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Abstract

The article investigates the process of circulation of knowledge which occurred during the first decades of the twentieth century between the South American researchers Edmundo Escomel (Peru) and Alfredo Da Matta (Brazil) and the Europeans Alphonse Laveran (France) and Patrick Manson (England) with regard to the definition and validation of espundia as a disease specific to South America, while simultaneously the need to insert this illness into the newly created group of diseases called the "leishmaniasis" was proposed. Sharing recent concerns in considering historical research beyond the limits imposed by the Nation-state as a category that organizes narratives, it dialogs with some apologists of global and transnational history, situating this specific case within this analytical perspective.

Keywords: leishmaniasis; *espundia*; tropical medicine; circulation of knowledge; asymmetries.

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The world of medicine underwent significant development as it moved from the nineteenth into the twentieth centuries. On one hand, the microbial doctrine of Louis Pasteur and Robert Koch laid down an instrumental theoretical and methodological framework for correlating infectious diseases and specific pathogenic microorganisms, such as bacteria, fungi and protozoa. On the other hand, studies by Patrick Manson and Ronald Ross on the concepts of "vector" and "intermediate host," as well as the substantiation of "the mosquito theory" by the commission headed by Walter Reed, permitted understanding of the transmission mechanisms for diseases deemed relevant in the main medical forums at that time (Neill, 2012; Benchimol, Sá, 2005; Benchimol, 1999; Caponi, 2003).

This set of assumptions provided new ways of understanding and addressing one of the main challenges of European imperialism in the regions it dominated: the so-called "tropical diseases" – a term its inventor called "more convenient than accurate" (Manson, 1898, p.XI) because it designated a broad group of diseases that, although prevalent, were not restricted to the world's tropical areas. The concept of tropical diseases was closely linked to imperialism and guided by a sense of incongruity directed at the populations in the colonialized regions, and the term was coined to demarcate a differentiation between what was considered European and the "others" (Arnold, 1996; Stepan, 2001; Neill, 2012).

In some countries in South America, the local medical elites were attentive to these developments in European medicine, were part of this discussion, and were collaborators and explorers of important frontiers in microbiology and tropical medicine. Guiding their methods, procedures, and practices with these new assumptions, certain groups of South American physicians gained prominence by conducting prevention campaigns, developing courses and disciplines in research institutes and universities, and responding to public health problems specific to their local realities through these recent canons (Kropf, 2009; Benchimol, Sá, 2005; Benchimol, 1999; Almeida, 2011; Cueto, 1989).

These local public health problems included the leishmaniasis,¹ a group of diseases created in 1906 after the redesignation (considering the study protocols by both Pasteur and Manson) of two pathogenic manifestations which until this point had been considered absolutely distinct: cutaneous leishmaniasis (known by many names; herein we have used "Oriental sore") and visceral leishmaniasis (also known as kala-azar). The former presented as a skin disease, with a clinical course considered benign and spontaneous cure in approximately one year; the latter manifested viscerally, was clinically severe, and could cause death. It was the morphological similarity observed between the pathogenic protozoa of these two diseases that forged the identification criteria for the existence of the leishmaniasis as a group of diseases (Grove, 2014; Jogas Jr., 2017).

Starting in 1910, a group of South American and European researchers began to advocate for the need to distinguish the types of leishmaniasis found in South America as a third form of leishmaniasis. Their main argument was that the pathogenic manifestations observed in the region presented mucosal lesions, more extensive and severe clinical evolution, and did not tend to recover spontaneously, even after a prolonged period of 15 or 20 years of suffering. However, as with kala-azar and Oriental sore, the protozoa found on this continent were also not morphologically different from those identified in Africa and Asia, leading to criticism of this notion of individualization (Carini, 1911; Miranda, 1910; Splendore, 1911).

The aim of this article is to demonstrate how the transnational perspective can be useful in analyzing the production of knowledge on the leishmaniasis, indicating the intersections of research as well as the asymmetries and divisions that existed between scientists on these two continents. I consequently propose to reflect on the ways in which some authors have sought new interpretations of the processes of construction and movement of scientific knowledge in order to consequently analyze the intertwined paths that led to understanding of the concept of the "leishmaniasis" and its relations with the emergence of microbiology and tropical medicine at the beginning of the twentieth century. Finally, I plan to specifically shed light on the process of constructing the expressions of *espundia* as a specific form of leishmaniasis in South America.

The transnational perspective and studies on the circulation of knowledge

At least during the past three decades, a significant portion of historians concerned with the processes of knowledge construction have been adopting the transnational perspective in their work. No longer considering science as a product of a particular nation, these studies have come to view it as the end point of a long transnational process, proposing new insights into how processes of circulation of knowledge occurred. Through this type of analysis, many studies have demonstrated the involvement of characters located on the peripheries of scientific production in a wide variety of knowledge areas (Raj, 2007; Fan, 2004).

In line with these new studies, Kapil Raj (2007, p.10, 11) resolved to reexamine the nature of scientific knowledge constructed after contact with Europeans and South Asians between the end of the seventeenth and nineteenth centuries, looking closely at areas of contact between specialists from these different cultures in the production of new knowledge. According to Raj, the study of the construction of scientific knowledge in these areas of contact can show that an important part of what became known as European science was actually constructed elsewhere (p.11).

In order to move forward in an alternative view of the construction and globalization of scientific knowledge through a reciprocal (albeit asymmetrical) process of movement and negotiation, this author set about to demonstrate that South Asia was not a space for simple application of European knowledge, nor a vast space to collect a variety of data to be processed in the metropolis. On the contrary, states Kapil Raj (2007), this region has been an active if unequal participant in the emergence of a global order of knowledge.

Meanwhile, Deborah Neill (2012) sought to examine the scientific networks formed by a relatively small group of researchers from different European countries who were dedicated to tropical medicine and worked in colonial territories in Africa and Asia. In this author's opinion, despite the sharp disputes that existed between the European nations at that time, this group of scientists who were disciples of the still-nascent medical field shared similar research agendas, training, and a certain "European heritage" which led them to success in constructing scientific networks and their scientific authority, in developing shared and complementary work, and in creating a professional apparatus (journals, societies, and conferences) of transnational structure in which knowledge, opinions, values, and policies were often conceived and shared beyond national borders (Neill, 2012).

Despite being heavily influenced by the transnational perspective, Neill's work is still marked by a Eurocentric vision of the construction of this field of medicine. By focusing on the work of researchers from France, Germany, England, and Belgium who were dedicated to constructing and legitimizing this medical specialty, the author ignored contributions from South America, and demonstrates a certain resistance to incorporating characters and scientific institutions located in the so-called "peripheral regions." It is precisely at this point that my research seeks to enter and propose new interpretations of the relationships established between researchers from Europe and South America, in an attempt to understand the true role played by actors from the periphery within the overall panorama of constructing and legitimizing this new medical specialty.

Starting from the model proposed by Fa-ti Fan (2012) in The global turn in history of science,² I wish to examine the nature of the relationships established between researchers from these two continents in the production of studies on the leishmaniasis, paying special attention to the different places from which each character spoke, and the representations of their respective institutions within a global plan of constructing, validating, and institutionalizing tropical medicine.

Before starting the next sections, I believe it is necessary to emphasize that the goal here is not to conduct an analysis along the lines proposed by Joseph Needham (1970) or demonstrate contributions made by South American (the river) to construct European/Western science (the great ocean), but rather to investigate the flows, interactions, divisions, and asymmetries that exist within an interactive yet asymmetrical process of constructing interactive knowledge between people, environments, and institutions located in different regions, without which it would be impossible or unlikely to define not only specifically *espundia* but other diseases considered tropical, as well as a deeper analysis of tropical medicine as a distinct medical specialty.

New channels and circuits of information: tropical medicine and the production of knowledge on the leishmaniasis

As mentioned, the category of "leishmaniasis" was created in the early twentieth century with the primary goal of encompassing two absolutely distinct diseases (cutaneous leishmaniasis, referred to here as Oriental sore, and visceral leishmaniasis) which were identified by their morphologically identical pathogenic protozoa. The purpose of this theme is to analyze the construction of this category and demonstrate its overlaps with the emergence of the fields of microbiology and tropical medicine between the end of the nineteenth century and the beginning of the twentieth century.

Before 1906, the year that leishmaniasis was created as a categorical designation, cutaneous leishmaniasis was already well known to European travelers under a series of regional names associated with the nature of its clinical evolution and/or its geographical distribution, such as "year-long sore," "Aleppo boil," and "Calcutta ulcer." These skin manifestations were considered the most common souvenir for those who ventured into the tropical regions of Africa and Asia during the eighteenth and nineteenth centuries, and their transmission was

associated with weather conditions or the poor quality of drinking water in certain regions (Killick-Kendrick, 2010; Manson, 1898).

According to the French physician Alphonse Laveran (1917, p.I),³ even though the skin ulcers were initially and "summarily" described in 1756 as "mal of Aleppo" by Alexander Russell in Syria, it was only after 1844 (as a result of epidemics during the French army's campaigns to conquer southern Algeria) that these manifestations came to be seen as a real problem from the point of view of the occupation of colonial territory, and began to be studied by European researchers.

Meanwhile, visceral leishmaniasis, which was also known as black fever, was characterized as "a ill-defined and very deadly disease prevalent of late years in Assam" (Manson, 1898, p.191), the part of India in which this disease was first described in 1882. And according to Laveran (1917, p.I), these manifestations were understood "by most authors" as a serious "form of paludisme (malaria)," which for quite some time had been restricted to the mountainous regions of that country. Its high mortality rates among natives and Europeans led to studies both locally in India and in Europe by physicians associated with the British empire.

Starting in the last quarter of the nineteenth century, in a move associated with the emergence and spread of microbiological principles, the tropical regions became an attractive destination for many young European physicians; these so-called "microbe hunters" saw in these locations the possibility to conduct original research which could not be done in their countries of origin in order to advance Western science. Furthermore, with the growth in European imperialism during the late eighteenth century and particularly in the early nineteenth century, the intensity and apparatus necessary for the success of these projects had been gradually increasing, encouraging greater contact between the colonized and the colonizers and transforming the characteristic diseases of these regions into the main threat to European intentions (Arnold, 1996; Worboys, 1996; Caponi, 2003).

It is against this backdrop that the Scottish physician Patrick Manson,⁴ considered the father of modern tropical medicine, returned to England after more than twenty years working in British holdings in the East. From that time onward, Manson made a deliberate effort to convince the English authorities of the need for specific education for those who would work in tropical regions. With the support of the Secretary of State for the Colonies at that time, Joseph Chamberlain, Patrick Manson was appointed medical officer to the colonial service in 1897, and received the support necessary to establish the instruction program he had wanted (Wilkinson, Power, 1998).

In 1898, he published the first edition of *Tropical diseases: a manual of the diseases of warm climates* (Manson, 1898), which would become the great guide to tropical medicine and be reprinted a number of times in the early twentieth century. The following year, Manson attained his objective with the British authorities with the founding of the London School of Tropical Diseases, which he led, and the Liverpool School of Tropical Diseases, which was controlled by the ascendant bourgeoisie of that port city, which was primarily concerned with the obstacles caused by the tropical diseases extant in the regions with whom they maintained commercial relations (Wilkison, Power, 1998).

Even in the first edition of his manual, Patrick Manson included Oriental sore and visceral leishmaniasis in a number of areas, considering these diseases real problems affecting

European life in the territories. According to Manson, even during a visit of only a few days to Baghdad, it was virtually impossible to avoid cutaneous leishmaniasis, while between 40 and 70% of the population residing in Delhi had already contracted skin ulcers. Manson linked Oriental sore with health and hygiene conditions, and believed that sanitary improvements significantly reduced chances of contamination; even though he stated that it was not possible to detect the susceptible population, he postulated that these ulcers were more prevalent at the beginning of the cold season in tropical countries, while they were more common at the end of winter and the beginning of summer in temperate climates (Manson, 1898, p.443).

As for visceral leishmaniasis, which at this time was considered specific to India, there was still debate about its possible relationship with malaria, since these two diseases shared endemic areas and chronic symptoms. Many autopsies of individuals diagnosed with visceral leishmaniasis also found the plasmodium parasite, the pathogenic agent of malaria. Because knowledge on visceral leishmaniasis was still in its infancy, Manson (1898, p.193) only published a brief note in this edition and concluded with the following statement: "It is evident that much clinical, etiological, and pathological work has yet to be devoted to the study of kala-azar before its true nature can be definitely affirmed."

After the foundation of the first two British schools and the publication of the first edition of *Tropical diseases* (Manson, 1898), the precepts of tropical medicine spread rapidly through the propagation of similar institutions in Europe and in other regions. Between 1900 and 1906, institutions along these lines were created in Germany, USA, France, Belgium, Sudan, and Brazil. In France, besides the Institut de Médecine Coloniale, the Société de Pathologie Exotique was founded in 1901 in Paris as a special section of the Institut Pasteur, and the *Bulletin de la Société de Pathologie Exotique (BSPE)* was founded in 1908. This society, which was directed by Alphonse Laveran and the zoologist Félix Mesnil, focused its concerns on the relationships established between protozoology, microbiology, and medical entomology, and also according to Caponi (2003), its creation reflected growing interest in tropical diseases which would occupy "increasing spaces" in Pasteurian concerns, especially in the work of researchers within the new institutes founded in non-European regions (Stepan, 2001; Worboys, 1996).

In 1903, amid the torrent of discoveries of new pathogenic microorganisms which characterized the early twentieth century (and which was the fruit of work carried out by the microbe hunters), the protozoans responsible for visceral leishmaniasis and Oriental sore were identified in completely different processes. The physicians William Leishman (1903)⁵ and Charles Donovan (1903),⁶ who were working in British possessions in India, published different and complementary articles in the *British Medical Journal* stating that they had found the microorganism that caused visceral leishmaniasis. That same year, this discovery was confirmed by Laveran and Mesnil, who proposed honoring the English duo by naming the protozoan responsible for this disease *Leishmania-Donovani*.

Meanwhile, the American physician James Homer Wright⁷, working in Boston, treated a girl who had recently immigrated from Armenia who presented a 12mm lesion on the left side of her face, which he diagnosed as an Aleppo boil. After conducting laboratory tests, Wright (1903) found a parasite that he considered the pathogen and dubbed it *Helcosoma*

tropicum. It is interesting to note that until this time, these diseases were still considered fully differentiated, i.e., no relation of identity was maintained.

It was only in the following year, 1904, that a connection began to be seen between these two diseases. Initially, Leishman himself published a new article in the same journal that had reported his findings the previous year, affirming that the microorganism he and Donovan had seen was similar to that identified by Wright with regard to Aleppo boil, but that the exact relationship between these two diseases still remained uncertain. The victor among the many proposals which emerged during the following years to designate and classify these protozoa came from German researcher Max Luhe, who proposed redesignating the pathogen for Oriental sore as *Leishmania tropica* in 1906, thus creating the group of diseases known as "the leishmaniasis." Also in 1908, the French researcher Charles Nicolle who directed the Institut Pasteur in Paris found that the different phases of *L. tropica* were all very similar to those of *L. donovani*, lending more strength to the idea of a group of diseases which, despite their different manifestations, had morphologically identical protozoic pathogens (Grove, 2014, p.156, 157).

From that time onward, the leishmaniasis became an important subject of research for practitioners of tropical medicine. After all, how could morphologically identical protozoa could cause absolutely distinct diseases? The main suspicions fell on potentially different biological cycles within the intermediate host. But, in fact, was there even an intermediate host? And if so, was it a fly, mosquito, gecko, or bedbug? And what about the different environments and climates in which these diseases were found? Did they have any connection to the different manifestations? These were some of the major issues that guided research on leishmaniasis at this time.

In South America, the researchers Adolpho Lindenberg⁸ (of the Instituto Bacteriológico de São Paulo) and Antonio Carini⁹ and Ulysses Paranhos¹⁰ (at the Instituto Pasteur in the same state) nearly simultaneously identified protozoa of the genus *Leishmania* in skin ulcers and other mucous membranes (in the mouth and nose) for the first time in Brazil and in South America, in laborers constructing the Northwest Brazil Railroad (Estrada de Ferro Noroeste do Brasil) in the rural area surrounding the city of Bauru in São Paulo (Lindenberg, 1909a, 1909b; Carini Paranhos, 1909a, 1909b). The so-called "Bauru ulcers" caused an epidemic so extensive that beds in the city's Santa Casa hospitals were filled, hindering progress on construction of the railroad. Initially understood as "anomalous," these pathogenic manifestations in the mucosal regions would soon gain enormous prominence in the research agendas of South American doctors, and this area became the hub for more dynamic studies on this group of diseases and promoted intensive scientific collaborations with European research centers.

As we shall see in the next section, from 1910 onward the search for some means to differentiate the protozoa in the Americas (and its anomalous manifestations) from the other leishmaniasis, as well as attempts to understand its transmission mechanisms, led to intersections in research between scientists from both continents and also divisions in the formation of selective transnational networks directed at understanding this group of diseases, or in the words of Laveran (1917, p.284) "a great confusion."

American tropics, protozoa, and leishmaniasis: a great confusion

After the publications by Antonio Carini and Ulisses Paranhos (1909a, 1909b) and Adolpho Lindenberg (1909a, 1909b) mentioned above, research on leishmaniasis gained considerable ground in South America. Mucosal lesions, which previously had been considered anomalous, became an important topic of research and allowed this disease to be diagnosed in different regions of South America (Rabello, 1925). The physician Bueno de Miranda (1910) from São Paulo seems to have been the first to draw attention to this type of manifestation found in that state. In a session at the Sociedade Paulista de Medicina e Cirurgia (the Society of Medicine and Surgery of São Paulo) in 1910, Miranda argued that these manifestations differed from cutaneous leishmaniasis and consequently demanded further investigation.

And the Italian physician Antonio Carini (1911), one of the scientists responsible for initially associating the Bauru protozoa with *L. tropica*, was also the first to write an article in *BSPE* reporting the existence of these ulcers in the nose and mouth, with appearances and clinical evolution that differed from traditional manifestations of Oriental sore in São Paulo. In this article, he stated that these manifestations were not rare in that state, and that although he had not found it, he continued to suspect that there was a specific protozoan responsible for this type of leishmaniasis (p.289).

Affonso Splendore (1911, 1912),¹¹ an Italian physician who worked in the bacteriological laboratory at the São Joaquim Hospital, also in the state of São Paulo, published articles in *BSPE* and *Archiv für Schiffs- und Tropen-Hygiene* describing three cases of this "new" form of the disease and naming them for the first time as "American leishmaniasis," believing that these manifestations were limited to the Americas.

Gaspar Vianna (1911), 12 a young doctor from Pará who at that time had just been hired to work at the Oswaldo Cruz Institute (Instituto Oswaldo Cruz, IOC), published a preliminary note in the journal *Brasil Médico* in 1911, in which he claimed to have identified protozoa which were "oval shaped," with a "nucleus located slightly above the median," that he deemed to belong to the genus *Leishmania*. However, the presence of a filament, "perhaps a rudimentary flagellum, not previously observed," "clearly" indicated that this was a new species of protozoan belonging to this genus. Vianna proposed naming it *L. braziliensis* and concluded his note by claiming to be "waiting for further studies for its detailed morphological and biological description" (p.411).

But this new species of *Leishmania* proposed by Vianna was received with great caution in the main medical forums at that time, both domestic and abroad. At the beginning of the 1910s, many researchers interested in investigating leishmaniasis suspected the existence of a distinct protozoan from South America. However, the distinction proposed by Gaspar Vianna did not win complete support for this differentiation. The main reason that led doctors and researchers to defend the idea was found in the disease (or rather, in the different clinical courses), not in the pathogens, which were morphologically considered identical (Jogas Jr., 2017).

It is also interesting to note that even though Gaspar Vianna was already part of the IOC, his work was not published this institution's journal (*Memórias do Instituto Oswaldo Cruz*) but rather in *Brasil Médico*, and even then as a preliminary note. It is not clear

why he did not publish in the journal of the institution he had just joined, but there is some evidence that Carlos Chagas did not agree with the idea that there was a particular protozoan in South America, and Oswaldo Cruz never commented on the issue. The first publication in Manguinhos journal would only come in 1914, with the article "Parasitism of the smooth muscle cell by Leishmania braziliensis" ("Parasitismo da célula muscular lisa pela Leishmania braziliensis") (Vianna, 1914).

Edmundo Escomel,¹⁴ a Peruvian physician who had returned to his country after a period of exchange at the Institut Pasteur in Paris, published an article titled "La espundia" in *BSPE* in 1911. In it, he reported observing several cases of a chronic disease characterized by granulous ulcers lasting several years, in the region of the Peruvian Amazon on the banks of the Madre de Dios River and in Sabaya and Sandia; this disease was popularly known as *espundia* and found especially near areas of forests "with lush vegetation, warm temperature, and great moisture" (Escomel, 1911, p.489, 490).

Even though he tried to identify it with known human and animal diseases in Peru, Escomel (1911, p.492) came to the conclusion that the differences between these and *espundia* were too great. He then described it as "a chronic, granular disease which exists within the forests of Peru and Bolivia, and probably other countries in South America," transmitted by an "insect without wings," whose pathogenic agent and treatment were still unknown, leaving these issues open for definition in subsequent works.

The following year, the researchers Alphonse Laveran and Louis Nattan-Larrier from the Sociéte de Pathologie Exotique published two articles in the journal of this institution suggesting "contributions" to the study of *espundia*. The first article from March of 1912 reported having received a piece of mucosa from the hard palate of a Peruvian patient (sent by Escomel) who had lived with *espundia* for 15 years, and claimed to have located protozoa of the genus *Leishmania* "greatly analogous to *L. tropica*, but demonstrating a peculiarity that seemed interesting to us" (Laveran, Nattan-Larrier, 1912b, p.177).

According to these scientists, despite the morphological similarity between these protozoa, the microorganisms which were found in the material sent by Escomel exhibited slightly different behavior and dimensions (Laveran, Nattan-Larrier, 1912b, p.177). However, in the conclusion of this article they modestly stated that "the observations reported in this note that tend to show that *espundia*, as it has been well-described by our colleague Dr. Escomel, has *Leishmania* as an agent, like yaws which was studied by Bueno de Miranda, Splendore and Carini" (p.179).

Four months later, Laveran and Nattan-Larrier published their second "contribution" to the studies on *espundia*. This time, they analyzed new materials sent by Escomel and described him for the first time as a corresponding participant in this scientific partnership; in the first paragraph, they announced that the protozoa found in the Peruvian tissue differed slightly from *L. tropica* and *L. donovani* because it varied from the known leishmaniasis in both its dimensions and behavior in culture. But in the final section, they reported that Charles Wenyon, an English researcher and professor at the Liverpool School of Tropical Medicine, had found the same alleged differential sign of South American leishmaniasis in protozoa from Oriental sore in Baghdad, and consequently discredited the alleged particularities of the American protozoan (Laveran, Nattan-Larrier, 1912a, p.489).

Consequently, Laveran and Nattan-Larrier (1912a, p.488, 489) pondered:

The study of *Leishmania americana* is too recent to allow us to draw conclusions about the morphological differences between this *Leishmania* and *L. tropica*, but the differences that exist from a clinical point of view between this leishmaniasis (yaws or *espundia*) and Oriental sore are undeniably evident; so even if we cannot observe any appreciable morphological difference between *Leishmania americana* and *L. tropica*, it is necessary to distinguish these parasites in the same way that *L. donovani* is distinguished from *L. tropica*, even though these two leishmaniasis are very similar from a morphological point of view.

Even with ongoing research invalidating the differentiating features of the American protozoan, the French researchers continued to defend the distinction between these leishmaniasis because of their different clinical characteristics. In the paragraph cited above, it is interesting to note that the same argument used to differentiate *L. donovani* from *L. tropica* was extrapolated to *L. americana*; in other words, its individualization was defended because of its different clinical characteristics and evolution. Finally, the researchers from the Société de Pathologie Exotique suggested abandoning the old names and designating the disease and the protozoan found in South America American leishmaniasis and *Leishmania tropica* var. *americana*, respectively (Laveran, Nattan-Larrier, 1912a, p.489).

Lizardo Velez Lopes (1913), another Peruvian doctor who was studying a pathogenic manifestation commonly known as *uta* in that country, published an article in the *Crónica Médica de Lima* reporting that he had found corpuscles of *Leishmania* in the tissue samples he analyzed; believing it to be a distinct species, he proposed naming it *L. peruviana*. However, despite having sent an article to the same French journal in which his fellow Peruvian published his research on *espundia*, his arguments and conclusions were not even published.

His work was reviewed by Laveran (1913, p.545), in the section devoted to correspondence, as follows:

In a letter from Trujillo (Peru) dated July 25, 1913, Dr. Velez announced that he had found *Leishmania* within an ulcerous disease which is known in Peru as *uta*. This disease, which is quite common in man, within certain areas of the Peruvian Andes has been confused with lupus tuberculosis. The short description that the author gives of the parasitic elements found within the serum from ulcers in *uta* patients is sufficient to demonstrate that this is indeed a leishmaniasis; *Leishmania* of *uta*, which Dr. Velez has proposed naming *L. peruviana*, differentiating it from *L. tropica* and *L. americana*, this is a very difficult issue to resolve and will require further studies. *A priori*, it is most likely that *uta* and *espundia* correspond to only one disease.

This was the only space in this issue of *BSPE* dedicated to the work submitted by Velez Lopes; his arguments were not presented, and his results were immediately challenged and discounted by the president of the scientific society.

The trajectory of Velez Lopes's idea is a good example of the division that exists amid processes of circulation of knowledge, as discussed by Fa-ti Fan (2012). As Fan has stated, not all things move in the same manner or through the same channels of information. Consequently, while his fellow Peruvian Escomel corresponded with and sent materials to the members

of the Société de Pathologie Exotique and published his work in *BSPE*, Velez Lopes and his ideas on *L. peruviana* did not even enter into the discussion on the leishmaniasis at that time. The reasons why these asymmetries and divisions affected the proposals of the two Peruvian researchers so differently are not easily traceable in studying the history, but we can find some evidence of possible reasons when we recall that Lizardo Velez Lopes (unlike Escomel) never studied with or had direct contact with any high-profile researchers or scientific institutions devoted to the study of tropical medicine. Therefore, I speculate that the summary disregard of his findings was associated with a possible lack of confidence in and recognition of his scientific activities. Even though Escomel also worked in the same peripheral context, he did participate in an international exchange at a research institution considered central, where he acquired the techniques and the canons of this nascent medical specialty.

In 1914, Patrick Manson (1914, p.III) released the fifth edition of *Tropical diseases*, "revised throughout and enlarged". In the introduction, the author stated that, due to "recent advances in tropical pathology, … the revision has become absolutely necessary if the manual is to continue to be of service to the student of tropical medicine" (p.V). Manson reorganized all of the contents and structure, and for the first time placed cutaneous and visceral leishmaniasis (which had been described in different groups in previous editions) as well as *espundia* (addressed for the first time in the manual) in a chapter entitled "Leishmaniasis" (p.199).

In the introduction to this chapter, Manson (1914, p.199) wrote:

Under the term 'leishmaniasis' three diseases are included, viz. kala-azar, Oriental sore, and espundia. These diseases, though clinically quite distinct and having each a definite topical and geographical distribution, are all associated with what appears to be the same organism, *Leishmania*. But though these organisms appear to be morphologically identical, it is by no means justifiable to consider that they are specifically identical. The leishmania form is common to many protozoa; it is merely a stage – an immature stage – and until the life story of the parasites of these diseases has been worked out, our judgment as to their identity or otherwise should be suspended. If it turn out to be the case that the germ causes of the various clinical forms of leishmaniasis are specifically identical, we shall have to conclude that the special pathogenic properties of theses germs have been conferred on them during their extracorporeal life, especially by passage through particular animal intermediaries. Herein lies a wide field for future investigation.

Because it is a manual used in teaching, in the propagation and understanding of the category "tropical diseases," Patrick Manson preferred caution with regard to classifying these protozoa, and even altered his manual in a meaningful way to group visceral and cutaneous leishmaniasis and *espundia* in a single chapter, stating that he preferred to withhold judgment as to their identity. However, he was clear about his tendency to believe (if the identities of the parasites were confirmed) that the intermediate hosts played a role in the process of acquiring "specific pathogenic properties."

The following year, Laveran (1915a, 1915b) published two new complementary articles in *BSPE*: "Leishmaniose américaine de la peau et des muqueuses." In the first article, he announced:

After doctors in the Americas for some time have reported the existence, in certain regions of South America, of diseases characterized by ulceration of the skin and mucous membranes, yet another great confusion reigned in the chapter of ulcerous diseases, so much so that diagnosis cannot be based solidly on knowledge of the pathogenic agent (Laveran, 1915b, p.284).

According to the president of the Société de Pathologie Exotique, one of the reasons for this current confusion was the multiple regional classifications associated with this disease. Therefore, "to escape from this chaos," it would be necessary to abandon the old names and adopt the designation of "American leishmaniasis of the skin and mucosa, abbreviated as American leishmaniasis" (Laveran, 1915b, p.284). Later in the article, Laveran conducted a broad survey of the literature which had been produced up to that point on American leishmaniasis, but warned that it was extremely brief with regard to work conducted prior to 1909 because of the confusion up to that point involving the history of ulcerous ailments in South America. He then mapped the endemic areas, clinical forms, and pathological anatomy.

In his second article in 1915, Laveran initially discussed the pathogenic agent of the American leishmaniasis. By focusing on the morphological similarity that existed between this protozoan and the *L. tropica*, Laveran stated that small differences had initially captured his and Nattan-Larrier's attention; however, the new research demonstrated that these alleged differential characteristics were neither constant nor exclusive to the leishmaniasis found in South America. The French researcher then began a broad dialog with what had been produced on the leishmaniasis protozoa and their classifications, leading him to cite (for the first time) and quickly disregard the work of the Brazilian researcher Gaspar Vianna and his proposed *L. braziliensis* (Laveran, 1915a, p.383).

According to Laveran (1915a, p.383):

In an ulcer in a patient from the state of Minas Gerais (Brazil), G. Vianna found leishmanias which after Romanowsky staining showed a red thread filament through its median section, not surpassing its membrane. Vianna proposed naming this *Leishmania*, which he considered part of a new species, *L. braziliensis*. The filament mentioned by Vianna seems to correspond to the rhizoplast which had already been noted by several other authors.

Finally, he stated his opinion about the protozoa from the American leishmaniasis:

From the morphological point of view, it is possible to state that no permanent characteristic exists to differentiate American *Leishmania* from *L. tropica*, but this does not prove that the two parasites are identical; *Leishmania donovani* has the same morphological characteristics as *L. tropica*, and furthermore there is an agreement that recognizes that two very different parasites are involved, one leading to kala-azar and the other to Oriental sore. It is also based on the pathogenic action of the parasite, on the symptoms and anatomical lesions that it generates, particularly in the nasal, oral, and pharyngeal mucousae, that we, Mr. Nattan-Larrier and I, propose not a distinct species, but another variety of *Leishmania* for Oriental sore, under the name of *L. tropica* var. *americana* (Laveran, 1915a, p.384).

It is interesting to note that, again, the argument used to defend the individualization of the American protozoan was the same used to distinguish *L. tropica* from *L. donovani*: their

different clinical conditions and evolutions. However, as with Vianna's proposal, there was no exclusive and consistent differentiating feature that supported the individualization of *L. tropica* var. *americana*, and, even so, the president of the Société de Pathologie Exotique discounted the proposal by the Brazilian researcher, claiming the credit for identifying and naming the South American parasite for himself and Nattan-Larrier.

In 1916, Escomel (1916) published a new article in *BSPE*. But this time, instead of new research on *espundia*, he suggested contributions to the study of American leishmaniasis by Laveran and Nattan-Larrier. In a short article, Escomel proposed classifying the different types of leishmaniasis which existed in South America, and particularly in his home country of Peru. Despite having called Laveran's 1915 work "the most precise guide to the study of this morbid entity," the researcher stated that "examination of many sick people who came from regions where American leishmaniasis is endemic has provided us with the opportunity to debate the existence of various clinical forms that seemed interesting to us" (Escomel, 1916, p.215). He then divided them into their cutaneous and mucosal forms and their respective variations, ulcerous, non-ulcerous, or papulo-tuberculosal, atrophied, lymphatic, and vine-like, unresolved continuity with the skin (like "Oriental sore"), and resolved continuity with the skin (similar to blastomycosis), and ultimately repeated an argument similar to Laveran's, stating that even though the American leishmaniasis protozoan was identical to that of Oriental sore, it would be at the very least necessary to consider it a variation of *L. tropica* because of their different manifestations and their clinical courses.

In this article from 1916, it is interesting to note that Escomel himself recognized and subjected himself to the asymmetrical relations that existed in the process of constructing knowledge on the leishmaniasis. In titling his article as contributions to the studies by Laveran and Nattan-Larrier, Edmundo Escomel reversed the logic and the meaning of the search. The scientist who proposed an original study on *espundia*, a disease located in his own country, instead was now just a collaborator with the French researchers, even though his participation and, above all, the information, materials, and specimens he sent were essential to permit the study.

Again referring to Fa-ti Fan's model, we can perceive although the asymmetries also affected Escomel's work and (volunteered) statements, they manifested themselves differently than they appeared with relation to Lizardo Velez Lopes, whose ideas were eliminated from the transnational circuits of tropical medicine. Escomel's work had always been and continued to be publicized by the French journal, and its editors recognized him as an important contributor, with access to clinical cases that continued to be essential in the production of this new scientific knowledge on the leishmaniasis.

Also in 1916, Alfredo Da Matta, ¹⁵ a researcher from Bahia, Brazil living in Manaus, the capital of Amazonas, published an article in *BSPE* proposing new classifications for this group of diseases, particularly those considered American. According to Da Matta (1916, p.502), there were five distinct species of leishmanias: *infantum, donovani, furunculosa, nilotic,* and *braziliensis*. The former two were related to kala-azar, which at that time did not exist in Brazil, while all the others corresponded to the cutanous, mucosal, and cutaneo-mucosal modalities observed in South America. In an article replete with illustrations, citations, and explanations, Da Matta dubbed the species responsible for Oriental sore *L. furunculosa*,

and also affirmed Laveran and Nattan-Larrier's assertion that *L. tropica* var. *americana* was nothing more than *L. braziliensis* in its cutano-mucosal manifestations, subsequently correlating each of these parasites with their respective clinical forms (p.502).

This article by Alfredo Da Matta is very important, considering the trajectory of research on the American types of leishmaniasis. Among other things, it is interesting to note that while the debate up to this point focuses on whether an American protozoan existed, Da Matta proposed the existence not of one but three pathogenic agents in South America, and presented photographs describing each of these pathogenic manifestations. Another notable point is the nomenclature Da Matta used to designate the protozoa involved with Oriental sore, *L. furunculosa*, in a nod to the nomenclature proposed by the Russian scientist Firth in 1891, *Sporozoa furunculosa* (Firth, 1891).¹⁶

It is not clear why this scientist adopted this classification, but considering that he worked in the Amazon, on the periphery from the viewpoint of where the major scientific institutions were active and had a presence but central with regard to observing the morbid processes of tropical diseases (Schweickardt, 2009), I believe that this position is a political stance by Da Matta. His goal may have been to acknowledge the Russian scientist, who like himself may be been marginalized for working in areas considered peripheral or exalted for presenting observations from places recognized as being of fundamental importance in understanding tropical diseases (Jogas Jr., 2017).

The following year, Laveran (1917) launched a book entitled *Leishmaniose: kala-azar, bouton d'orient, leishmaniose américaine*. According to this author, this book containing over five hundred pages was meant to gather the scientific knowledge produced on the leishmaniasis over the previous 14 years. After an overview of the history of this group of illnesses, the president of the Société de Pathologie Exotique devoted a chapter to each modality, the last of which was "Leishmaniose américaine de peau et muqueuses." In it, Laveran reproduced the text of his two articles from 1915, almost paragraph for paragraph; however, he did make some changes that have drawn attention for their connections with the work by Da Matta and Escomel in the previous year (Laveran, 1917).

In addition to using the photographs from Da Matta's article to illustrate the different modalities of the American leishmaniasis, Laveran also adopted the nomenclature proposed by the two South American researchers (lymphatic, atrophied, vine-like, papulo-tubercular). But the most significant change in the 1917 book was related to the pathogenic agents of the American leishmaniasis. In assigning the name *L. tropica* var. *americana*, Laveran (1917, p.494) added the following paragraph:

This opinion is not unanimous; some authors consider *Leishmania americana* to be identical to *L. tropica*; others denote a distinct species under the name *L. braziliensis*; others still admit that the American leishmaniasis could be caused both by *L. tropica* and by *L. braziliensis*.

Unlike in his articles in 1915, for the first time Laveran acknowledged the possibility that these American manifestations were caused by both *L. tropica* and *L. braziliensis*. It is interesting to note that it was only after 1916, with the work conducted by Da Matta in the Amazon, that the idea contributed by Gaspar Vianna (now deceased) gained new strength

and recognition in the transnational debate on the construction of knowledge on this group of diseases.

At the end of the 1910s, knowledge about the leishmaniasis in general, and the American variations in particular, was incomplete, much less stable. Quite to the contrary, during the 1920s and in subsequent studies on this group of illnesses, the leishmaniasis became even more complex with the refinement of studies on the leishmania protozoa. The correlation between the different species of sandflies and the transmission of the distinct manifestations of these diseases began to occupy more space in the research agenda during the years following the era portrayed in this article, and it was only in the 1960s, through complex techniques involving molecular biology, that researchers who were still concerned with the existence of features differentiating the American protozoa were able to identify a way of characterizing them.

Final considerations

This article is simultaneously an effort towards and an exercise in thinking about one part of the production of knowledge on the American leishmaniasis from a global and transnational perspective. It is clear, however, that the process of constructing knowledge described here is an emblematic case for us to consider the manner in which the circulations of knowledge, specimens, and skills occurred with regard to the asymmetries and divisions that exist amid the production of new scientific knowledge.

In this specific case, perhaps in a superficial analysis, we may be led to mistakenly think of an entirely connected world in which different experts from South America and Europe cooperated with each other, exchanging information, techniques, materials and data almost naturally in a continuous flow, with the pure objective of building a universal understanding of this group of diseases. However, in deepening our analysis and tracing the origins of the ideas and their respective proponents, we perceive subtleties that may indicate contributions, disputes, asymmetries, deletions and divisions that, after this knowledge was stabilized, do not appear as visibly as they were during the process described herein.

During the fervor of studies on the leishmaniasis, Escomel's *espundia* quickly drew the attention of Laveran, who went on to study it in the Société de Pathologie Exotique, creating research intersections and fostering interactive circuits. However, at that time the work of Gaspar Vianna and Lizardo Velez Lopes did not enjoy the same access to the main scientific journals in Europe dedicated to tropical medicine. *L. braziliensis*, which was proposed in 1911, only gained strength and projection in 1916 through Da Matta's work in the Amazon. Escomel, who initially proposed original studies on *espundia*, went on to be a mere collaborator in the studies by Laveran and Nattan-Larrier on *L. tropica* var. *americana*. And Velez's theory about the existence of *L. peruviana* would only enter the international discussion in the 1960s, when the *L.* responsible for *uta* was individualized, and in a merely memorial sense, was named *L. peruviana*.

The nationalist components included in the construction of scientific knowledge on the leishmaniasis should also be highlighted. By naming "their" leishmanias *brasiliensis* and *peruviana*, respectively, Vianna and Velez Lopes demonstrated the intentionality of associating

their research with their respective nationalities, illustrating the tensions existing within a scientific field that claimed to be universal while simultaneously seeking national prestige.

The study of the leishmaniasis played a significant role in consolidating the research institutes devoted to the practice of tropical medicine in South America, and also played a fundamental role in positioning the researchers from these institutes within the global panorama involving the creation and institutionalization of this new field of practice, research and teaching. It also permitted open and direct dialog between physicians from different continents who, by forming a network of selective and asymmetrical researchers, managed to build unified knowledge about these pathogenic manifestations of the leishmaniasis in the terms, concepts, procedures, and practices of microbiology and tropical medicine.

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NOTES

- ¹ According to the World Health Organization (WHO), the leishmaniasis are currently understood as a complex of predominantly rural antropozoonoses transmitted by a vector (sandflies), caused by 22 protozoa species in the genus *Leishmania*, with different pathogenic manifestations that affect humans and animals. They are classified as neglected tropical diseases, and are endemic to more than 98 countries and territories on four continents; approximately two million new cases are estimated to occur each year, and 350 million people live in risk areas. They are often subdivided into three types of pathogenic manifestations: visceral (the most severe form, with 90% of cases registered in Bangladesh, Brazil, Ethiopia, India, Nepal, and Sudan), cutaneous (with 90% of cases registered in Afghanistan, Saudi Arabia, Algeria, Brazil, Iran, Turkey, Syria, and Sudan) and mucocutaneous (with 90% of cases recorded in Bolivia, Brazil, and Peru). See OMS (2010).
- ² According to Fa-ti Fan (2012, p.253), because of the hazards associated with the use of the concept of "circulation," it is important to keep critical questions in mind when applying this concept to specific historical cases. For example, "What was being circulated? Considering that things do not circulate equally, it is necessary to distinguish between different things which are in circulation. What were the areas or spaces of circulation? Certain people or things could circulate in certain areas, but others could not. If this was the case, what were the boundaries of circulation, the borders that marked the areas of circulation? Who and what facilitated the circulation? What were their meanings and mechanisms? What were the barriers and obstacles? Another thing to ask is what happened to the objects of science during circulation. Did they undergo mutations, transformations, or reconfigurations?"
- ³ Charles Louis Alphonse Laveran (1845-1922) was a prominent French physician who founded the Société de Pathologie Exotique, linked to the Institut Pasteur. His achievements included identification of plasmodium as the causative agent of malaria in the 1880s and the 1907 Nobel Prize for Medicine for his work with protozoa (Charles..., n.d.).
- ⁴ Patrick Manson (1844-1922) was a Scottish physician known as the first researcher to conduct studies linking the life cycle of filaria worms to blood-sucking insects, in 1880. It was through his studies on lymphatic filariasis in English colonies in the East that Manson proposed the foundations of the field of tropical medicine and came to be considered the father of modern tropical English medicine (Sir..., s.d.).
- ⁵ William Boog Leishman (1865-1926) was a Scottish physician trained at the University of Glasgow. He was the director of the Royal Army Medical Corps, which took him to India, where he conducted his first works on the causal agent of visceral leishmaniasis. In 1897, he returned to England to work at the Netley Hospital, where he continued to conduct research on this disease. In 1903, he published the first article about the alleged causal agent of visceral leishmaniasis. However, he was unable to reach a consensus on the taxonomic classification of the microorganism he found (Colonel..., s.d.).
- ⁶ Charles Donovan (1863-1951) was an Irish doctor who worked in the Indian Medical Service. During his time in India, he conducted work on the etiological agent responsible for visceral leishmaniasis, independent

of Leishman's studies. His conclusions proved that the disease involved a specific protozoan parasite, and also put an end to discussions of its relationship with plasmodia, the causative agent of malaria (Dutta, 2008).

⁷ James Homer Wright (1869-1928) was an American doctor from Baltimore who worked at Massachusetts General Hospital in Boston from 1893 until his death in 1928. In 1896, at only 27 years old, he assumed leadership of the newly-founded laboratory of pathology at this hospital. In 1903, he described the protozoan responsible for Oriental sore as *Helcosoma tropicum*, upon examining an Armenian girl who had just immigrated to the USA (Lee, Young, Castleman, 2002).

⁸ The physician Adolpho Carlos Lindenberg (1872-1944) was born in Rio de Janeiro and trained in dermatology in Europe (in Berlin, Vienna and Paris). When he returned to Brazil he moved to São Paulo, where he helped found the Department of Dermatology at Santa Casa and the Faculdade de Medicina de São Paulo. He was responsible (along with Antonio Carini and Ulysses Paranhos) for first identifying the leishmaniasis parasite in South America (Proença, n.d.).

⁹ Antonio Carini (1872-1950) was an Italian physician invited by the São Paulo government to assume leadership of the Instituto Pasteur of São Paulo in 1906. He conducted studies in the areas of microbiology and parasitology of animal and plant diseases. Together with Ulysses Paranhos, he was responsible for identifying protozoa of the genus *Leishmania* for the first time in South American, in the city of Bauru, São Paulo, at the same time as the work conducted by Adolpho Lindemberg at the Instituto Bacteriológico de São Paulo (Teixeira, 1995).

¹⁰ Ulysses Paranhos (1885-1931) was a doctor from São Paulo trained at the Faculdade de Medicina da Bahia who helped found the Instituto Pasteur of São Paulo, and also served as the secretary of the Sociedade de Medicina e Cirurgia de São Paulo (the Society of Medicine and Surgery of São Paulo). Together with Antonio Carini, he was one of several physicians responsible identifying the so-called Bauru ulcers with the genus *Leishmania* during construction of the Northwest Brazilian Railroad (Teixeira, 1995).

¹¹ Affonso Splendore (1871-1853) was an Italian physician trained at the University of Rome. In 1899 he traveled to Brazil, where he settled in the city of São Paulo. He conducted research along with Adolpho Lutz at the Instituto Bacteriológico de São Paulo. He is considered the first researcher to visualize the causal agent of toxoplasmosis. He was also the first researcher to propose designating the pathogenic manifestations of leishmaniasis found in South America as American (Meira, s.d.).

¹² Gaspar Vianna (1885-1914) was a researcher from Pará who, during his training at the Faculdade de Medicina do Rio de Janeiro (FMRJ), had been close to professor Eduardo Chapot-Prévost, the chair of microbiology. With the departure of the researcher Henrique de Rocha Lima from the IOC to further his studies in Germany and promotion of Carlos Chagas to head of the department of this institute, Oswaldo Cruz searched for a new histologist for Manguinhos to fill the subsequent gap. Most likely on the recommendation of the department head at FMRJ, the director of IOC personally invited Vianna to be part of that institute and devote himself to studies related to the parasite involved in the new illness, Chagas disease (Gaspar..., s.d.).

¹³ In this and other quotes from texts published in other languages, a free translation has been provided.

¹⁴ Edmundo Escomel (1880-1959) was a Peruvian doctor born in the city of Arequipa who graduated from the Universidad Nacional de San Agustín in 1902. After graduation, he traveled to France to conduct research at the Institut Pasteur. He edited the *Crónica Médica* of Lima and the *Revista de Bacteriologia e Higiene* of La Paz, and was also a corresponding member of several foreign societies and medical journals (Naquiravelarde, 2006).

¹⁵ Alfredo Augusto Da Matta (1870-1954) was a doctor from Bahia who graduated from the Faculdade de Medicina da Bahia in 1893. After graduation he moved to Manaus, the capital of Amazonas, where he conducted scientific research for fifty years. He was the founder of the Sociedade de Cirurgia e Medicina do Amazonas (The Amazonas Society for Surgery and Medicine) and was head editor of *Amazonas Médico* (Schweickardt, 2009).

¹⁶ Before James Wright described the protozoan responsible for Oriental sore, the Russian scientist H.R. Firth (1891) had published a description of this parasite and called it *Sporozoa furunculosa*. However, his arguments were not strong enough for him to be recognized as the first scientist to describe this microorganism.

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