in the tropical setting, where many other diseases with 46 47 similar initial presentation co-circulate: Hepatitis A; Yellow Fever; Schistosomiasis (Bilharzia) or 48 Blackwater fever (malaria)⁴. Before being a neglected tropical disease, however, leptospirosis 49 was a public health concern in now-developed countries. The French Royal Society of Medicine 50 received 80 communications on « bilious epidemics » in France from 1782 to 1784 alone, many of which may have been leptospirosis outbreaks ⁵. In the absence of endemic Yellow Fever in 51 52 Europe, the principal differential diagnoses in leptospirosis outbreaks were malaria, typhoid and 53 viral hepatitis A. Clinicians, however, knew the febrile cycles associated with malaria well and routinely used bark of cinchona, including in febrile jaundice cases ⁶. Typhoid was similarly 54 lethal in the pre-antibiotic age but rarely associated with jaundice ⁷. The issue of viral hepatitis is 55 56 more complex, but this was a widespread, benign childhood disease before public hygiene improved, with most infections remaining symptom-free ⁸. At the end of the 20th Century, 57 58 seroprevalence remained high in European populations, with antibody prevalence of approximately 50% around age 20 in Spain and around age 40 in the Czech Republic⁹. The 59 prevalence of protective antibodies was likely much higher in the 19th C when most enlisted 60

61 populations described below would have been born and raised on farms or in urban slums.

62 Moreover, oliguria is rarely documented in type A nonfulminant hepatitis 10 .

In temperate settings, leptospires may have caused a devastating outbreak among Patuxet (Plimouth) indians in New England in the early 17th C ^{3,11} or in Minorca in 1745 ¹². JAF Ozanam (1773-1837) mentioned community outbreaks of "epidemic jaundice" in Berlin in 1699 and 1702, in Hungary in 1703 and 1705, in Rome in 1709 and in now-Belgium and the Netherlands in 1719 ^{5,13}. Most of the well-documented epidemiological records available on what may be considered to be leptospirosis, however, were documented by military doctors in Europe.

These clinical epidemiologists were struck by the brutal character of "epidemic jaundice" outbreaks even among healthy adults; they described environmental or occupational exposures leading to jaundice which bore similarities to "typhoid" or "typhus" but was less lethal and not always febrile.

Sir John Pringle (1707-1782) relates the account of "epidemic jaundice" among British troops in Flanders in 1743¹⁴. Outbreaks and their dynamics were described in Europe, for example in now-German troops besieging Paris, causing 799 cases amongst 33,380 Bavarian troops stationed around Paris in Feb-May 1870 with an estimated attack rate of 2.4% ⁵. Many other such epidemics were described elsewhere in Europe and no doubt detailed in other languages ¹⁵. But the best-described epidemics - in French medical literature at least - occurred in closed settings with documented denominators ¹⁶.

E. Fritsch dit Lang (1833-1877) described epidemics among French garrisons in 1859,
during the second Italian independence war against Austria. Outbreaks among garrisons in Pavia
and Civita-Vecchia near Rome occurred among 71/1,022 troops (6.9% attack rate, no deaths) and
47 cases including 21 severe (4 deaths) among stationed troops, respectively ^{5,6,16}. The latter

outbreak was associated with soldiers' bathing in waters contaminated by sewage, one of the first
 mentions of a telluric origin ¹⁵.

86	In Gaillon, France, Carville cited by Lavéran documented in 1859 a 5-month prison outbreak
87	of 47 cases of "severe epidemic jaundice" (ictère grave épidémique) associating frisson,
88	headache, extreme fatigue, oliguria in some, abdominal tenderness and vomiting. After 6.5 days
89	on average the presentation progressed to jaundice, vomiting, epistaxis, hematemesis or
90	petechiae, albuminuria and caused 11 (23.4%) deaths ^{16,17} .
91	Two well-documented outbreaks with thorough clinical descriptions occurred in garrisons in
92	and around Paris in 1865 : One in May in Saint-Cloud ^{18,19} and the other in July-August at
93	Caserne Lourcine, in Paris ¹⁷ . These epidemics were at the time attributed to drinking or exposure
94	to biocontaminated water from uncleansed or rat-infested reservoirs. Others in Arras, France,
95	documented "epidemic jaundice" cases in 1864, 1865 and 1867 associated in time and space with
96	the cleansing of water reservoirs and muds ^{15,16} .
97	Alfred Kelsch's overview of military data and epidemiological
98	perspective

99 Louis Félix Achille Kelsch (1841-1911) (Figure 1) was a French military doctor and 100 epidemiologist. A contemporary of Louis Pasteur, he was well aware of the microbial theory but 101 resisted the notion that microbes were the sole agents of disease, his view being that these were 102 necessary but not sufficient to cause disease and anticipating individual vulnerability and host-103 pathogen response ²⁰.

Kelsch who became a professor at Val-de-Grâce - Paris's military teaching hospital - wrote a
reference textbook on diseases in the army, with a focus on "essential jaundice" ("ictère

essentiel") ^{16,21}. In the authors' opinion, this provides one of the best and most comprehensive
views of what was later identified as leptospirosis.

With first-hand field experience in Algeria in 1878, he later built upon his own and many others' knowledge ⁵ to clinically delineate the leptospiral disease paradigm. Kelsch also noted the seasonality and the "circumscribed nature of disease" ¹⁵, thereby not ascribing outbreaks of "catarrhal jaundice" solely to seasonal factors. The following are the authors' translation of Kelsch's conclusions from French ¹³:

113 « The two jaundices are associated: Simple jaundice is reported in severe jaundice 114 epidemics, and vice versa; Sporadic cases of the latter sometimes occur during 115 epidemics of « catarrhal jaundice » ; The latter, by some attenuation of its traits, such 116 as muscle pains, prostration, epistaxis, often reminds one of the presentation of the 117 former; Severe jaundice has its benign forms, and simple jaundice is often marked by 118 severe presentations [...] ¹⁶ The [geographically] circumscribed nature of the disease 119 bears undoubtable witness to the [geographical] limitation of its cause » ²¹.

120 Kelsch concluded:

121 "1/ That sporadic or epidemic « catarrhal jaundice » is a specific, infectious
122 disease; 2/ That the infectious agent develops outside of the body; 3/ That the foci in
123 which it generates are ponds, muds, soils rich in organic matter of animal or vegetal
124 origin, and the waters in which these substances are in suspension; 4/ That, these
125 infectious foci being common to malaria and dothienenteria (typhoid), this explains
126 concurrent epidemics of jaundice and intermittent fever (malaria) or typhoid which
127 are sometimes reported » ^{21,22}.

Like L. Landouzy (1845-1917) in 1883 ^{23,24}, Adolph Weil published his detailed clinical report on what is now termed Weil's disease in 1886, considering it to be an abortive form of "typhus" perhaps due to climactic factors ¹. In his 1894 re-edition Kelsch writes:

"We do not yet know the pathogenic agent of epidemic jaundice [...]. But although
we remain ignorant of the essential cause, epidemiology enables us to at least delineate
its origin and the conditions which underlie its development [...]. In summary, the
analysis of observations published to date brings us to conclude that neither clinical
experience, etiology, nor anatomical pathology allow us to see Weil's symptomatic
complex as a single and undivided affliction by essence"²¹.

137 The pathogenic agent of leptospirosis was some years later identified thanks to work by Nobel prize-winners Inada and Ido²⁵ and Wolbach²⁶, among others²⁷. The link with rats was 138 quickly established by Ido et al. ²⁸ as well as Mikinosuke Miyajima (1872-1944) who in 1915 139 140 identified S. icterohaemorragiae in Fukuoka (Kyūshū, Japan) houses and coal mines, and rural rats, with suggested prophylactic measures ²⁹. Noguchi was the first to question and study the 141 142 survival of leptospires in various media, including soils ³⁰. We now know that infection by pathogenic leptospires is mostly pauci- or asymptomatic and can cause a very wide range of 143 144 symptoms ³¹, confirming "Weil's disease" to be only one of multiple possible presentations of 145 leptospirosis.

The role of rats and domestic animals in the epidemiology of leptospirosis is now wellestablished. Work is currently being performed, notably at the Institut Pasteur in New Caledonia,
on the diversity and persistence of *Leptospira* in soils, strongly supporting the intermediate,
telluric reservoir of leptospirosis ^{32,33}.

- 150 As suggested by Kelsch 130 years ago in a prefiguration of Hill's criteria ³⁴ and supported by
- 151 our current knowledge on host-pathogen interactions in leptospirosis ³⁵, the role of contaminated
- soils and muds as intermediate reservoir deserves to be further explored and better understood.

- 153 Figure 1: L.F.A. Kelsch (source: U.S. National Library of Medicine Digital Collections
- 154 available at https://collections.nlm.nih.gov/catalog/nlm:nlmuid-101420156-img)





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