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► **To cite this version:**

D. Sereno. Leishmania (Mundinia) spp.: from description to emergence as new human and animal Leishmania pathogens. *New Microbes and New Infections*, 2019, 30, pp.100540 -. 10.1016/j.nmni.2019.100540 . hal-03484389

HAL Id: hal-03484389

<https://hal.science/hal-03484389>

Submitted on 20 Dec 2021

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Historical note

Leishmania (Mundinia) spp.: from their description to their emergence as new human and animal *Leishmania* pathogens

Running title: History of *Leishmania (Mundinia) spp.* identification

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2

3 **Abstract**

4

5 During the last 20 years, *Leishmania (Mundinia)* spp. have emerged as new causative
6 agents of human and animal leishmaniasis. We provide a historical view of these
7 parasites, from their initial description to their emergence as pathogens, to help
8 avoiding future confusion in species assignment of these newly emerging pathogens.

9

10

11 More than one billion people are at risk of contracting visceral (VL) or cutaneous
12 (CL) leishmaniasis. Visceral leishmaniasis causes 20,000 to 30,000 deaths annually, and
13 CL affects the quality of life of millions, causing disability and permanent scarring after
14 healing (<http://www.who.int/leishmaniasis/en/>). The first account of human
15 leishmaniasis dates from the middle ages, but the discovery of *Leishmania* parasites as
16 causative agents only occurred in modern times. Until recently, it was thought that the
17 etiological agents responsible for leishmaniasis belonged almost exclusively to the
18 subgenus *Leishmania* in the Old and New Worlds and to the subgenus *Viannia* in the
19 New World. This view is currently challenged [1].

20 Between 1995 and 2002, human and animal CL and VL caused by noncanonical
21 *Leishmania* parasites were reported in geographically distant areas (Thailand,
22 Martinique, Switzerland, Australia, and Ghana). In Martinique, reports of cutaneous-like
23 infections date back to 1917, but the etiological agent was not formally characterized
24 until 2001 [2,3]. A draft genome of the isolate was released in 2013, and the species
25 named *L. martiniquensis* was included in the *Leishmania* subgenus [3]. In Thailand, prior
26 to the description of first autochthonous VL cases in 1999, leishmaniasis were only
27 diagnosed in travelers returning from the Middle East. In 2008 a new species is
28 suspected of being the etiological agent of VL cases in Thailand [4]. In West Africa, CL
29 cases caused by *L. major* have been documented. In Ghana, from 2002 to 2003, 8,876
30 possible CL cases were reported, and *L. major* and another *Leishmania* sp. were
31 identified [5]. Surprisingly, animal cases (horse, cow, and red kangaroo) of CL were
32 detected in North America, Europe, and Australia [6,7,8]. The enigmatic *Leishmania*
33 parasite responsible for CL in horses is genetically closed to the suspected new species
34 identified in Thailand. The name "*Leishmania siamensis*" was used at the time [7],

35 nevertheless given the lack of adherence to the international code for zoological
36 nomenclature, the name "*Leishmania siamensis*" is considered a *nomen nudum*. In 2014
37 clues emerged to incriminate *L. martiniquensis* in some CL and VL cases reported in
38 Thailand since 1999 [9]. Surprisingly, all these pathogens were genetically related to a
39 parasite previously isolated from a guinea pig in Brazil, *L. enriettii* [1,9]. In 2018, the
40 subgenus *Mundinia* was created [1]. It encompasses Leishmania species responsible for
41 human and animal diseases, previously gathered in the *L. enriettii* complex, *L.*
42 *(Mundinia) martiniquensis* previously assigned to the subgenus *Leishmania* [1], and *L.*
43 *(Mundinia) orientalis*, a newly described species responsible for CL in Thailand [1,10]. A
44 schematic timeline the *Mundinia* subgenus of characterization is given (figure 1).

45 Strikingly, the last 20 years have seen parasites of the subgenus *Mundinia*
46 emerging as new human pathogens, causing VL and CL in HIV+ and HIV- patients. These
47 parasites challenge our current knowledge of the worldwide distribution and
48 physiopathology of leishmaniases. To elucidate the underlying factors triggering the
49 worldwide emergence of *L. (Mundinia) spp.* and to address the future risks for human
50 and animal health, we have to investigate the vectors and hosts involved in the
51 transmission cycles of these pathogens.

52

53 **Acknowledgements**

54 We thank anonymous reviewers for their helpful suggestions, corrections and
55 comments on a previous draft of the manuscript.

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114 **Figure Legend**

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116 **Figure 1: Historical events leading to the identification of *L.(Mundinia)* spp. as**
117 **newly emerging *Leishmania* pathogens worldwide.** CL, cutaneous leishmaniasis; VL,
118 visceral leishmaniasis. Dashed lines refer to the absence of molecular identification of
119 the etiological agent. In Asia, members of the *Mundinia* (Shaw, Camargo and Teixeira
120 2016) subgenus are currently identified only in Thailand. In Africa, they were isolated in
121 Ghana and are referred as “Ghana strains”. In Europe the presence was reported in
122 Deutschland (Bavaria) and Switzerland. In North and South America, they have reported
123 in the United State of America (Florida), Brazil (Curitiba, Sao Polo) and Martinique
124 Island, respectively. Described species belonging to the *Mundinia* subgenus are:
125 *Leishmania (Mundinia) enriettii* (Muniz & Medina 1948), *Leishmania (Mundinia)*
126 *martiniquensis* (Desbois, Pratlong & Dedet, 2014), *Leishmania (Mundinia) orientalis*
127 (Bates & Jariyapan 2018), *Leishmania (Mundinia) macropodum* (Barratt, Kaufer & Ellis,
128 2017) plus parasites responsible for CL in Ghana ; «Ghana strain».

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