

Bacteria or parasite? The controversy over the etiology of sleeping sickness and the Portuguese participation, 1898-1904*

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Abstract

The etiology of sleeping sickness was unknown until the early twentieth century. This African disease soon became the main obstacle to European colonization. Sending scientific missions to the colonies to monitor its progression *in loco* thus became inevitable. Portugal sent the first research mission to Angola in 1901, and the Royal Society of London sponsored two British missions to study the disease in Entebbe (1902 and 1903). Their results led to a controversy in which Portugal was involved from 1898 to 1904, on the national and international circuits, analysed in this article.

Keywords: tropical medicine; sleeping sickness (trypanosomiasis); Annibal Bettencourt (1868-1930); Charles Lepierre (1867-1945); Aldo Castellani (1877-1971).

At the end of the nineteenth century, there were two trends which marked the progress of a number of European countries on the imperialist scene: the scramble for Africa, in the sense of colonialist expansion, and specialization in the biological sciences, in which tropical medicine became one of the beneficiaries. The interest shown by governments and the scientific community in sleeping sickness was directly connected with the high epidemiological levels recorded between 1894 and 1910, particularly in Africa, and the lack of scientific and medical preparation to confront the disease. In the program of colonization, African human trypanosomiasis therefore took on an important role with the international medical community.

With the founding of the first research and teaching centers specializing in tropical medicine in England, France, Germany, the United States and Portugal, tropical medicine became part of a transnational and interdisciplinary effort seeking to establish a new concept of disease (Worboys, 1976), specifically of tropical diseases (Arnold, 1996). The etiology of these diseases was therefore a burning question in this new area of study. The classical view of microbiology, which had governed European and American programs for the study of germs since 1890, was beginning to show signs of inadequacy in explaining the specific features identified in tropical diseases. Sleeping sickness represented a disquieting threat to the permanence of Europeans in Africa, because it killed a large number of people, thereby damaging the colonial policies of various European powers. For this reason it was one of the most widely studied tropical diseases in Europe (Bradley, 1980). Given the importance of such a typically African disease, medical missions were sent to African colonies by various countries, with the aim of identifying the agent responsible for the disease. The difficulty in determining this was the cause of a controversy between 1898 and 1904, which involved specialists of various nationalities, including Portuguese.

The Portuguese government, through the Ministry for the Navy and Foreign Affairs, sent the first mission for studying sleeping sickness to Angola, the jewel in the imperial crown, in 1901, charging it with the task of studying the disease in this province, together with the etiology and transmission of malaria (Comissão..., 1901, p.496). The mission comprised the most eminent researchers in the fields of microbiology and tropical medicine: Annibal Bettencourt, director of the Real Instituto Bacteriológico Câmara Pestana (Royal Câmara Pestana Institute of Bacteriology)¹, head of mission: Annibal Celestino Correia Mendes (1870-?), doctor on the Angola health staff; Ayres Kopke (1866-1947), naval doctor, director of the microbiology laboratory at the Navy Hospital; José Gomes de Rezende Junior (1871-1905), an army doctor from the Câmara Pestana Institute of Bacteriology, and João Brás de Gouveia (1865-?), laboratory assistant at the same institute. In turn, the Royal Society of London (RSL) gave its support to the sending of the first British mission for the study of sleeping sickness to Entebbe (Uganda) in 1902. On the recommendation of Patrick Manson (1844-1922), two of his students were included in the mission, George Carmichel Low (1872-1952), head of mission, and Aldo Castellani, and also Cuthbert Christy (1864-1932), an army doctor with the West African Field Force, with medical experience in tropical regions. The second mission arrived in Entebbe in 1903, and included David Nunes Nabarro (1874-1958) as substitute for Low, David Bruce (1855-1931) as substitute for Christy, and Castellani, who would remain there for some time thereafter.

The scientific argument which would bring the researchers from the Portuguese and British missions into opposition centered on the interface between bacteriological and parasitological theory. The former was based on Pasteurian assumptions with regard to the concept of disease; the latter arose from the realms of natural history. Bacteria or parasite; this became the fundamental question in the controversy.

In England, the controversy started at a time when tropical medicine based on laboratory investigation was being consolidated under the leadership of Patrick Manson, a distinguished figure from the School of Tropical Medicine in London, who enjoyed the direct support of Joseph Chamberlain (1836-1914), secretary of state for the colonies, and of the RSL, of which he was a member. In Portugal, the controversy had its beginning at a time in which tropical medicine still did not exist as an institutionalized scientific field, and bacteriology represented, *par excellence*, the area of support for experimental medicine.

The debate was carried on at two levels, national and international, and in two phases. Besides the dispute between Portuguese and British doctors, there were internal arguments in both countries. As far as the phases of the debate were concerned, the first centered on the identification of a bacteria, which was supposedly responsible for the disease; the second on the identification of a parasite and its relationship with the cause of the illness.

At the internal level, in Portugal, during the first phase of the controversy, the debate began with regard to a bacterium which was supposed to be the cause of the disease, and pitted Annibal Bettencourt against António Pádua and Charles Lepierre (1901-1903). The dispute then moved to the external plane, involving Annibal Bettencourt and Aldo Castellani (1902-1903), both of them proposing bacteria as the cause, the argument being about who was the discoverer. In the United Kingdom, Castellani disputed with David Bruce (1903-1904). For the latter, the cause of sleeping sickness was a parasite. This dispute was reflected in Portugal, opposing Annibal Bettencourt against Correia Mendes and Ayres Kopke (1904), the latter two adopting the same position as that of Castellani-Bruce.

During the first phase of the controversy, between 1902 and 1904, at the national level, the discussion produced differing concepts of rigor in scientific investigation and involved a strategy for disclosing results to the international scientific community, so as to demonstrate and confirm the scientific authority of the Portuguese doctors, on the basis of work known since 1898. Among the protagonists in the debate were Bettencourt and his team, from the Câmara Pestana Institute of Bacteriology, and Cagigal and Lepierre, from the Microbiology Laboratory of the University of Coimbra, which are laboratories, as we shall see, with very different resources and public visibility. In 1903, at the international level, an argument broke out between the members of the first two missions to study the disease, organized by Portugal and Great Britain respectively, the first led by Annibal Bettencourt, and the second by Aldo Castellani, who disputed being the discoverer of the bacteria, a meningococcal infection having been initially identified as the causal agent of the disease. After the identification of trypanosomes in patients, carriers of the disease, by Castellani in 1903, the debate entered a second phase, both in England and in Portugal. It was now a question of establishing the relationship between trypanosomes and the etiology of the disease. In Great Britain, debate continued between the protagonists of the first

and second missions to study the disease, David Bruce being opposed to Aldo Castellani, and the outcome of this dispute would put an end to the controversy surrounding the causal agent of the disease.

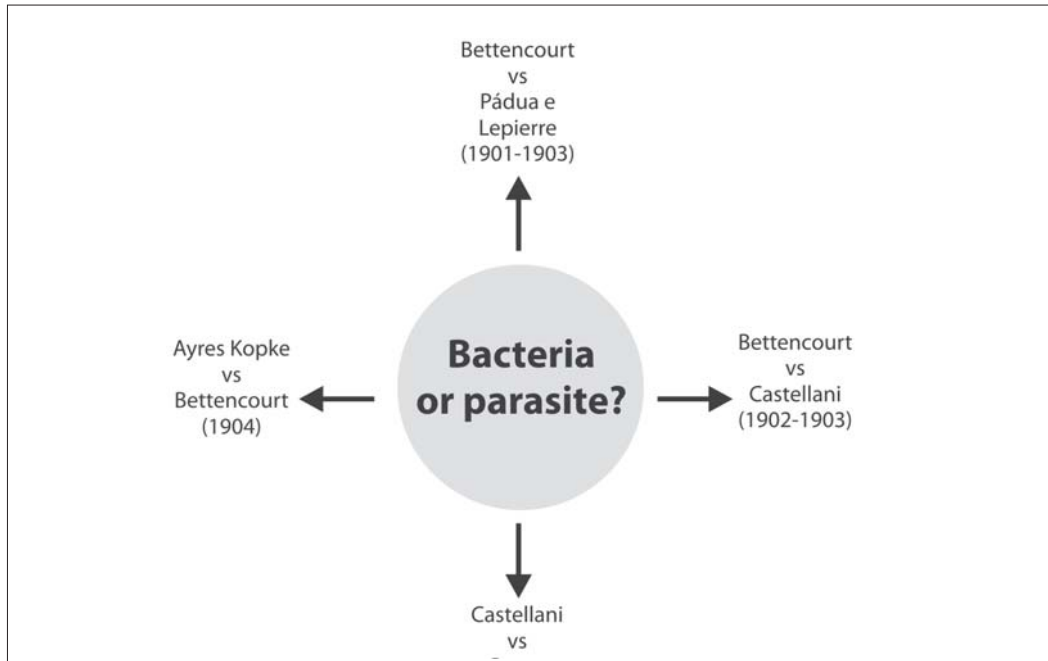


Figure 1: Diagrammatic representation of the core of the bacteria-parasite controversy in sleeping sickness (1901-1904) (Diagram prepared by the author)

In Portugal, a disagreement arose between Annibal Bettencourt, who continued to defend the same position, and Ayres Kopke and Correia Mendes, who considered that sleeping sickness was in fact caused by a parasite, identified by them in the blood and in the cephalorrhachidian fluid of patients in the Colonial Hospital of Lisbon. The disagreement between the members of the 1901 mission was related to the fact that, at the time, they had not succeeded in breaking away from the bacteriological paradigm then being developed at the Câmara Pestana Institute of Bacteriology, with the result that, after 1902, with the institutionalization of tropical medicine and the foundation of the School of Tropical Medicine in Lisbon, where Ayres Kopke and Correia Mendes worked, the acceptance of the parasitological theory did not offer any resistance. From 1904, both sides moved in the direction of the English theories and arrived at a position of support for Castellani and Bruce.

The mission to study sleeping sickness: the doctors of Lisbon

Sleeping sickness, today known as African human trypanosomiasis, is caused by a protozoan parasite of the genus *Trypanosoma*, which is transmitted by the bite of an insect, the tsetse fly (genus *Glossina*), which is the carrier. The disease follows three stages,

which coincide with the development of the parasite: the first stage, when the parasites invade the blood flow and the lymphatic system, characterized by the appearance of cervical ganglia, a feverish condition and drowsiness; the second, when the parasites lodge themselves in the central nervous system and multiply, causing greater lethargy; and the third stage, when inflammation of the cerebral meninges occurs, leading to coma and death.



Figures 2 and 3: Photographs of patients observed by Ayres Kopke in the first and second phases of the disease (Source: Kopke, s.d.)

In 1902, when the controversy began over the etiology of this disease, it was simply thought that it was a case of a contagious disease, given the high rate of incidence among Africans. The positions of the participants in this debate were obviously a reflection of their scientific training and their authority inside and outside the medical community, and were based on a variety of motives, which were not only of a scientific nature, but also political. All those who took part, for one reason or another, longed to play a leading part in the history of the etiology of tropical diseases, on the knowledge of which depended their control and the success of European colonization in Africa.

The mission, supported by the Portuguese government, had access to resources which were unthinkable in other circumstances, in view of the economic constraints which were discussed in the country at the time. The government supplied practically everything which the mission demanded for the success of its work, to judge by the manner in which its members addressed the naval minister (Relatórios..., 1901, p.5):

The manner in which Your Excellency has liberally endowed us with the necessary means for the performance of the task entrusted to us and has accepted the results of our investigations affords us the opportunity to record at this time our gratitude to the person who has totally understood the large scope of all the measures.

In fact, a mission of this kind had obvious advantages for both parties: for the government which, against a backdrop of international competition for African territories, showed its earnestness in the effective occupation of African territory, which depended directly on controlling the advance of the disease; for the doctors, because it gave rise to wider opportunities for intervention and professional development.

The Society for Medical Sciences in Lisbon had a decisive influence on the Portuguese government, and also on the announcement of this mission (Bombarda, 1900b), in arguing for a change in colonial policy, in which medicine would play an important role, giving substance to the principles declared at the Berlin Conference: "it is necessary for Portugal to send a scientific expedition, made up of men familiarized to research, which will in our part of Africa search for a solution which will have consequences for questions of humanity and questions of interest" (Bombarda, 1900b, p.268).² To underline the relevance of Portuguese medical participation in the colonial project, the Society went even further, emphasizing the importance of medical missions as a guarantee of European colonization in Africa (Bombarda, 1900b, p.268):

Germany, England, France, Austria have increased the number of their scientific expeditions, and Africa and Asia have seen the learned men from European laboratories tear themselves away from the comforts of life to go to these far-off and sometimes barbarous locations, and in the face of dangers and inclement climates to study at close quarters some of these terrible illnesses, which are the scourge of humanity.

Against a background of imperialist rhetoric, the doctors advocated a position of scientific supremacy and moral authority, to the extent that they showed themselves ready to abandon their comforts, while possessing the means to overcome the problems for health posed by an inhospitable environment, considered to be the main obstacle to effective colonization.

With Angola as its destination, given the vital importance of this colony to the government, the mission first made a stop at the Ilha do Príncipe, staying there for 15 days, which was primarily a scientific decision. The stay was important, given the small size of the island and therefore the possibility of studying the evolution of the disease among its inhabitants from various points of view, with a greater degree of effectiveness than could be obtained in Angola.

The bulk of the mission was made up of researchers from the Câmara Pestana Institute of Bacteriology, including its leader, Annibal Bettencourt. The Institute was the result of a set of initiatives in furtherance of bacteriological investigation in Portugal, beginning with a bacteriological study of Lisbon water and of rabies, in a similar manner to what was happening in France and Germany, such studies being launched under the direct influence of the Society of Medical Sciences. In 1901 bacteriology had already been institutionalized for nine years, constituting a recognized and sufficiently prestigious area of study, which gave it power and influence in relation to other areas of medicine, such as tropical medicine for example, which would only become institutionalized in 1902. Through the Câmara Pestana Institute of Bacteriology passed the most influential figures of modern Portuguese medicine in the first half of the twentieth century, who were trained

there in Pasteurian principles and practice, before directing their own laboratories or research institutes – Câmara Pestana (1863-1899), Annibal Bettencourt, Carlos França (1877-1926), Marck Athias (1875-1946), Henrique Parreira (1895-1945), Ayres Kopke – and Ricardo Jorge (1858-1939), names which show the uniqueness and the prestige of this medical research unit on the Portuguese scene. The results obtained by it lent particular distinction to the Medical School of Lisbon, overshadowing, to some degree, the University of Coimbra – the only one in the country until 1911 – which did not possess an institute with the same infrastructure and features as those of the Câmara Pestana Institute.

Also a member of the mission was a doctor from the health staff of Angola, Annibal Correia Mendes, who was accustomed to dealing with the disease in that colony, especially at the Maria Pia Hospital in Luanda³; and Ayres Kopke, a naval doctor who since 1897 had devoted himself to laboratory research into tropical diseases in the rudimentary microbiology laboratory of the Naval School, of which he was the director. His first works on paludism (malaria) date from this time, and were referred to by Alphonse Laveran (1845-1922) in his work *Traité du paludisme* (1907). In 1902, Kopke was appointed director of the School of Tropical Medicine in Lisbon, owing to the scientific prestige he had achieved in the field. As regards sleeping sickness, he would make his name through the research of therapeutic medicine in the first stage of the disease, a task to which he devoted his entire career.

Despite the fact that it had expertise in the principles of Pasteurian bacteriology, the mission sent to Angola nevertheless showed certain heterogeneity. Laboratory medicine was still a recent achievement in Portuguese medicine. The impulse given by the prestige of the Câmara Pestana Institute of Bacteriology and the contributions of Ricardo Jorge, in the spheres of epidemiology, hygiene and public health, would only be given substance with the reform of medical teaching in the Faculties of Medicine in 1911 (Amaral, 2006). Despite being trained in bacteriology at the Institute, owing to their subsequent links with tropical medicine, Correia Mendes and Kopke would distance themselves from the position of the mission led by Bettencourt. They would give priority to research into the vectors, which was the object of teaching and research at the School of Tropical Medicine in Lisbon. This was an institution which had been modeled on the schools of tropical medicine in Liverpool and London, symbols of the recognition of tropical medicine as an autonomous discipline, at the turn of the nineteenth and twentieth centuries (Amaral, 2008).

The microbiologists of the University of Coimbra

The Department of Microbiology and Chemical Biology at the University of Coimbra, founded in 1882, was the first laboratory of its type to be created in Portugal (Lepierre, 1906), ten years before the Câmara Pestana Institute of Bacteriology. Founded by Augusto Rocha (1849-1901), a doctor and professor of microbiology at the University, it attracted a certain public recognition within the Portuguese scientific community (Pita, 2006, p.49), largely owing to the contributions of Charles Lepierre. The latter had concluded the course in chemical engineering at the School of Industrial Physics and Chemistry in Paris in 1887, where he was a student of the Portuguese chemist, based in France, Roberto Duarte

Silva (1837-1889). In 1891 Lepierre was given the job of laboratory head in Coimbra, where he remained director for twenty years. Trained in the French tradition, and very close to the microbiologists of Pasteurian tradition, Lepierre developed microbiology in Portugal by establishing a complete laboratory program for analyzing drinking water in the city and suspect produce from the municipal slaughterhouse, at the same time as he gave his support to medical microbiology, and consequently to the hospital of the University of Coimbra, particularly in the domain of medico-legal examinations. In this context he carried out the first bacteriological examination of a patient there who had come from Benguela (Angola), who was diagnosed with sleeping sickness on the basis of specific clinical symptomatology. Lepierre and António Olimpio Cagigal (1867-1933), a fifth year student in the medical course, published in 1898 (Cagigal, Lepierre, 28 jan. 1898), a work – which became a work of reference – on the possible cause of the disease, a bacteria which they had identified in bodily matter taken from that patient. These results were publicly defended in 1899 by António de Pádua (1869-1914), a professor of medicine who had graduated from the University of Coimbra and was director of the Department of Microbiology between 1902 and 1903. Pádua added to the internal debate over the results obtained by Lepierre and Cagigal in Coimbra and by the mission of the doctors from Lisbon (Pádua, Lepierre, 1904).

Although Lepierre and Pádua achieved considerable prestige at the national level in the field of bacteriology (Pereira, Pita, 1998), neither of them was chosen by the Portuguese government to form part of the first mission officially charged with studying sleeping sickness in 1901. In addition to having no influence with the Society for Medical Sciences, with its headquarters in Lisbon, their results in microbiology were not comparable to those of the Câmara Pestana Institute of Bacteriology.

The British protagonists

In the United Kingdom, the protagonists in the debate examined in this article were members of the first two missions of the RSL appointed to study sleeping sickness in Uganda. George Low, Aldo Castellani and Cuthbert Christy formed part of the first mission. The first mentioned had a knowledge of tropical medicine in its geographical, biological and pathological aspects; the second was a graduate in microbiology, and Christy, for his part, had interests in zoology and natural history. Low had studied medicine at the University of Edinburgh and had been invited by Patrick Manson, in the same year as the opening of the School of Tropical Medicine in London, to join his teaching staff. He had been sent by Manson to Heidelberg, to make a specialist study of the techniques for handling mosquitoes, thereby contributing to clarifying the importance of the life cycle of the mosquito and its relationship with malaria (Manson-Bahr, 1956, p.158-162; Cook, 2007, p.127-144). Later he devoted himself to investigating the role of arthropods as vectors of parasite-caused diseases in the tropics, particularly in the transmission of lymphatic filariasis through *Plasmodium falciparum*, the agent of malaria (Low, 1900). His future career was directed towards natural history and ornithology, ending his academic career at the Liverpool School of Medicine.

Castellani had finished the course of medicine at Florence in 1899, with a thesis on the isolation of the typhoid fever bacillus from the blood. He spent some time in the microbiology laboratory of Walther Kruse (1864-1943), at the University of Bonn, where he specialized in techniques for the identification of bacteria. He studied with Manson at the School of Tropical Medicine in London, and in 1900 was invited by him to join the teaching staff (Cook, 2007, p.197-209; Castellani, 2010). At the end of the mission to Uganda he travelled to Ceylon, returned to England, but ended his career in Lisbon, at the Institute of Tropical Medicine.

Christy, like Low, had studied at the University of Edinburgh, and there he became interested in natural history and zoology. He took part in various expeditions to South America and to India, before being chosen for the RSL mission. He was an army doctor and would later become well known at the Liverpool School of Tropical Medicine (Christy, 1932), directed by George Low. His relationship with the other members of the mission in Uganda was never easy. For temperamental reasons and because he disagreed with the decisions of Low, he was forced to return to Great Britain before the end of the mission.

David Bruce, a doctor in the British army and a graduate of the University of Edinburgh, had achieved some fame in 1894 through the discovery of the bacteria responsible for Malta fever in Natal (South Africa), later called brucellosis after him. In 1889 he concluded his studies in experimental bacteriology at the laboratory of Robert Koch (1843-1910), specializing in techniques for the cultivation of micro-organisms and the production of vaccines. He was also a researcher with an interest in tropical veterinary medicine, owing to his training and the interest in zoology and natural history that he showed in his youth. He identified the presence of trypanosomes in cattle, linking it with the "fly disease" known as nagana (Cook, 2007, p.145-156; Esch, 2007, p.109-127). His varied training and his interest in the relationship between vectors and parasites would be crucial in the debate on the etiology of sleeping sickness in humans, as we shall see later.

David Nabarro, who was also a doctor in the British army, had begun his clinical career as a laboratory assistant in histology and physiology at University College London, where he had graduated, and after a few years became assistant in pathology and bacteriology (O'Connor, 1991, p.162-163). He was appointed as a member of the commission for the study of sleeping sickness, in Uganda, with the aim of confirming trypanosome as the etiological agent of the disease and of ascertaining the method of transmission and its role in a possible insect-carrier life cycle, from a histo-pathological perspective. His training in histology and parasitology would determine his future career.

The contributions of Aldo Castellani unleashed a controversy with regard to the results of the second mission, which was also nourished by the prudent position of the RSL in relation to Castellani's results. In fact, the Society refused to publish the results obtained by him in Entebbe, probably because it considered his conclusions to be premature and because it was more inclined towards an interpretation of a parasitological nature with regard to the etiology of sleeping sickness (Cook, 1933). On his own initiative, and with the support of Walter Kruse, Castellani published his work, which we will quote below, and later claimed to be the discoverer as opposed to Bruce in discovering the etiology of sleeping sickness. This dispute constituted the final phase of the controversy examined in this work.

All of the members of these study missions and also the members of the Malaria Committee of the RSL were important figures in the history of sleeping sickness, not only from the experimental point of view, but also with regard to their knowledge of the tropics. They had a wide-ranging scientific background in the fields of bacteriology, parasitology, natural history, zoology, physiology and histology, as opposed to that of the Portuguese doctors, whose training was more specialized and, therefore, limited.

Prelude to the controversy: the identification of a species of bacteria

The first Portuguese work on the causal agent of sleeping sickness was carried out by António de Carvalho Figueiredo, in 1889, based on a patient at the Saint Joseph Hospital, in Lisbon (Azevedo, 1891). The patient died less than a month later, and it was therefore possible to study cultures of micro-organisms *post-mortem*. Figueiredo found two types of bacilli, isolated and in pairs, cylindrical, arranged in longer or shorter chains, in a similar way to *coccus*, and, as regards the chains, to *streptococcus*. These mobile aerobic organisms developed relatively well in meat juice, agar and gelatin, but not in a culture formed of potatoes and albumin. They colored effectively in the presence of aniline, and not in the presence of Gram. As they had been obtained from a single cadaver, these results were not considered meaningful, but contributed towards the suspicion that the disease was of a microbial nature and that the blood and the cephalorrhachidian fluid were possible habitats for the pathological agent (Cagigal, Lepierre, 1897b, p.470-472).

In 1897, in the blood of a young black Angolan aged 16, who was suffering from sleeping sickness and was interned in the Coimbra Hospital, Cagigal and Lepierre identified another bacterium which they imagined was the agent of the disease (Cagigal, Lepierre, 1897a, p.493-494; Cagigal, Lepierre, 1898, p.3). This analysis had two objectives: firstly, to identify the pathogenic agent in the biological fluids; secondly, to inoculate the isolated agent in laboratory animals, with a view to testing whether in fact they were dealing with the agent of the disease in humans.

Observation of the principal symptoms of the 'pathological sleep' led the authors to the hypothesis that the causal agent of the disease was a micro-organism which inhabited the blood. They therefore took various samples during the evolution of the disease, in feverish and non-feverish periods, and also from the cadaver. Laboratory analysis was carried out with strict attention being paid to the indications in the manuals of tropical diseases, as adopted in the Pasteur institutes. Various microscopic preparations were made, some without coloring, others colored with aniline, and various culture mediums were employed: gelatin, agar, potato starch, albumin, meat juice and peptone. Growth in all the culture mediums was very difficult, and it was only after a month of repeated immersions in serum that the first results were obtained. The bacillus observed in the blood did not develop except in serum, and very slowly in gelatin. These samples revealed the existence of a single microbial culture which the authors called "sleeping sickness bacillus" (Cagigal, Lepierre, 1897a, 1897b). According to Cagigal and Lepierre, it showed the following characteristics (Cagigal, Lepierre, 1897b, p.472-474):

It is a short rod the ends of which are slightly thicker than the mean thickness and differs from that observed in the blood only in its dimensions;... they are scarcely motile, they color with aniline and discolor under the Gram method; they possess spores;... it is a true aerobic microorganism.

Intrapericardial, intrapleural, and intraperitoneal fluids and fluid from the third ventricle were taken at the autopsy. Each one of them was used to create cultures on sheets of gelatin, in serum and in meat juice. Apart from the bacillus identified in the patient when he was still alive, it was only in the cultures of the intraperitoneal fluid that it was possible to observe the *Bacillus coli*, which was subsequently inoculated into rabbits, guinea pigs and chickens, with its virulence enhanced in some cases (Cagigal, Lepierre, 1897a). The authors claimed that they had observed and described the true agent of the disease which had carried off Gô [the name of the patient] (Cagigal, Lepierre, 1897a, p.494). In 1904, António de Pádua and Lepierre admitted that their observations should be submitted to experiments to corroborate them, bearing in mind that they had utilized only one clinical case (Pádua, Lepierre, 1904, p.8).

The work of the Portuguese mission in Angola was planned so as to include a stay on the Ilha do Príncipe. This stop was strategically advantageous for the mission to Angola, a colony which merited greater attention, given its size and the riches associated with it. The threat of devastation through sleeping sickness was evident in Príncipe, as the island was small and had a high incidence of the disease (the settled population had diminished drastically from three thousand inhabitants in 1885 to eight hundred in 1900). Without this specific cause of mortality, the demographic make-up of the island was normally stable. These features were not to be ignored for the purposes of the exploratory mission in all the colonies, which included the acquisition of knowledge of the local environment, both in relation to the living conditions of the population and in relation to natural phenomena (Correia Mendes et al., 1909, p.4). On the island, studies were made of the development of the disease (clinical and experimental observation), which associated it with the increase in the flow of trade and the importation of workers (Relatórios..., 1901, p.9). In the report, the hypothesis was admitted that the disease on the island was linked with “farms which were hot, humid and with abundant vegetation” (Relatórios..., 1901, p.23). This assumption linked it in a general way with the environmental characteristics of tropical climates. For the Portuguese colonial administration, the mission was important to the extent that it sounded a warning as to the gravity of the illness, which would make the colony uninhabitable within a short space of time. At this stage the idea began to grow that the high mortality rate in Príncipe was due to sleeping sickness, which was the main obstacle to its colonization (Bruto da Costa, s.d., p.88, 90).

On the basis of the observations carried out on the island, the team began to look for explanations for the etiology of the disease. It was accepted that it was transmissible and contagious (A doença..., 1901, p.301), but the team was a long way from being able to put forward an explanation of an etiological nature, because there was no experimental evidence to show the existence of any micro-organism, even on the international plane. The sick were sent to Portugal for the purpose of being studied in the hospitals of Lisbon, Porto and Coimbra, given that conditions for their treatment in the hospitals of the colony

were inadequate, through lack of resources and specialist clinical information on tropical diseases. From 1902, the Colonial Hospital in Lisbon received most of these patients.



Figure 4: Carrier sufferer from sleeping sickness, Ilha do Príncipe, 1901 (Image kindly loaned by Luís Marto)

On their arrival in Luanda, the team installed themselves in the Maria Pia Hospital, and had certain facilities at their disposal there: the bacteriology department assigned to them by the head of the health service and director of the Hospital, José de Brito Freire e Vasconcellos; two small rooms, one used as the room for cultures, sterilization, and the preparation of histological samples, the other as a photography room, and there was even a third room for the accommodation of patients. Working conditions were rudimentary, notwithstanding the good will and cooperation of the medical staff of the hospital. The equipment which the mission had brought from Lisbon comprised microscopes, tables for slant sample viewing, reactants and equipment currently used in the laboratory, some of it adapted so as to function with a petrol generator. Working areas were small; laboratory materials ran out; the local equipment was obsolete or would not function due, for example, to the lack of gas in the town (Relatórios..., 1901, p.14).

The mission of Annibal Bettencourt could count on the experience of two local doctors from the health staff of the Province of Angola, Alberto de Sousa Maia Leitão e Annibal Correia Mendes, although only the latter was appointed a member of the mission. Maia Leitão was given the task of travelling to the areas of the province with the highest incidence of cases, to carry out an epidemiological study, bearing in mind the symptomatology and etiology of the disease (Leitão, 1901). From the general conclusions of the report that he presented, I note the following: the disease was prevalent in all the areas visited to the east of Luanda; the mortality rate among indigenous children was high (90%); the indigenous persons who emigrated to Ilha do Príncipe (four or five per year) did not return; the mortality rate was always higher than the birth rate; sleeping sickness led inevitably to death (Leitão, 1901, p.127-128). These observations simply confirmed the lethal nature of the disease, which seemed to be highly contagious and capable of developing in a short space of time (Doença..., 1901).



Figure 5: The Maria Pia Hospital in Luanda (Primeiro congresso..., 1924)

Meanwhile, the other members of the mission concentrated on the clinical symptomatology and microbiological research on pathogenic agents and their effects on laboratory animals (Bombarda, 1901). Microscope analyses of samples of blood and cerebrospinal fluid from carriers of the disease, colored with aniline or with Gram coloring, revealed that the bacteria cultures had difficulty growing in the media traditionally used, whether liquid or solid (agar, gelatin or meat juice). The culture medium that gave the best results was that of Martin, which was obtained by soaking pork liver. In the cultures obtained in this way, the mission identified a micro-organism described as a *diplo-streptococcus* and designated 'hypnococcus'. In 46 of the 48 samples grown *intra-vitam* and *post-mortem*, a bacillus was isolated which was similar to the *diplococcus* of Weichselbaum, a *diplo-streptococcus* distributed in pairs, immotile, of rounded shape and sometimes elliptical (Relatórios..., 1901, p.32-33). The mission had great difficulty in finding a culture medium which was viable for this micro-organism. However, such a high frequency led the mission to conclude that the disease was a meningo-encephalitis of a microbial nature, as described in the report:

Its pathogenic power in animals, the facts of transmission as related by the patients and the persons who live with them, and the progressive and invasive nature of the illness lead us to the conclusion that these are elements which we consider sufficient to accept that sleeping sickness is of a microbial nature and that the diplo-streptococci found by us are the etiological agent.

The results were initially published in the first report sent to the Overseas Ministry in 1901, and in *Medicina Contemporânea* (A doença..., 1901a, p.325-328; 1901b, p.319). Considered national heroes, the authors were decorated by don Carlos I. The encouraging conclusions of the Portuguese mission were presented to a public meeting at the Geographical Society

of Lisbon, and at the same time a fuller report was published, which included illustrations of anatomical parts, cultures and microscope preparations, in a de luxe edition, at the government's expense. An abridged version of this second report was published in 1902 in *Revista Portuguesa de Medicina e Cirurgia Práticas* (Doença..., 1902). The Navy minister praised the mission to the Society for Medical Sciences, thanking it for the influence it had had on the government, and for the advancement of Portuguese prestige in a European medical context.

The final version of the report was published in French in 1903. Its last two editions showed an intention to display, for internal and external consumption, the scientific competence of the Portuguese mission, and to give a measure of the capacity of the Portuguese state to occupy and administer its territories in Africa. The mission was thus transformed into an important element in the recovery of national pride, which had been wounded following the humiliation of the English ultimatum.⁴

Between 1901 and 1904, various articles were published in five medical periodicals with a wide circulation: *Medicina Contemporânea* (Lisbon), *Jornal da Sociedade de Ciências Médicas* (Lisbon), *Revista Portuguesa de Medicina e Cirurgia Práticas* (Lisbon), *Movimento Médico* (Coimbra) and *Coimbra Médica* (Coimbra). These represented the principal vehicles for the controversies over the etiology of sleeping sickness, which involved the results obtained by the microbiologists of Coimbra or by Castellani, as opposed to the positions taken up by the Bettencourt mission.

All the other missions were realized by the School of Tropical Medicine of Lisbon and showed the importance of sleeping sickness in the defense of national interests and for the acceptance of Portuguese tropical medicine, as a specialized field of medical activity. Between 1902 and 1935, the School undertook eight scientific missions, six of which were concerned with sleeping sickness: to Ilha do Príncipe in 1904, 1907 and 1911; to Mozambique in 1910 and 1927; and to Guinea in 1932. All of them aimed to map the disease and develop therapeutic action programs capable of lowering its pathological rates until it was finally eradicated. Work was carried out both *in situ* and in the School of Tropical Medicine in Lisbon, to which were sent entomological specimens, biological samples and the patients themselves. In addition to a reduction in the mortality rate due to the disease, the consequences of which for the economy were evident, the missions also wished to demonstrate the 'justice' of Portuguese claims in relation to their African territories, by showing medical expertise in tropical diseases. The medical community thus had the opportunity to show itself at the forefront as a decisive element in the development of Portuguese colonial policies.

The controversy in Portugal: Bettencourt vs. António de Pádua and Charles Lepierre, 1901-1903

The results of the Bettencourt mission were not well received throughout the Portuguese scientific community, and the main opponents naturally came from the group of microbiologists at the University of Coimbra, who claimed to be the discoverer of the bacillus which caused the disease. The doctors at Coimbra claimed that their bacillus was

the same as that described by the mission. The Society of Medical Sciences of Lisbon, who had had a decisive influence on the decision of the Portuguese government to send the mission of 1901, immediately defended the merits of the results (Bombarda, 1901; A doença..., 1903); however, the team at the University of Coimbra, led by António de Pádua and Charles Lepierre, became involved in an open confrontation, criticizing the value of the microbiological observations and the rigor in presenting the concepts and the results of the mission. The entire dispute developed around the 'sleep bacillus', the meningococcus identified by Cagigal and Lepierre in 1898, and the 'hypnococcus' identified by the Bettencourt mission.⁵ Lepierre adopted a cautious attitude, but the mission's position was categorical. For the former, the bacillus found could be the etiological agent; for the mission, the true agent responsible for the disease had been found. The mission was clearly concerned to demonstrate its scientific authority, which it skillfully associated with the need for Portugal to show its capacities as a colonial power.

The main arguments in this internal controversy were to be found in the context of bacteriology as a scientific methodology, and the dispute centered on the validity of the observations, phenomena and methods which were the analytical elements in the problems of the controversies (Machamer, Pera, Baltas, 2000).

Bettencourt argued that the sleep bacillus of Coimbra could not be the same as the one the mission had identified, because it possessed different characteristics (Lepierre, 1903b, p.179). Lepierre and Pádua countered this argument by saying that the differences were

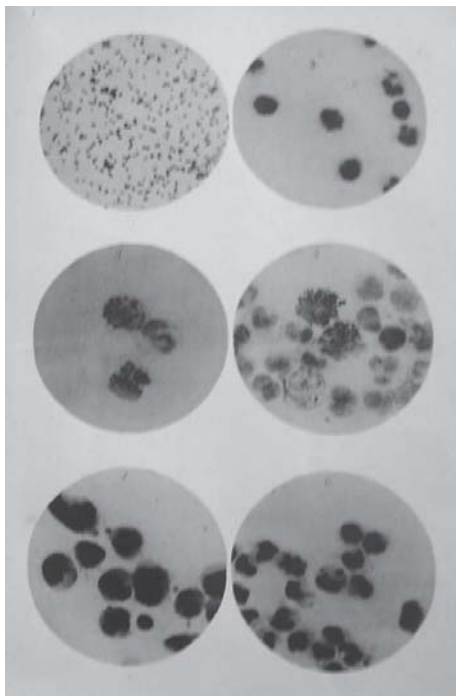


Figure 6: Cultures of 'hypnococcus' in agar, better viewed in plates 3 and 4 (Bettencourt et al., 1901, p.333)

not grounds for supposing the presence of a different micro-organism, and that the mission was not quite up to date with regard to the most recent research in the field, which was in fact the case. Four basic aspects were identified in the confrontation between Bettencourt and António de Pádua and Charles Lepierre, starting with the criticism made by the mission of the results obtained in Coimbra: the simultaneous identification of the bacillus and of the spores in the culture and the long time taken for laboratory animals to react to the inoculation of the bacillus, thereby giving grounds for a distinction between the 'sleep bacillus' of Coimbra and the 'hypnococcus' of Lisbon. Conversely, criticisms centered on the strangeness of the ruthless claims for the discovery. Added to this was the lack of clarity in explaining the results, particularly when referring to *in-vitam* or *post-mortem* situations, and in some cases also, the accusation that the mission doctors had falsified their results – because of the differences which existed

between the first and second reports of the mission – with the aim of building up a stronger case.

Comparing these arguments, we are led to conclude that, although the differences may not have been significant between the two bacilli, this fact by itself would not be enough to affirm that the ‘sleep bacillus’ and the ‘hypnococcus’ were the same microbiological entity. A comparison of the results does not seem significant in resolving the fundamental question, probably because it would be necessary to find other means of discriminating between bacilli of such similar characteristics, which might invalidate the assumptions of the debate itself. The criticisms made in Coimbra of the way in which the mission compared on a theoretical plane with other researchers seem to make sense in the development of the controversy, which went beyond national frontiers and even reached Aldo Castellani in Uganda.

Twists and turns in the controversy: Bettencourt vs. Castellani, 1902-1903

The Malaria Committee of the Royal Society, which supported the choice of Low, Christy and Castellani for the first mission for the study of sleeping sickness, was particularly concerned with the microbiological methods employed by its members and the possibility of the parasite *Filaria perstans* being in some way connected with the disease. At this stage Miguel Bombarda, in Lisbon, also considered that the views of Manson could not be ignored by the Portuguese researchers, whose laboratory investigations pointed towards a bacterial cause (Bombarda, 1900a, p.412).

When they arrived in Uganda in 1901, the British mission were aware that trypanosomes had been identified in the peripheral blood system by Robert Michael Forde (1861-1948), in Gambia, in patients with ‘trypanosome fever’, and confirmed by Joseph Everett Dutton (1874-1905). However, neither of these authors, nor even Manson, associated this pathology with sleeping sickness (Cook, 1933, p.225). The latter, based on the observation of three patients, accepted that the disease was caused by *Filaria perstans*, because he had identified embryos of this nematode in the blood of the patients. However, he took notice of the results of the Bettencourt mission and sent them direct to Low (Cook, 1933, p.225), who passed them on to Castellani, recently established in his new laboratory. Like the Portuguese mission, the mission of Low had excellent conditions and equipment for carrying out microbiology projects in Uganda (Cook, 1933, p.221). On October 15, 1902, Low reported to Manson that Castellani had encountered a *streptococcus* or similar organism in cases of sleeping sickness, and considered this to be the cause of the disease. Castellani hurriedly sent a preliminary report to the Royal Society, stating that he had found a micro-organism in eight of the ten *post-mortem* samples of cephalorrhachidian fluid. The Society’s reaction to these results was skeptical (Boyd, 1973, p.95), probably because Castellani was a foreigner, he was still inexperienced and he did not base himself on a significant sampling of experimental results. For these reasons it decided not to publish his report and considered the possibility of sending another mission to confirm his results, which did in fact happen. Unhappy with this decision, Castellani submitted the article to the *British Medical Journal* on November 14, 1902, which published it the following year (Castellani, 1903c). In this

article, Castellani claimed for himself the discovery of the etiological agent of sleeping sickness, and rejected any analogy between his bacteria and the 'hypnococcus' of Bettencourt, because of the characteristics of the micro-organism – in the same way as what happened between Bettencourt vs. António Pádua and Charles Lepierre. Referring to the Portuguese mission, Castellani began by stating that it had only collected samples from the blood of patients – which was untrue (Relatórios..., 1901, p.33) – because the micro-organism did not grow in the culture media currently used in laboratories, contrary to what the Portuguese mission had stated (Relatórios..., 1901, p.34-35), and that it did not observe whether the blood of the patients had any agglutinant capacity in relation to the 'hypnococcus'. Castellani claimed he had identified a *diplococcus*, a variety of *streptococcus*, motile and of variable aspect, in sleeping sickness patients. Charles Lepierre and António de Pádua had admitted that an absolute difference existed between the two cocci discovered by the Bettencourt mission and by Castellani, for which reason they could not be the same micro-organism, bearing in mind the different criteria used in the microbiological identification (Lepierre, 1903a, p.261; Lepierre, 1904, p.53-54) – particularly the agglutination tests, which the Portuguese mission were unaware of. However, Bettencourt hurriedly wrote to Castellani and published two articles, one in *A Medicina Contemporânea* (Bettencourt, 1903a), the other in the *British Medical Journal* (Bettencourt et al., 1903b), admitting that the two bacilli were similar and that acclaim for the discovery should be assigned to the Portuguese authors and not to the Italian bacteriologist. Thus in *Medicina Contemporânea*, he says (Bettencourt, 1903a, p.95):

our investigations were not limited to cultures and microscopic examination of the pathological fluids of the organism. We also studied numerous sections, particularly of nerve tissue, and we were the first to find in them and confirm the presence of hypnococcus. How is it possible that the microbe which we obtained so many times in a pure culture is not the same as that in the sections, given the morphological similarity? And how could the microbe of Castellani, isolated from the same regions of the organism where ours were taken from, during life and *post mortem*, not be the same one as we observed in our sections? In view of all this, we have no doubt that the microbe of Castellani is the same as the one we described and that his investigations are full confirmation of ours... the question of who was the discoverer is relatively unimportant and no-one... can dispute that it should be attributed to us; but the work of the member of the English mission, carried out independently from our work, in a region far away from where we worked, does not lose its own value on this account nor the importance that it has for understanding the etiology of hypnosis.⁶

In reply, Castellani repeated that his bacillus was different from the one isolated by Bettencourt, because it reproduced well in gelatin and other culture media, in which the microbe isolated by the Portuguese team did not develop. In addition, he claimed in August 1903 (Castellani, 1903b) that Bettencourt had altered the results in his second report to bring them closer to his, an opinion shared by the group of microbiologists at Coimbra. It should be noted that Castellani sent his arguments to Lepierre and Pádua, as well as to Bettencourt (Pádua, Lepierre, 1904, p.101).

However, by November 12, 1902 Castellani had already moved on in his investigations when he identified, to his surprise, a trypanosome in a sample of cerebrospinal fluid taken

from a patient who had been clearly identified as a carrier of the disease (Castellani, 1903b, p.501).⁷ The identification of the parasite was not easy, for which reason he employed a variant of the experimental method normally used to identify this type of protozoan. Castellani placed a sample of cerebrospinal fluid in a centrifuge for 15 minutes, and examined the supernatant under a microscope (at medium resolution power), where he viewed the trypanosomes which, being motile could be identified more easily (Castellani, 1903b, p.501). In this way, he was forced to change his investigative target from bacterium to parasite. He observed the latter in twenty out of 34 cases analyzed (a very high percentage) and concluded that, owing to its similarity to the parasite of Dutton, he was probably dealing with a variant (Castellani, 1903b, p.507). Even so, he did not miss the opportunity of calling it *Trypanossoma ugandense*⁸ (Kruse, 1903; Cook, 1933, p.225), as opposed to that of Forde-Dutton, *Trypanossoma gambiense*, even in research carried out after he had left the mission in Uganda (Castellani, 1910). Castellani went on with his work, and in August 1903 completed his series of investigations into sleeping sickness, maintaining that it was caused by trypanosomes found in the cephalorrhachidian fluid and that, in the final stages of the disease, infection could occur accompanied by streptococci (Castellani, 1903b, p.507-508).

In the same month, in the second report that it published, the Portuguese mission once more claimed to be the discoverer of 'hypnococcus', the *diplo-streptococcus* of Castellani (Bettencourt et al., 1903a), at the same time as it refuted the new theory of the author to the effect that the cause of the disease was a parasite (Bettencourt, 1903b). This report, published in French, was aimed at the Pasteurian microbiologists, in an attempt to canvass support for the Portuguese mission's claim to be the discoverer, to the detriment of Castellani. However, the *Journal of Tropical Medicine* immediately published a hard hitting commentary on the results of the Portuguese mission, so that Castellani concluded, "except from the point of view of the geographical distribution of sleeping sickness, the report of the Portuguese mission merits scant attention" (Report..., 1904, p.230).

The circulation of the results of the Portuguese mission among the doctors who were investigating sleeping sickness worried Castellani, because it constituted a threat, not only to his own prestige but to that of the mission which had been entrusted to him. In these circumstances, he quickly changed to a 'trypanosome' in an attempt to restore his place at the head of the discovery and etiology of sleeping sickness (Cook, 1933, p.225). However, this was not the end of the argument, either for him or for the Portuguese mission.

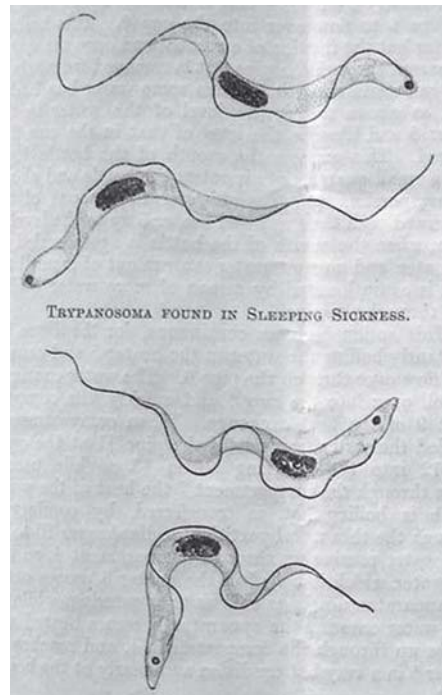


Figure 7: Trypanosoma identified by Aldo Castellani (Castellani, 1903a, p.205)

Epilogue (1903-1907): Castellani vs. Bruce and Kopke vs. Bettencourt

The second English mission arrived in Entebbe on March 16, 1903, as a result of the need to send reinforcements to the colony, firstly owing to the high rate of incidence of the disease, and secondly because of the need to confirm the results obtained by Castellani. The Malaria Committee of the Royal Society deemed it advisable to surround Castellani by a more experienced team, made up of David Nabarro and David Bruce. These two opened up a new argument in the competition to find the cause of the disease, which this time brought Castellani and Bruce into opposition. The former claimed to have discovered the trypanosome, and consequently the etiological agent of sleeping sickness; Bruce, in his turn, claimed that it was he who had established the relationship of the parasite with the disease, because Castellani had only identified the parasite and was still attached to the a:'streptococcus' responsible for a secondary infection in the latter stages of the disease. The controversy was resolved in the Malaria Committee of the Royal Society in 1904 (Boyd, 1973).

When he arrived in Entebbe and examined the results obtained by Castellani, Bruce concluded that these did not confirm the pathogenic character of the parasite, because the Italian had not established any relationship between it and the host, contrary to what he had found: nagana in cattle was transmitted to humans by the tsetse fly (Boyd, 1973, p.101). Castellani reacted immediately. He sent various letters to the Royal Society claiming the discovery of the etiological agent of sleeping sickness, but he did not meet with success. The Malaria Committee of the Royal Society, chaired by Ray Lankester, a friend of Bruce, decided that although Castellani had identified the parasite, he had not established its relationship with the etiology of the disease, while Bruce had done so because of his additional contributions to the work of his predecessor, which had provided an explanation of the mechanism by which trypanosoma was transmitted to man (Boyd, 1973, p.102-105). The claims of Castellani would be maintained in the British medical press until almost the beginning of the 1930s, although without any result which was favorable to him.⁹ Because of his training in natural history, Bruce was more qualified to think in terms of the connection of the parasite with the tsetse fly and to explain the mechanism of the disease, involving agent, carrier and host, rather than Castellani, whose training had concentrated on the identification of micro-organisms in the school of Kruse, and these considerations were of importance in the decision of the Society.

In Portugal too, the argument continued between Bettencourt and the researchers of Coimbra. The former maintained his line of argument until the end (A doença..., 1903; Bettencourt, 1903b, p.163-165), but two members of the mission disassociated themselves from the positions argued by their superior. In 1903, following the evidence presented by Castellani of the existence of trypanosomes in patients who were carriers of the disease, Correia Mendes and Ayres Kopke redirected their researches and arguments in favor of a parasitic etiology for sleeping sickness. In 1904, Correia Mendes examined a case in a European, which was a rare occurrence, looking for parasites in the blood, and on identifying trypanosoma, wrote as follows (Correia Mendes, 1904, p.152):

I have observed hundreds of individuals afflicted with this disease [sleeping sickness] and I do not think I am wrong in saying that this is a case of hypnosis, which is particularly interesting in view of the fact that I have found in the blood the trypanosome to which

the English assign the cause of the disease ... given its rarity in individuals of the white race, such a coincidence cannot fail to be taken into consideration, leading us to believe that trypanosoma plays an important part in sleeping sickness.

Ayres Kopke, in his turn, developed in the laboratory of tropical bacteriology and parasitology of the School of Tropical Medicine a research project which consisted in the clinical observation and investigation of certain patients in the Colonial Hospital in order to study the role which trypanosoma and 'hypnococcus' might play in the etiology of the disease, as well as the action produced by the two associated agents.

In the course of these investigations, Kopke disassociated himself from the position of the mission of 1901, admitting, like Castellani, that *streptococcus* represented only a secondary aspect of the evolution of the disease. Kopke accepted completely the theory of the parasite responsible for sleeping sickness: the trypanosome identified by Castellani and confirmed by Bruce and Nabarro. Gradually the new parasitic thesis was accepted by the other Portuguese doctors on the mission. After 1904, the bacterial theory of sleeping sickness was definitively abandoned, and the consensus of the national and international scientific communities united around the parasitic theory.

Final considerations

The devastation caused by sleeping sickness in Africa, where mortality rates were extremely high, leading sometimes to a drastic reduction in available manpower, led the doctors in colonizing countries to give priority to the discovery of its cause. The political scramble for Africa was succeeded by the competition to discover the cause of sleeping sickness. The Portuguese mission to study the disease, the first of the European missions to be sent to African territory with this aim, in 1901, unleashed a string of controversies, not only among members of the Portuguese medical community, but also between Portuguese and British doctors, and even between British doctors.

The importance given to the Portuguese mission of 1901 by the Portuguese government, and the way in which its members published their results within and without the Portuguese scientific community, can be seen as an attempt to recover national pride, after the plan for the 'Pink Map' had been frustrated. The discovery of the etiological agent for sleeping sickness would bring renown to Portuguese medicine and would be a demonstration of the capacity of the Portuguese to effectively occupy their African colonies.

The Portuguese mission started the controversy over the causal agent of the disease (bacteria or parasite), after the publication of its results in 1902. On the domestic level, the prolonged and bitter debate between the bacteriologists of Lisbon and Coimbra represents a contest for scientific authority within the Portuguese medical community. The microbiology section at the University of Coimbra could hardly compete with the Câmara Pestana Institute of Bacteriology, either in resources or in national prestige. However, in the dispute between the researchers of Lisbon and Coimbra, it appears that the latter had a greater grasp of medical microbiology, probably due to their experience in association with the University Hospital, where various clinical cases were encountered which assisted microbiological investigation. In any event, it was very difficult to accept the arguments

of these researchers with regard to the 'sleep bacillus', because their results were based entirely on the history of a single case of the disease.

The results of the mission were rapidly known by the English mission in Uganda. The debate, which centered on a bacillus (*streptococcus*), led Castellani to contest the conclusions of Bettencourt, making use of his expertise in microbiology – particularly in the use of agglutination tests for the selective identification of bacteria (Castellani, 1902). Although these tests had sometimes failed to identify *streptococcus*, and the results obtained from inoculated animals were not very satisfactory, if this micro-organism was not the result of a secondary infection, Castellani was probably in the best position to challenge the Portuguese stance, in an international context: his techniques were more specific and his experience in tropical diseases wider, owing to his connections with the School of Tropical Medicine in London and with Manson.

The outlook of Annibal Bettencourt and of a large part of the Portuguese medical community was profoundly influenced by the Pasteurian tradition, which prevented the identification of the true etiological agent of sleeping sickness. Nevertheless, the heated debate within and outside Portugal was crucial for the history of tropical medicine (Benchimol, 2010), in that the arguments between a Pasteurian agenda and a medicine of vectors (Benchimol, 1999, p.396) were at the epicenter of the emergence of a new discipline. As argued by Sandra Caponi, these controversies enabled them to find new objects, concepts and study methods which did not necessarily result from the pattern of investigation started by Pasteur (Caponi, 2002, p.115).

From the acceptance of trypanosoma as the agent responsible for the etiology of the disease, at an international level, the doctors who took part in the mission, but who did not belong to the Câmara Pestana Institute of Bacteriology, Correia Mendes and Ayres Kopke, easily distanced themselves from the position taken by the mission headed by Bettencourt. While the bacteriologists from the Institute remained faithful to the scientific agenda of the institution and to Pasteurian orthodoxy, that is, to 'the hunt for microbes', in a search which already had ten years of history, Correia Mendes and Ayres Kopke, who since 1902 had been linked to the School of Tropical Medicine – which was modeled on the School of Tropical Medicine of London and the views of Patrick Manson – were more prepared to follow the evolution of tropical medicine. At the prestigious British institution, both microbial medicine and the medicine of vectors were equally prized. For António de Pádua and Charles Lepierre also, it was easier to accept the discovery of trypanosoma by Castellani, owing to the independence they enjoyed in relation to the Portuguese government, making it easier for them to adopt a contrary position.

In the debate between Portuguese and British doctors, the positions of Bettencourt and of Castellani are illustrative of the struggle for primacy, which also existed between the two English missions, through Castellani and Bruce. If Portuguese nationalism was exacerbated by the ghost of the rivalry between Portugal and England over African territories, this extended to the Portuguese doctors, who were equally in competition with the doctors of the English mission. As regards Castellani, one of the central figures in the controversy, he showed himself very concerned from the outset to take on the principal role in the race to find the cause of sleeping sickness. The pressure that he brought to bear on the Royal

Society to publish his work on 'streptococcus', or on the etiology of sleeping sickness associated with trypanosoma, the dispute with the Portuguese mission, and the exchange of correspondence and dispatch of biological material to Walter Kruse in Germany, before the publication of the results by the Royal Society, are examples of this attitude.

It was the Portuguese chase after bacteria which persuaded Castellani to take the microbiological road, where he felt himself to be on sure ground, but it was also *streptococcus* which was the cause of the argument which developed with Bruce, which he never succeeded in resolving in his favor. Bruce argued that Castellani had not come up with an etiological explanation for the disease, because he was only concerned to identify and describe his *streptococcus*. However, the chance identification of trypanosoma by Castellani and his rapid change in the techniques for identifying micro-organisms (agglutination tests), in order to identify parasites (centrifuges), seems to show his view that a micro-organism identified in only a few cases and under very particular experimental conditions was not the correct road for the investigation in question.

By 1904, an answer had been found to the fundamental question in the controversy: was the pathogenic agent that caused sleeping sickness a bacterium or a parasite? However, the rivalries between the main protagonists in the debate continued for some time, particularly in the United Kingdom, where they lasted, within the medical community, until the end of the 1920s.

Although the climax of this controversy occurred between 1902 and 1904, there is a lot of historiographical material for the period between 1908 and the end of the 1920s involving Castellani and Bruce (Castellani, 1908; Nabarro, 1913a, 1913b, 1917a, 1917b; Chalmers, 1913, 1918; Ross, 1926). Why? Probably because the bacterial solution for the etiology of the disease did not involve important figures in the history of European tropical medicine, as the period of its dominance was very short. Neither Bettencourt nor Castellani were sufficiently known to the Malaria Committee of the Royal Society, of which Patrick Manson was a member. Bruce, on the contrary, was very influential in the British scientific community, which was a reason for the length of the argument with Castellani. This work has attempted to contribute to a better understanding of the twists and turns of this controversy, which have passed by unnoticed in the most recent historical writing on the problematical etiology of sleeping sickness. The problem had involved a significant part of the Portuguese medical community, at the height of a debate between a Pasteurian agenda and the medicine of vectors, in order to discover the etiological agent responsible for sleeping sickness.

NOTES

* This paper was originally presented in 2008, at the 6th Step Meeting, in Istanbul (Turkey), having been pre-circulated among those taking part in the meeting, with the title "Discovering exotic pathologies: bacteria or parasite in sleeping sickness, controversies at the Lisbon School of Tropical Medicine (1898-1904)".

¹ The Royal Câmara Pestana Institute, founded in 1892, along the lines of the Pasteur Institutes in Paris, was an institution of great prestige at the time in the field of bacteriology.

² In this and other citations of texts from non-English languages, a free translation has been provided.

³ Built in 1886, the Maria Pia Hospital has been known since the independence of Angola as the Josina Machel Hospital, as a tribute to the wife of Samora Machel (President of Mozambique from 1975 to 1986), due to her importance in the struggle for women's rights. It is still today one of the most imposing buildings in the city of Luanda, owing to its grand design, on which the surrounding works of recent years project a great importance.

⁴ The Berlin Conference (1884-1885) set up a new legal framework for European occupation of African territory, based on effective occupation. For Portugal, the first country to set up colonies in Africa, Portuguese claims based on historical rights would only be valid if they were backed up by an authority to instill respect for the rights acquired and guarantee freedom of trade and movement. In 1886 Portugal made its colonial pretensions known, in the form of the 'Pink Map' – a map which linked the coast of Angola with that of Mozambique. The Portuguese government then made various attempts at effective occupation, in a colonial dispute with England. England responded to one of these attempts with the Ultimatum of January 11, 1890. The letter required the immediate withdrawal of Portuguese military forces from the territories between Angola and Mozambique, under the threat of a massive military invasion by England. Portugal retreated, retaining only its authority in Angola and Mozambique.

⁵ This controversy can be followed in the *Revista Portuguesa de Medicina e Cirurgia Práticas* (between November 15, 1901 and October 15, 1902) and in *Movimento Médico* (between December 1, 1901 and January 15, 1902). The former gives the position of the Bettencourt mission, the latter that of the Coimbra researchers. The controversy can also be followed in its totality in *Medicina Contemporânea* (between 1901 and 1904).

⁶ Hypnosis was a word used as a synonym for sleeping sickness.

⁷ Castellani sent a letter from Entebbe to the Malaria Committee of the Royal Society on April 5, 1903 entitled, "On the Discovery of a Species of Trypanosoma in the Cerebro-Spinal Fluid in Cases of Sleeping Sickness", which was received on May 8 and read on May 14, 1903.

⁸ Aldo Castellani kept in regular contact with Walter Kruse, who had already said that the trypanosoma identified by Castellani ought to be called *Trypanosoma Castellani*.

⁹ When he returned to London in 1908 and discovered that Ray Lankester had published a book the previous year – entitled *The Kingdom of Man* – in which the history of sleeping sickness attributes Bruce to be the discoverer of the etiology of the disease, Castellani returned to the defence of his position in the *British Medical Journal* and in *The Times* newspaper, where Low, Christy, Nabarro, Kruse and Robert Koch, among others, joined in his defence. Compare the various articles on sleeping sickness published in the *Journal of Tropical Medicine and Hygiene* or in *The Times* between 1908 and 1926.

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