



Between black and miscegenated population groups: sickle cell anemia and sickle cell trait in Brazil in the 1930s and 1940s*

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Abstract

The article examines medical and scientific studies of sickle cell anemia published in Brazil in the 1930s and 1940s, when the vast majority of physicians and scientists believed that miscegenation played a significant role in the epidemiology of the disease in the country. Special focus is placed on hematologist Ernani Martins da Silva, of the Oswaldo Cruz Institute, who conducted blood analyses around the interior of Brazil with the purpose of classifying miscegenated and allegedly pure population groups based on the presence of sickle cells and the racial distribution of blood groups. The article explores the ambivalences stemming from associations between sickle cell anemia and the 'black race' during this period.

Keywords: history; sickle cell anemia; sickle cell trait; miscegenation; Brazil.

In this analysis of the relations between race and disease as reflected in Brazil's earliest medical and scientific studies on sickle cell anemia, published in the 1930s and 1940s, our goal is to explore uncertainties regarding the associations drawn between sickle cell anemia and the notion of 'black race' from a historical perspective. We identify the physicians and scientists who studied the disease and offer our understanding of its early history in Brazil, in hopes of fostering new studies on the role of sickle cell anemia by Brazilian medicine. We also show how the history of naturalized concepts can be rife with doubts and debates.

The term sickle cell disease (SCD) is applied to disorders caused by a specific change in the hemoglobin molecule, an oxygen-carrying molecule that is one of the most abundant within red blood cells. Genetic alteration causes one amino acid to be replaced with another in the protein chains that make up hemoglobin (with β_6 glutamic acid replaced by valine – Hb S), thereby altering the molecule's structure. This change lowers the affinity between the oxygen molecule and hemoglobin, prompting the formation of long hemoglobin chains that clump into intracellular bundles concentrated at the ends of the red blood cell and thus distort the cell into the crescent shape from which it gains its name (Andreoli et al., 1997, p.371).

A person whose mother and father both code for the hemoglobin variant Hb S will present the genotype Hb SS and thus be born with sickle cell anemia. The sickle cell trait is present when only one copy of this gene is inherited, with the carrier presenting the genotype Hb AS (Hb A being the abbreviation for normal hemoglobin). Carriers of the sickle cell trait do not display clinical symptoms since they have less Hb S than Hb A, making any structural changes to the molecule unlikely and meaning that their red blood cells rarely become sickle shaped. Other SCDs occur as the result of the combination of Hb S with other hemoglobins with altered structures. Hb D and Hb C, for instance, produce genotypes Hb SD or Hb SC, resulting in milder clinical presentations than actual sickle cell anemia (Hb SS). Patients who are homozygous for other hemoglobins, like Hb CC and Hb DD, can also present diseases that are milder than sickle cell anemia. Like carriers of the sickle cell trait, patients who have only one copy of a gene that causes production of modified hemoglobin (Hb AD or Hb AC, for example) display no clinical symptoms. Of all altered hemoglobins, Hb S is the most common (Wintrobe et al., 1981a, p.822, 1981b, p.856-859).

SCD displays a variety of clinical symptoms, which can be acute or chronic. The greater the proportion of Hb S, the more serious the presentation of the disease. Carriers of Hb SC present a milder disorder than carriers of Hb SS. Acute symptoms are caused primarily by the blockage of blood vessels by sickle-shaped erythrocytes or by tissue hypoxia, brought on by abnormal blood perfusion. Sickle cells make the blood more viscous, as they lack the flexibility of the normal cell's double-concave shape. One of the most common acute symptoms is pain crises caused by tissue ischemia, most generally affecting the abdomen, lungs, joints, and bones. One of the organs most often affected by the obstruction of blood vessels is the spleen, which often fails to function during the earliest years of childhood. Since this organ is vital in fighting infections before the organism has developed antibodies, the immunological response is compromised and he thus is more susceptible to infection.

Chronic symptoms stem mainly from the injuries caused by tissue hypoxia. Such symptoms include renal and heart failure, chronic ulcers, avascular necrosis (especially the head of the humerus and of the femur), and damage to the eyes (Andreoli et al., 1997, p.372; Wintrobe et al., 1981b, p.841, 844).

Sickle cell anemia is held to be one of the best examples of natural selection. It is believed that the altered hemoglobin gene (Hb S) remained stable for generations because it afforded carriers of the sickle cell trait protection against malaria.¹ This association was deduced after it was observed that carriers of the sickle cell trait in regions of Africa where malaria is endemic presented greater resistance than others to infection by *Plasmodium falciparum*. In the 1990s, research on people with sickle cell anemia showed that the gene Hb S may have appeared in more than one region of Africa and in places in Saudi Arabia and India (Naoum, Naoum, 2004, p.77-78).

In the mid-1990s, in the early days of debates over the adoption of affirmative action policies in Brazil, sickle cell anemia came into the spotlight as a genetic disease specific to the 'black race,' a consideration that would justify the creation of policies specific to the 'health of the black population' (Maio, Monteiro, 2005; Fry, 2005). Along with interest in the topic came the realization that there were no historical studies on any Brazilian medical scholarship exploring the relationship between sickle cell anemia and the black race. In the present article, we address such scholarship from the 1930s and 1940s, when the first Brazilian publications of clinical, hematological, and anthropological studies appeared. Sickle cell anemia was recognized as part of the nation's nosological picture in the 1930s, when studies were published on its clinical and pathological forms. Research became more diversified the following decade, when many studies focused on the correlation of sickle cell rates and Brazil's racial diversity.

The 1950s saw a paradigm shift in interpretations of sickle cell anemia, with concepts imported above all from population genetics, studies on natural selection, and molecular biology.² These new biomedical hypotheses regarding sickle cell anemia were concomitant with social changes that in the 1950s started lending new vigor to the fight against racism in the United States, especially the civil rights movement. The conjoining of new medical and social concepts was what consequently led to a reshaping of the meaning of sickle cell anemia as a racial disease (Tapper, 1999; Wailoo, 1997, 2001, 2003).

In Brazil in the 1930s and 1940s, the association between sickle cell anemia and the black race often accompanied the view that miscegenation had lent the epidemiology of the disease unique features in this country. This interpretation was in consonance with the budding idea that Brazil's large miscegenated population was unique. Furthermore, while there is now a scientific consensus that the disease originated in Africa, opinions then differed about whether sickle cell anemia occurred only in blacks and about whether it had first emerged among African peoples.

We present our argumentation in three sections. The first discusses U.S. medical and scientific studies linking sickle cell anemia to the black race – research that grounded investigations by Brazilian physicians and that informs us about the context in which scientific knowledge was being produced in the United States. By exploring specific questions – such as how a diagnosis was arrived at, the relation between SCD and the black race,

and inaccuracies regarding clinical manifestations – we can better understand how these elements were adopted and adapted into the Brazilian context. The first section also looks briefly at the significance of early research into sickle cell anemia in Africa itself.

The second section examines clinical, hematological, and anthropological research conducted in Brazil in the 1930s and 1940s, with a special focus on studies that used sickle cell anemia as a way of elucidating the interface between disease and race. Lastly, the third section primarily analyzes work by Oswaldo Cruz Institute (Instituto Oswaldo Cruz – IOC), an important biomedical research center in Rio de Janeiro, hematologist Ernani Martins da Silva, who launched a multi-disciplinary research program on sickle cell anemia and took it to various corners of Brazil.

Sickle cell anemia in the United States in the first half of the twentieth century

Our analysis of U.S. articles relied on historiographic studies of sickle cell anemia in the United States, especially the extensive research of anthropologist Melbourne Tapper (1999) and historian Keith Wailoo (2001), which contains interpretations of the relation between the context in which knowledge was produced and the meanings assigned sickle cells and the disease they cause. We selected the U.S. articles that Brazilian physicians used most often as the sources for the key concepts they adopted in their understanding of sickle cell anemia. Our intent was to first present the concepts then accessible by physicians in Brazil and to next see how these concepts were molded to a Brazilian interpretation of the disease.³

These medical articles on sickle cell anemia often began by referencing the work published by physician James Bryan Herrick in the *Archives of Internal Medicine* in 1910. Although uncommon forms of blood cells were already the topic of analysis, the notion that sickle cells caused a disease was first voiced in this publication.⁴ The symptoms of fever, chronic and acute rhinitis, swollen lymph glands, cardiac alterations, and leg scarring were observed in a patient with sickle-shaped red blood cells. The patient's clinical exam was accompanied by hematological testing that detected chronic anemia, eosinophilia⁵, and the presence of elongated, sickle-shaped red blood cells. While James Herrick (1910) stressed that the observed set of clinical symptoms did not portray any disease documented in the literature, he asserted that the patient's hematological status was the key feature of his clinical profile.

After describing Herrick's article, it was customary to move on to R.E. Washburn's 1911 study of a clinical case greatly resembling Herrick's, particularly as far as his hematological profile (Washburn, 1911, cited by Cook, Meyer, 1915). An article by Jerome Cook and Jerome Meyer then followed, describing a clinical case similar to the others. It would next be suggested that these cases represented a specific disease, which was acquired hereditarily and whose emergence depended upon the presence of 'black blood' (Cook, Meyer, 1915).

After this history of sickle cell anemia would often come an explanation of the 1917 study of hematologist Victor Emmel, who devised a microscope technique for identifying sickle cells in bloods samples (Emmel, 1917). The historical description would close with articles by John Huck and by Virgil Sydenstricker and collaborators, both published in

1923, which suggested, respectively, that the disease was transmitted according to Mendel's laws, through a dominant character, and that it manifested in two phases, an active and a latent (Huck, 1923; Sydenstricker, Mulherin, Houseal, 1923).

While these studies did mention the key features ascribed to sickle cell anemia up until the early 1950s, we agree with Wailoo (1991, p.185) when he pinpoints the debate at the 75th session of the American Medical Association, held in June 1924, as a milestone in the history of the disease. Following an address by Professor Virgil Sydenstricker, with the University of Georgia's Medical Department, the discussion turned to who had first identified sickle cell anemia and what features should be considered specific to the disease – in other words, what features should be considered in diagnosing the disease.⁶

Although Sydenstricker's paper (1924), which described his research and the discussions that followed its presentation, was not cited quite so often in historical references, we have chosen to highlight it here because it was a road mark for subsequent research. The debate at the American Medical Association was a watershed in the history of sickle cell anemia, forging a consensus about the disease's specific characteristics, one that remained practically unchanged through the 1930s and 1940s.⁷ The most emblematic feature of the disorder was the sickle-shaped red blood cells, interpreted either as a sign of disease or as proof of a pathological yet asymptomatic condition. Since few argued that these red blood cells were benign, their role as agents or products of pathology was the subject of much discussion through the close of the 1940s.

During his talk before the American Medical Association, Sydenstricker (1924) pressed home his idea that sickle cell anemia could be divided into two phases: an active phase, signaled by a greater quantity of sickle cells in the blood as well as by the seriousness and variety of clinical symptoms; and a latent phase, corresponding to a low number of red blood cells in the blood and the absence of clinical symptoms. The disease's symptoms and clinical evolution were still a matter of debate, however, since its clinical manifestations had yet to be definitively delineated. Additionally, there was the challenge of determining what phase the person presenting sickle cells was in, and this meant it was impossible to make any prognosis about the disease.

Diagnosis was hampered by these question marks surrounding the hematological presentation of the disease and by the variety of symptoms, which were not specific and could mimic other illnesses. In 1935, Eldridge Campbell, a surgical resident at The Johns Hopkins Hospital, warned that physicians needed to be more aware of the clinical symptoms of sickle cell anemia, since many cases were misdiagnosed as appendicitis or some other illness responsible for abdominal pain (Campbell, 1935). Furthermore, a good share of the diagnostic efforts by doctors in the southern United States focused on diseases then of greater concern to the region, while sickle cell anemia was relegated to a secondary plane in epidemiological terms.⁸ Doctors were not familiar with the procedure used to visualize sickle cells, and so they analyzed blood to find the parasites that caused malaria, for example (Wailoo, 2001, p.64).

It was not only the issue of technique that kept the disease invisible. In the United States, it was a common notion that blacks were "a naturally diseased people" (Wailoo, 2001, p.56) and thus spreaders of disease. Interpretations of sickle cell anemia did not

deviate from this, since they were underpinned by the same theoretical framework. The explanation offered up by physicians Travis Winsor and George Burch (1945), of Tulane University's Department of Medicine, in Louisiana, is an example of this. Winsor and Burch used the varied clinical presentation of sickle cell anemia to reinforce the notion that black people supposedly had a propensity to disease:

Like syphilis, sickle cell anemia may present many clinical syndromes. Some of these are easily recognizable, while others may imitate many disease states such as rheumatic fever, tuberculosis, Hodgkin's disease ... Like syphilis, the disease may be so subtle as not to enter the mind of the clinician. *Because of the fact that sickle cell anemia is such a great imitator and because it may remain so subtle, it is necessary, again as in syphilis, to study the blood routinely for sickle cell anemia in all Negro patients.* ... As in the case of routine serologic examinations for syphilis, this has resulted in the unexpected discovery of many patients with sickle cell anemia (p.793; emphasis added).

The relation drawn between sickle cell anemia and syphilis reflects the belief not only that black people's bodies harbored disease but that their 'black blood' did so as well. In the case of sickle cell anemia, this link between the black race and the disease was even more significant because of the absence of a specific etiological agent, like the syphilis bacteria, and because of the presence of a blood alteration believed intrinsic to the organism. A hereditary disease that occurred almost solely among blacks made for a more convincing argument than the incidence of any other kind of disease within this racial group (Tapper, 1999, p.14).

We find this association between sickle cell anemia and people classified as black right from the outset of the process to characterize the disease⁹, and it was always mentioned in scientific papers. In the late 1920s, according to Tapper (1999, p.16-28), the release of articles identifying sickle cells in the blood of white people fueled debates over the disease's alleged racial specificity. From that point forward, many studies adopted criteria for delimiting race, such as the analysis of physical features and research into family ancestors, all in an effort to identify a black heritage among carriers of such cells (Castana, 1925; Archibald, 1926; Cooley, Lee, 1929; Rosenfeld, Pincus, 1932; Lawrence, 1927; Cook, Mack, 1934; Haden, Evans, 1937; Ogden, 1943). It is worth reiterating that this focus on the observation of sickle cells in whites was intended to tease out a hidden black ancestry.

Yet detecting sickle-shaped cells in whites did not shake the widespread belief that the disease was racially specific. To the contrary, the effort then shifted to calling into question the racial purity of the 'white' person presenting sickle cells. A fine example is found in a discussion by two physicians at New York's Brooklyn Jewish Hospital, Samuel Rosenfeld and Joseph Pincus (1932), concerning the presence of sickle cells in the blood of three generations of a white family. Although they in principle agreed that sickle cells could be found in 'white blood,' we see them retreating at the end of their argument:

since it is known that the sickling trait is a dominant character in its hereditary transmission and since interbreeding between the colored and the white races is more or less constantly taking place in many regions, including this country, we may in future generations expect the presence of this peculiar blood trait in an increasing number of apparently white descendants. Because of the tendency to deny such descendancy by those who are free of

all Negro features, no history will be obtained of such racial origin in affected individuals, *thereby increasing the number of apparently pure white cases of sickle cell anemia* (p.681; emphasis added).

The use of sickle cells as racial markers belonged to a period when other blood characteristics were also used to identify and compare human races. At the time, blood groups were accepted as inherited characters, believed to be distributed across races at different rates (Schneider, 1983).¹⁰

In 1937, William Warrick Cardoso, pediatrician at Provident Hospital in Chicago, published a study that sought to verify the relation between sickle-shape erythrocytes and a specific blood group (Cardoso, 1937, p.627-628). So research into sickle cells was not limited to clinical studies. The possibility of using these as racial markers reshaped the history of the disease, as evident in anthropological research exploring a number of questions, such as the differences between blacks in Africa and the United States (Tapper, 1999, p.34). In the next section, we will see how scientific research conducted in Africa first sought to establish whether sickle cells were specific to the black race. Once this correlation had been established, investigations turned to elucidating the differences between rates of sickle cell anemia among African and U.S. blacks.

The racial specificity of sickle cells in Africa

In the wave of genetic and anthropological studies based especially on blood group rates, research was done on the rate of sickle cells in tribal groups in different regions of Africa, as a way of better understanding ancestry (Singer, 1953; Hiernaux, 1955). The late 1940s saw an abundance of research on sickle cells in French, Portuguese, Belgian, and British colonial Empires in Africa (Evans, 1944; English, 1945; Findlay, Robertson, Zacharias, 1946; Robertson, Findlay, 1947; Gosden, Reid, 1948; Beet, 1949; Lehmann, Raper, 1949; Van den Berghe, Janssen, 1950; Hiernaux, 1952; Jelliffe, Humphreys, 1952; Lehmann, Cutbush, 1952; Foy, Kondi, Hargreaves, 1952; Singer, 1953; Foy et al., 1954).

The idea that the disease had originated in Africa was not embraced straightaway. In a 1942 article published in the journal *África Médica*, Carlos Trincão, chief of Laboratory Analyses at Lisbon's Civil Hospitals, suggested that the few studies done in Africa had not yet proven that sickle cells were specific to blacks. He added that the number of whites identified as presenting sickle cells surpassed that of African blacks (Trincão, 1942). For Foy and collaborators (1954), for example, the racial specificity of sickle cells remained in question, although by that time more than fifteen statistical surveys had been conducted among African populations, revealing a high incidence of sickle cells.

The earliest research in Africa was aimed first at confirming or refuting the hypothesis that sickle cells, along with the disease deriving from them, were inherent to members of the black race. This specificity was accepted subsequent to statistical studies¹¹, and research moved to investigate differences in the presentation of sickle cell anemia between African and U.S. blacks. Most studies reported high rates of sickle cells, reaching as much as 20% to 40% in some populations.

In 1950, physician Alan B. Raper (1950, p.52) of Kampala Medical Laboratory in Uganda suggested that miscegenation, especially with whites, had resulted in a greater number of cases of this disease in the United States. That same year, a Philadelphia physician by the name of John H. Hodges (1950, p.809) also argued that the mixing of the races had boosted the incidence of 'sickling' among U.S. blacks. In a 1952 editorial, the *British Medical Journal* also raised the hypothesis that interbreeding with whites had boosted the rate of this type of anemia in the United States (Editorial, 1952, p.427).

Prior to this African research, in an article published in the U.S. journal *The Archives of Internal Medicine*, Diggs, Ahmann, and Bibb (1933) had suggested that miscegenation pushed up the rate of sickle cell trait among blacks. They posited that lighter-skinned people presented a higher rate of incidence while those with dark skin presented the lowest rates (p.774). From these conclusions came the conjecture that even though sickle cells were hereditary, the condition could also be brought on by miscegenation with 'white blood.'

Findings from studies done in Africa were used in the United States in the effort to establish differences between African and U.S. blacks. For Tapper (1999, p.31-34), this was the goal of the research program known as anthropathology, a term coined by physician Julian Lewis. It was believed that by identifying racial differences in susceptibility to diseases, these differences would be less perceptible than those already pinpointed by traditional anthropology, and sickle cell anemia was one of its focal points. It was thought that this new methodology would enhance both racial classification and the determination of ancestral background. The interpretation that more Africans displayed the sickle cell trait and that more U.S. blacks had sickle cell anemia dovetailed perfectly with the widespread notion in the United States that black and white miscegenation led to physical degeneration, including the emergence of disease.

During the first decades of the twentieth century in the United States, sickle cell anemia fit into the following interpretative framework: it was specific to the black race; it was detected through observation of sickle cells in the blood and associated with a varied gamut of symptoms; and it manifested in two phases: active and latent. Moreover, it is worth emphasizing the belief that miscegenation influenced the epidemiology of the disease by increasing the cases of sickle cell anemia in the active phase. Although in Brazil it was also thought that blacks were more prone to certain pathologies, there were marked differences between the views of U.S. physicians and their Brazilian peers.

Blood, race, and sickle cells in Brazil, 1930-1940

The first Brazilian article on sickle cell anemia was written by physician Álvaro Serra de Castro¹² and published in the *Jornal de Pediatria* in 1934.¹³ The article presents five clinical cases taken from studies conducted at São Francisco de Assis Hospital in Rio de Janeiro. Although Castro (1934) offered no statistical data on his findings, he presented the results of systematic analyses of eighty black children that were part of his search for sickle cells, thereby qualifying his paper as one of the first studies on the incidence of sickle cell anemia in Brazil.

Between 1935 and 1940, four articles on sickle cell anemia appeared in the Brazilian literature, all stemming directly or indirectly from Álvaro Serra de Castro's findings. In 1935, Arcanjo Penna de Azevedo, a pathologist at the Oswaldo Cruz Institute, published a brief exposition on the autopsy of one of Castro's patients; two years later, he released another histological study of a sickle cell carrier (Azevedo, 1935, 1937). In 1939 and 1940, two medical interns belonging to the same team as Serra de Castro published papers on hereditary anemias, which included reference to cases of sickle cell anemia (Azevedo, 1939; Santos, 1940).

Most physicians studying sickle cell anemia in Brazil in the 1930s and 1940s saw it as an important disease in terms of the country's public health problem given the large population of blacks and mestizos, an argument that in fact served as a justification in selecting the topic for research (Castro, 1944; Capriglione, 1945; Ballvé, 1946; Carini, 1946; Frimm, 1947; Costa, 1949; Jahara, 1949; Carvalho, 1949). As part of his qualifying exam to become a *livre-docente* (full professor) of Medical Pediatric Practice at the National Faculty of Medicine (Faculdade Nacional de Medicina – FNM), Álvaro Serra de Castro (1944, p.10) stressed that sickle cell anemia represented a “medical and social problem” for Brazil, since a large share of those affected by it, i.e., blacks, were considered “the country's great human mass.” In an article in the journal *O Hospital*, Gastão Rosenfeld (1944, p.846) asserted that the “lower economic and cultural level” of Brazilian blacks hampered their access to hospital care and therefore contributed to the scarcity of studies on sickle cell anemia in Brazil.

We believe there was little knowledge of sickle cell anemia among Brazilian physicians, save for some pediatricians and hematologists, with this lack of information extending to its very existence as a disease. Sickle cell anemia was difficult to diagnose because of its non-specific clinical symptoms and doctors' unfamiliarity with the necessary hematological exam, known as the Emmel test.¹⁴ A number of publications called attention to the challenge of diagnosing the disorder (Capriglione, 1945, p.58; Castro, 1944, p.76; Jahara, 1949, p.322; Nunan Filho, 1949, p.77; Rocha, 1946, p.61-62; Rosenfeld, 1945, p.120), such as an article by the physician Antonio Carini (1946, p.103), scientific director of the Paulista Biology Laboratory (Laboratório Paulista de Biologia – LPB), an important institution founded in 1912: “it is our understanding that here in Brazil, where there is a large percentage of blacks and mestizos, laboratory technicians must be able to recognize this hematological feature and be quite familiar with the technique required to discover latent cases.”

Brazilian physicians' lack of familiarity with the disorder is also evident in Carlos Estevão Frimm's medical thesis.¹⁵ Frimm (1947, p.4) said he had taken an interest in the topic because such a large number of cases were available and gaps had been left to fill in: “The study of Drepanocytosis has a history of only 37 years, and many of its chapters are still largely open to original contributions of great importance. Scholars in our country thus have an excellent opportunity to help refine understanding of this morbid state, thereby enhancing the merits of Brazilian medical science while also contributing to alleviating a malady found in a large share of the world's population.”¹⁶

Although there was little awareness of the existence of the disease, the physicians working on it were in contact with each other and often exchanged research material. Doctors found that their main motivation for studying sickle cell anemia came from working with outpatients, where they encountered clinical cases of the disease. Hematologists, for their

part, were concerned with studying blood disorders, while other scientists were concerned with the relations between race and disease, keeping in step with a widespread interest in Brazil. The latter group was comprised mainly of those devoted to statistical studies of the incidence of the disorder in Brazil. In the 1940s, such surveys often appeared in articles and theses on sickle cell anemia. The incidence of the syndrome was evaluated based on the racial classification of those studied.

The first Brazilian paper presenting statistical data on the incidence of sickle cells was published in August 1942 by Captain João Maia de Mendonça, an Army doctor and hematologist with the Army Institute of Biology (Instituto de Biologia do Exército – IBE) in Rio de Janeiro. Adopting the nomenclature proposed in Edgard Roquette-Pinto's "Notas sobre os tipos antropológicos do Brasil" (1928), Mendonça separated 1,045 individuals into *melanodermos* (blacks), *faiodermos* (descendants of blacks and whites), *xantodermos* (descendants of whites and Indians), and *leucodermos* (whites). He further sub-divided melanodermos and faiodermos into three groups, based on "pigment distribution": light, medium, or dark (Mendonça, 1942). In this racial classification, the descendants of blacks could therefore display grades of black ancestry, as manifested in their skin tone.

In this particular study, Mendonça (1942) wanted to identify the proportion of *meniscocitêmicos* (see Table 1), that is, healthy carriers of sickle cells. He found: (a) no cases among the thirty *xantodermos*, and 0.99% of cases among *leucodermos* (six *meniscocitêmicos* out of a total of 598); (b) sub-divided into light, medium, or dark pigmentation, 2.4%, 9.5%, and 7.4% of *faiodermos* carried sickle cells; and (c) likewise divided into light, medium, or dark pigmentation, *melanodermos* presented 7.1%, 9.8%, and 11.3% (p.384).

In 1944, Mendonça published a second study, motivated, according to him, by the discrepancies between his previous findings and those of U.S. authors Huck (1923) and Diggs, Ahmann, and Bibb (1933). He disagreed with Huck about the notion that the sickle-shape characteristic of red blood cells was transmitted in accordance with Mendel's laws, through a dominant character. For Mendonça (1944, p.83), the absence of positive cases among *leucodermos* was in contradiction with "the great interbreeding that has taken place in Brazil." The second point of disagreement derived from the finding that *meniscocitemia* was more common among *melanodermos* and *faiodermos* with darker skin tones, contrary to what Diggs, Ahmann, and Bibb (1933) had observed, that is, a higher incidence among lighter-skinned blacks.

In his second study, Mendonça obtained an incidence of 0.15% for his group of *leucodermos*, a result he still deemed inconsistent with Brazilian reality; he had expected to find more *leucodermos* with sickle cells in their blood owing to the "great interbreeding" of the people of Brazil. Mendonça's two studies were guided by the issue of miscegenation, with a larger number of *leucodermos* chosen, unlike any other Brazilian study. Out of all 1,974 people analyzed in the two studies, 1,232 were *leucodermos*, with a *meniscocitemia* rate of 0.56%. He also continued to contrast his results with those of Diggs, Ahmann, and Bibb (1933), asserting that people with more mixed blood displayed a lower proportion of sickle cells. He obtained the following percentages in his second study: *faiodermos*, 1.24% (light), 9.09% (medium), and 6.26% (dark); *melanodermos*, 4.76% (light), 3.70% (medium), and 9.09% (dark).

Table 1: Nomenclature adopted in Brazilian studies of sickle cell anemia in the 1930s and 1940s

Disease caused by sickle cells	<i>Anemia falciforme</i> (Sickle cell anemia)	<i>Anemia drepanocítica</i> (Drepanocytic anemia)	<i>Eritrofalcemia ativa</i>	<i>Anemia meniscocítica</i>
	<i>Falcemia, siclemia</i> (Sickle cell anemia, sicklemia)	<i>Drepanocitemia</i> (Drepanocytemia)	<i>Eritrofalcemia latente</i> –	<i>Meniscocitemia</i> –
Condition of carrying sickle cells	<i>Síndrome falciforme</i> (Sickle cell disorder)	<i>Drepanocitose</i> (Drepanocytosis)	<i>Eritrofalcemia</i> –	<i>Meniscocitose</i> –
Red blood cells	<i>Hemácias falciformes</i> (Sickle cells)	<i>Drepanócito</i> (Drepanocyte)		<i>Meniscocito</i> –
Healthy individual presenting sickle-shaped red blood cells	<i>Siclêmico</i> (Sickleemic)	<i>Drepanocitêmico</i> –		<i>Meniscocitêmico</i> –
Sick individual presenting sickle-shaped red blood cells		<i>Drepanocitanêmico</i> –		<i>Meniscocitanêmico</i> –

N.B.: These terms are found in publications by Castro (1944), Capriglione (1945), Silva (1945a, 1945b), and Frimm (1947).

Miscegenation proved an issue to be addressed in Brazilian studies of sickle cell anemia in the 1940s. In a review of the medical thesis of Rio Grande do Sul physician Carlos Estevão Frimm, Maia de Mendonça (1948) stressed his argument that miscegenation could prevent transition from the latent to the active phase and thus influence the epidemiology of sickle cell anemia in Brazil. For Mendonça, contrary to what was argued in the United States, miscegenation could be a viable way of preventing sickle cell anemia.

The suggestion that sickle cell anemia was on the decline in Brazil because of miscegenation is in line with the ideology of *branqueamento* ('whitening'), a notion dating to the nineteenth century that posited that the biological interbreeding of whites and blacks would lead to a predominantly white society (Skidmore, 1976; Santos, 2010). In the case of sickle cell anemia, mixing with whites could actually help eliminate a disease.

Miscegenation could also supposedly explain why it was impossible to ascertain the incidence of sickle cell carriers based on, for example, a projection of black people in the country (Mendonça, 1948). In his thesis, Carlos Estevão Frimm (1947, p.127) calculated that 1,051,579 people in Brazil were sickle cell carriers, based on the number of 'persons of color' identified in the 1940 census.

The lengthy medical thesis by Frimm (1947) contains 11 chapters on such topics as clinical and hematological symptoms of the disease, forms of prevention, and racial distribution. Conducted in 1945, Frimm's research on the incidence of drepanocytosis in Rio Grande do Sul was based on 250 blacks and *pardos* (mixed-race) from Porto Alegre's

Santa Casa de Misericórdia hospital and the Asilo São Benedito orphanage for girls. Sickle cells were detected in eight patients from Santa Casa and in three girls from the orphanage. With a view to studying the relation between the active and latent phases of the disease, Frimm chose both sick and healthy people for his groups. At the suggestion of Ernani Silva, he also did research among Indians at the Nonoai Indigenous Post (Posto Indígena de Nonoai) in Rio Grande do Sul as a further contribution to studies on the racial origin of the disease (p.145). Besides looking for sickle cells, Frimm ascertained the blood types of the 101 Indians at the Nonoai Post.

João Maia de Mendonça's 1948 comments on Carlos Estevão Frimm's thesis show how U.S. medical knowledge on sickle cell was selectively applied to the Brazilian context. In his medical thesis, Frimm (1947, p.127-128) calculated the number of Brazilians with sickle cells in their blood based on statistics from Brazil's 1940 census (which gave the number of "individuals of color" residing in the country) and also on U.S. data, the latter indicating the proportion of sick to healthy sickle cell carriers. Using this method, Frimm concluded that "the Brazilian population had 1,051,579 *people with Drepanocytemia* and, of these, 52,579 had *Drepanocytic Anemia*, that is, the disease itself" (p.128; emphasis in the original). When Mendonça (1948) reviewed Frimm's thesis in *Revista Brasileira de Medicina*, he stated that this projection was not corroborated by other Brazilian authors, himself included, who argued that "in Brazil, interbreeding may have attenuated or altered the still unknown factors that transform a *drepanocitêmico* [carrier of the sickle cell trait] into a *drepanocitoanêmico* [carrier of sickle cell anemia]" (p.553). The suggestion that miscegenation was leading to a decline in sickle cell anemia in Brazil shows how something deemed detrimental to the population in the early twentieth century had been transformed into a possible aid in eliminating a pathology.

The bulk of research on the rate of sickle cells across different racial groups grew out of outpatient work at big city hospitals. In *Brazil-Medico*, Abdon Hermeto and Oswino Penna Sobrinho (1945), physicians at the Clinical Research Laboratory at São Vicente de Paulo Hospital in the city of Belo Horizonte, gave the rates of drepanocytemia for a group of two hundred children: it was found in 8.33% of blacks, 5.37% of mulattoes, and in none of 72 whites.

As a hematologist with the Medical and Surgical Pediatric Clinics at the Belo Horizonte Faculty of Medicine (Faculdade de Medicina de Belo Horizonte), Oswino Penna Sobrinho was also involved in the research on the incidence of sickle cells conducted by pediatrician Berardo Nunan Filho (1949) as part of the latter's qualifying thesis for the chair in Pediatrics at the faculty. Tests indicated sickle cells were present in 21 of 230 "black and mestizo" children, three of thirty mothers, and none of thirty white children (p.20).

In 1946, in the city of São Paulo, J. de Moura Andrade and L. Amato investigated sicklemia (see Table 1) in 330 blacks and mestizos, 209 of which were hospitalized; they found a 4.8% incidence of sicklemia but only one actual case of sickle cell anemia (cf. Araujo, 1961, p.90). In the state of Bahia, physicians Álvaro Pontes Bahia, João Pedroza Cunha, and José Peroba (1949) performed blood analyses on five hundred children at a clinic of the Bahian League Against Infant Mortality (Liga Bahiana Contra a Mortalidade Infantil). Like hematologist João Maia de Mendonça, the physicians in Bahia used Roquette-

Pinto's racial categories. The children were racially divided as follows: 146 *melanodermos* (blacks), whose incidence of sickle cells was 0.8%; 304 *faidermos* (descendants of whites and blacks), with an incidence of 1.4%; and fifty *leucodermos* (whites), who showed no indication of sickle cells (p.233).

The number of studies attempting to establish incidence rates among those with the disease and those presenting sickle cells in their blood were fewer in number. At the hospital Santa Casa de Misericórdia de Santos, physicians Edmir Boturão and Edgard Boturão (1947) published the results of blood tests on 358 hospitalized patients, divided into 64 whites and 294 blacks. The purpose was to elucidate active forms of the disease, whose incidence was still unclear in Brazil, according to these doctors. However, the article confined itself to analyzing the relation between race and "disease by sickle cells" (understood to be the presence of such cells regardless of symptoms). The number of people with sickle cells totaled 6.8%, with blacks and mulattoes presenting rates of 8.6% and 4.5%.

As with statistical research, the purported racial specificity of sickle-shaped red blood cells comes up often in other studies consisting basically of descriptions of clinical cases. Some publications call this specificity into question, such as an article by Arcanjo Penna de Azevedo (1935), who did not regard sickle cell anemia as an "innate feature of [the black] race" (p.1182). In a lengthy article appearing in *Arquivos de Clínica*, Luiz Capriglione (1945) had something different to say on the subject. Although he included an "ethnological exam" as part of his clinical analyses, Capriglione underscored the ideas of Italian physician L. Pontonti, who was skeptical about the assertion that sickle cell anemia was a disease of blacks alone (p.14). Like Portuguese physician Carlos Trincão, Capriglione suggested that in the absence of data from black Africa, no assertion about any racial specificity could be made about the sickling of red blood cells. He also wrote: "For a long time, European hematologists did not concern themselves with this unique morbid process. Studies from the United States made it specific to the black race, and so only hematologists and clinical doctors from regions that are home to this racial element have devoted themselves to its study" (p.14).

As we saw earlier, little research on sickle cell anemia had been conducted in Africa prior to 1945, and in Brazil this cast doubts on what U.S. physicians had to say, since their Brazilian peers considered them racist. Given the abundance of data from the United States and the absence of data from Africa – considered the place of black people's origin – it was hard to definitively assert that the disease was racially specific. In turn, this lingering doubt fed the persistent Brazilian idea that sickle cell anemia was heavily influenced by miscegenation. We can observe this lack of definition about the presence of the disease among whites in an article published in the *Jornal de Pediatria* by Asdrúbal Costa (1949), pediatrician at the University of Brazil's Institute of Child Health (Instituto de Puericultura, Universidade do Brasil):

However, is drepanocytosis found only among blacks or mixed-race blacks? *This question has yet to be satisfactorily settled.* ... Even if we allow that *falcemia* is restricted to blacks and Negroid mestizos, clinical evidence leads us to state that amongst us we should not exclude the hypothesis of drepanocytosis occurring in an apparently white person, presenting hemolytic anemia. ... Ever since the earliest days of the formation of the Brazilian

people, there has been frequent miscegenation between Caucasians and Negroids (p.72, 77; emphasis added).

The conviction that miscegenation played a role in the epidemiology of sickle cell anemia in Brazil, plus the failure to prove that the disease was racially specific, left Brazilian physicians with uncertainties and hampered their efforts to define the disease. In the next section, we will see how investigators began searching for sickle cells among indigenous populations in their attempts to clarify the question of a correlation between sickle cell anemia and the black race. It was believed that these doubts could be eliminated by conducting research among isolated population groups. The hematologist Ernani Silva¹⁷, of the IOC, was the first in Brazil to undertake studies to identify sickle cells in indigenous populations; he also inaugurated research that incorporated concepts from anthropology in interpreting sickle cell anemia in Brazil.

From medicine to anthropology: Ernani Martins da Silva's research program

Of the physicians and scientists carrying out statistical surveys on the incidence of sickle cell anemia in Brazil in the 1940s, Ernani Silva, scientist from the Oswaldo Cruz Institute's Hematology Section (Seção de Hematologia) was the leading representative of anthropological research on the disease in this country. By Brazilian anthropological research into sickle cell anemia, we mean studies on indigenous populations, on populations not residing in urban centers, and on non-hospitalized people conducted with the sole objective of investigating the relation between disease and race.

Ernani Silva was with the IOC's Hematology Section throughout the 1940s, where he did all his hematological work. The section was devoted to studying the processes involved in blood production and regeneration, especially the symptom of anemia. Implemented by section head Walter Oswaldo Cruz¹⁸, this research was meant to "draw a hematological map" of Brazil (Cruz, 1939, p.280). The main goal was originally to study the relation between parasites, changes in blood components, and diet, but blood tests were soon broadened to include other indices as well.

Based on measurements of the presence of sickle cells and the racial distribution of blood groups, Ernani Silva developed a hematological anthropology of Brazilian 'racial types.' The logic behind the studies was to identify 'pure' white, black, or indigenous groups as well as mixed groups. Brazilian studies on blood groups had begun in the 1920s and were especially concerned with proving paternity and identifying populations in racial terms. In the 1930s, this research expanded and was used in legal medicine as a way of identifying people (Faria, 1952).

Studies conducted on the racial distribution of blood groups help us understand how the definition of blood influenced the day's medical understanding of sickle cell anemia (Ribeiro, Berardinelli, Roiter, 1934; Fávero, 1935; Biocca, Ottensooser, 1944; Silva, 1948d; Silva, 1949; Ottensooser, Pasqualin, 1949). Back then, Brazilian medical thought assumed that a person's heredity was determined by a combination of blood types from his ancestors, according to the so-called theory of blood mixture (Dreyfus, 1947, p.776). This theory underpinned Ernani Silva's work, in which he measured the proportion of miscegenation

based on a mathematical formula devised by physician Fritz Ottenssooser¹⁹ from the LPB. An individual's racial mixture was calculated based on blood group frequency, which was the way of ascertaining if someone belonged to a 'pure' group and of ascertaining the proportion of white, indigenous, or black blood in the case of mestizos. Ottenssooser's formula stands as an example of the theory of blood mixture, as it draws a relationship between a blood characteristic and a person's racial origin.

As part of their professional relationship, Fritz Ottenssooser and Ernani Silva also shared data on the blood groups of indigenous populations (Ottenssooser, Pasqualin, 1949). In a 1944 article on blood groups in Indians, Ottenssooser and the physician and anthropologist Ettore Biocca²⁰, both of whom worked at the LPB, averred that examinations of blood characteristics were more precise than the ones anthropology used in the racial classification of individuals, like skin color and nose shape. They argued that although all four blood groups (A, B, AB, and O) were found in most peoples, the only difference being the incidence of each, other blood characteristics could decrease doubts about racial classification (Biocca, Ottenssooser, 1944, p.113).

In 1945, Ernani Silva published his first paper on sickle cell anemia, in which he suggested that sickle-shaped red blood cells could be used as parameters for racial classification in the fields of anthropology and ethnography (Silva, 1945a, p.329-331). He believed that once it had been established that sickle cells were a determinative feature of the black race, hematological testing to detect these cells could serve as yet another tool for studying black heritage, alongside research on blood group distribution and other classification methods used in physical anthropology. Furthermore, from Ernani Silva's view, hematological analyses could be joined with other research then available on the topic, conducted by anthropologists Nina Rodrigues, Arthur Ramos, and Melville Herkovits.

According to Ernani Silva (1945a), 1,374 sickle cell tests were done on individuals and on autopsy material at the IOC, with the following results: sickle cells were found in 63 of the 610 samples of autopsy material (10.2%); in 93 of the 890 people in the "Negroid ethnic group" (10.4%); in 11 of the 140 people in the "Negroid-Caucasian ethnic group (mulattoes)" (8%); in 9 of the 100 in the "Negroid-Caucasian-Mongoloid group" (9%); in none of the 120 in the "Caucasian ethnic group"; and none of the thirty in the "Mongoloid ethnic group." The scientist also researched 88 people from 12 families and found sickle cells in 19% of them (p.320).

As stated earlier, doubts remained about the racial specificity of sickle cell anemia. Part of the effort to put an end to these was the search for sickle cells in "groups clearly displaying no miscegenation with Negroid elements" (Silva, 1945a, p.331). Since it was believed that certain indigenous communities still remained isolated, one way of investigating the racial specificity of red blood cells would be to search for sickle cells among these groups. In his medical thesis, Carlos Estevão Frimm (1947, p.145) was clear about his goal in investigating indigenous groups: "the first section of this study stressed ... our interest in ascertaining whether there is an incidence of Drepanocytosis among 'pure' Indians, for such findings may afford a valuable contribution to the issue of the exclusive Negroid racial incidence of the disorder under study." In blood analyses of 101 indigenous of "*caingangue* and *guarani*" ethnicity, Frimm found no sickle cells (p.152).

From 1945 to 1947, Ernani Silva traveled to Brazilian states and federal territories (Maranhão, Amapá, Mato Grosso, and Pernambuco), collecting blood from different population groups, mainly indigenous ones, in hopes of ascertaining the racial distribution of blood groups and detecting the presence of sickle cells. He published the results of these trips in a number of articles (Silva, 1948a, 1948b, 1948c, 1948d, 1949).

Ernani Silva's article with his findings from blood analyses that were performed to identify sickle-shaped cells was published in the journal *Science* in February 1948, including a table showing the number of indigenes examined, their respective ethnic origins, and research locations. Blood tests were done on 1,545 indigenes distributed among the following ethnic groups and locations: Pariukur, Galiby, Caripuna, Crossing intertribes, and Emereillon, in Amapá; Canella (Ramkókamekra), Apinayé, Crossing Canella-Apinayé, and Guajáára, in Maranhão; Tereno, Cayá, Caduéo (Guaycurú), Guarany, Laiano, Quinquinau, and Crossing intertribes, in southern Mato Grosso; Boróro, in northern Mato Grosso; and Fulniô (Carnijó), in Pernambuco. Three 'sickleemics' were found among the Fulniô, which, in the scientist's words, was a "highly miscegenated tribe"; another four sicklemics were of "Tereno Indian, white, and black" descent in the indigenous villages of Taunay and Lalima, in Mato Grosso (Silva, 1948a, p.221).

In Ernani Silva's other articles, his ethnological interpretations based on hematological data show that the cultural and biological dimensions of the term race were being confused. Many of the anthropology works referenced in his studies served to provide information on the culture of indigenous populations and to underpin his conclusions about the degree of contact these people had had with non-indigenous populations (Silva, 1948b). Thus, he determined the miscegenation or racial purity of indigenous groups based on his blood and ethnographic analyses. Photographs of indigenes with their utensils and in typical dress are accompanied by tables of hematological data, illustrating how miscegenated or pure they were (Silva, 1948d). The idea of racial purity vs. miscegenation thus embraced biological notions (represented by blood analyses) as well as sociocultural notions (represented by their preservation of habits and customs). Combining a broad range of perspectives, from physical characteristics to the analysis of the culture of groups classified as blacks, Ernani Silva's approach to sickle cells from an anthropological perspective reflected theoretical and methodological changes that took place in the 1930s, when social scientists gradually shifted the importance of the concept of race to the concept of culture in their endeavor to understand race relations in Brazil.

Ernani Silva's pioneer work in Brazil, which blended research on the racial distribution of blood groups with the rate of sickle cells and correlated these findings with the anthropological literature, drew him closer to the field of anthropology. His place among anthropologists was firmly established with the publication of papers in specialized journals such as the *American Journal of Physical Anthropology* and *Revista do Museu Paulista* and with his 1946 lecture before the Brazilian Society of Anthropology and Ethnography (Sociedade Brasileira de Antropologia e Etnografia) at the invitation of the anthropologist Arthur Ramos (Azeredo, 1986, p.194). What sparked anthropologists' interest was Ernani Silva's idea that sickle cells could be used to study blacks in Brazil.

Based on anthropological studies, Ernani Silva became spokesman of the idea that sickle cells and the disease they caused displayed epidemiological features in Brazil that were distinct from those seen in the United States, owing to the distinct social make-up of Brazilian blacks. The underlying assumption was that greater miscegenation had taken place in Brazil, something he had proven with his own hematological research and his anthropological observations.

Ernani Silva did blood analyses on a variety of populations around Brazil, classifying them as Indians, whites, blacks, or mestizos. This initiative shaped a research program that sought to ascertain the degree of miscegenation within Brazilian populations by means of hematological analysis. The program undertook studies and recruited physicians and scientists to work on the topic. The physician Carlos Estevão Frimm, for example, went to the IOC to receive Ernani Silva's guidance in his studies among indigenous populations in Rio Grande do Sul, while Luis Capriglione obtained a good share of his bibliography from Ernani Silva. This type of scientific exchange also traveled abroad, with Ernani Silva's findings appearing in *Science* and in *Genetics and the race of man*, by William Boyd.²¹

Carlos Estevão Frimm embraced the suggestion to link hematological and anthropological knowledge, including in his research the examination of indigenous populations of Rio Grande do Sul. Like Ernani Silva, he also compared hematological rates with his ethnological observations of the populations under study, and his thesis includes photographs of the indigenes he observed. As mentioned before, the point of researching indigenes was to confirm that sickle cells were specific to blacks, while simultaneously assessing miscegenation. So despite all the misgivings about the racial specificity of sickle cells, these cells underpinned research, as Frimm (1947, p.27-29) explains:

The Brazilian cultural anthropological school has made a valuable contribution, in that many of the elements involving blacks are more clear-cut now than ten years ago. ... We must mention in the first place professors Nina Rodrigues and his heir Arthur Ramos; the latter shall serve as the basis of concepts to be expounded upon regarding the origin and acculturation of blacks. ... Relatively recent data from African paleontology and paleoethnology indicate that our conceptions about the origin of African blacks are not yet firmly grounded. ... For the purposes of studying Drepanocytosis, it would be most interesting to establish parallels between the incidence among African blacks and those brought to the Americas several centuries ago.

In the 1930s, a renewed interest in Brazilian topics put the black question in the spotlight among intellectuals, in part because blacks were being valorized in such socio-anthropological studies as Gilberto Freyre's *The masters and the slaves*. If the black had been viewed as a dissonant element within the Brazilian population in the early twentieth century, he was viewed as a constituent part of national identity starting in the 1930s and represented a counterpart to the threat of 'cultural degeneration' posed by the large number of immigrants to Brazil (Corrêa, 1998, p.266-271).

The research program drawn up by Ernani Silva pointed to methods of analysis and also predicted what problems would be encountered in studying a disease like sickle cell anemia. He believed miscegenation was a distinguishing feature of Brazil and also of the

epidemiology of sickle cell anemia in the country. For Ernani Silva, miscegenation hampered the possibility of arriving at a trustworthy estimate of the frequency of sickle cells.

According to Ernani Silva (1945a, p.327), problems identifying sickle cell carriers would be overcome through the widespread application of blood tests. On top of the question of miscegenation, the scientist added two more obstacles to the achievement of a reliable estimate: the hereditary nature of the disease could lead to an overestimation of its incidence, while the internal migration of blacks could also interfere, either by inflating or deflating the true numbers. One of his articles presents a map of the main places where blacks were greater in number, such as Brazil's sugar-producing Northeast. For him, the migration of blacks, especially to Brazil's large urban centers, should be taken into account when analyzing the results of sickle cell tests (p.329).

Another argument that spoke in favor of establishing surveillance methods and systematic identification of sickle cell carriers was the differentiated patterns of racial classification presented in the United States, Cuba, Colombia, and African nations or colonies. Blacks in the United States were identified on the basis of their African heritage, thus including even those who appeared to be white, whereas Brazil's classification defined blacks by their physical appearance; therefore, any comparison would be impossible given these dissimilar parameters, in the argument of Ernani Silva (1945a, p.324).

Any estimate of the presence of sickle cell anemia in the Brazilian population was thus flawed not only because of miscegenation but also because research findings here could not be compared with those from other countries, given differences in racial classification. Since the disease was assumed to represent a public health problem, because of the large number of blacks in Brazil, Ernani Silva (1945a, p.327) suggested the following measures:

- a) taking a census of sickle cell individuals and mandating that this information appear on identification cards;
- b) the systematic application of sickle cell tests on newborns;
- c) surveillance of sickle cellemics, including their mandatory appearance before public health authorities periodically (most especially when the first signs of the disease presented themselves), and inclusion of sickle cell testing as part of the biological evaluation required during pre-nuptial testing.²²

This concern with locating all sickle cell carriers came on the heels of alarming statements about the alleged ability of sickle cell anemia to spread among the Brazilian population. When Ernani Silva (1945a, p.328) says that "a sickle cell person should be considered potentially sick (an apparently healthy carrier) and [it is] even possible to compare him to a carrier of the germ, in the sense used in the prevention of infectious diseases," what we have is the image of the sickle cellemic as a threat to public health in Brazil.²³ And he was adopting the negative eugenics perspective (Stepan, 1991, p.103) when he proposed state surveillance of carriers of sickle cell anemia, an outlook visible in his pre-nuptial testing proposal, for example.

Another argument favoring the systematic application of sickle cell testing in Brazil was that it might enhance understanding of the relation between healthy and sick carriers of sickle cells, about which there was still no consensus. We can easily perceive clinical concerns mixing in with the issue of racial interference in the prognosis and dissemination of the

disease when we look at explanations on prevention and treatment, exemplified in the suggestion about pre-nuptial testing found in the doctoral thesis of Carlos Estevão Frimm (1947). In the following excerpt, we once again find a comparison with the United States:

Individual statistical confirmation of Drepanocytemia should be undertaken with only the well-being of our colored population in mind. *We should not, however, view this problem in the exaggerated fashion of certain U.S. authors, who, regarding the topic from a solely racist point of view, see Drepanocytosis as yet another argument, this time a biological one, for justifying the drafting of laws aimed at banning marriage between whites and blacks.* In refutation of these ideas, we should not forget that all races have their own characteristic diseases and if blacks transmits sickle cells to Caucasians, the latter have in exchange passed on to the former a substantially higher number of morbid entities (p.128; emphasis added).

Frimm's critique of more radical negative eugenics shows how the racial dimension of sickle cell anemia held heavy sway in perceptions of the disease. Although Frimm and Ernani Silva were somewhat in agreement about the question of pre-nuptial testing, the latter put forward suggestions about reproductive control over sicklemics, arguing that blacks were starting to migrate to major centers and that sicklemics, who were for the most part black, would spread the disease. Frimm's and Ernani Silva's views of the racial dimension of sickle cell anemia reflect the existence of distinct approaches to prevention of this disease.²⁴

Final considerations

In the 1930s and 1940s, the bulk of Brazilian studies on sickle cell anemia that sought to understand the course of the disease, its main features, means of diagnosis, and possible cures and forms of prevention were grounded in medical and scientific articles from the United States. Brazilian research, however, always highlighted the differences between the racial contexts in these two countries.

Medical interest in sickle cell anemia in Brazil emerged at a time when intellectual views on the concept of race were starting to change. Beginning in the 1930s, under Vargas, the matter of race was no longer seen as condemning the country but was instead viewed in a positive light; Brazil was a nation of mestizos, a 'melting pot,' where interactions between blacks, mestizos, and whites were to be valued. Miscegenation was a sign of Brazil's uniqueness, which contrasted with racism in the United States, where racial and cultural mixing was condemned.

In Brazil in the 1930s and 1940s, miscegenation was considered essential to understanding sickle cell anemia, given its purported influence on the epidemiology of the disease. This idea can be found in the vast majority of scientific articles published at the time, above all those proposing to use blood analyses to identify allegedly pure or miscegenated groups.

Ernani Silva stood out among the Brazilian physicians who studied the disease because of his efforts to ascertain the degree of purity and racial miscegenation through the identification of sickle cells. Furthermore, he was a strong supporter of the notion that miscegenation was a unique aspect of sickle cell anemia in Brazil. He adopted the idea

promoted by his section chief at IOC, Walter Oswaldo Cruz, that Brazil should be hematologically mapped by identifying miscegenated and racially pure groups using blood tests to detect sickle cells and ascertain the racial distribution of blood groups. The maps appearing in his 1945 and 1948 papers illustrate his goal of surveying the number of sickle cell carriers in Brazil by geographic region.

At the close of the 1940s, while Ernani Silva traveled into the interior of Brazil to measure miscegenation rates, research was mounting on the frequency of sickle cells in the colonial territories of Africa. At that time, Brazil had amassed about ten statistical surveys on rates of the sickle cell trait and sickle cell anemia, encompassing some 5,500 tested individuals. Yet doubts remained about the racial specificity of the disease, and these constituted the prime motivation for research into supposedly isolated indigenous groups.

The research on indigenous populations conducted by Ernani Silva, and to a lesser extent by Carlos Estevão Frimm, was characteristically interdisciplinary, combining knowledge from hematology and anthropology. Blood analyses were compared with the information consulted in books but mainly with the scientists' own observations about the social context of the tested individuals.

At the end of that decade, interest in sickle cell anemia had been evinced not only in the number of papers published but also the attention afforded the disease at scientific meetings of specialists in pediatrics and hematology. In July 1949, the Second Congress of the South American Confederation of Pediatrics (Segundo Congresso Sul-americano..., 1950) was held in Buenos Aires, where the Brazilian delegation presented on neuroanemias, shigellosis, and drepanocytosis (p.74). The last topic was the subject of Ilda Widmann Costa Santos, who had described clinical cases of sickle cell anemia nine years earlier. On May 21-26, 1950, the First Brazilian Congress of Hematology and Hemotherapy was held in Petropolis, Rio de Janeiro; sickle cell anemia was the theme of the paper given by Carlos Estevão Frimm, official rapporteur for the topic Treatment of Anemias (Anais..., 1950). At the second meeting, held in Santos, São Paulo, on May 20-26, 1951, drepanocytosis was also one of the top issues discussed (Segundo Congresso..., 1951).

In January 1950, sickle cell anemia was a key subject in the collection of articles on hematology published in the journal *O Hospital*, where it was referred to as one of the most important diseases in hematological studies. According to editor João Maia de Mendonça (1950, p.19), this set of articles was an effort to contribute "to the development of Brazilian hematology with this collection of works, while also show[ing the existence of] a nucleus of specialists."²⁵

New understandings of the disease came to light in the late 1940s and early 1950s. In 1947, based on clinical observations, geneticist James Neel determined that sickle cell anemia differed from the sickle cell trait and that an asymptomatic individual would never fall sick with the disease. He further established that sickle cell anemia presented when sickle cells were inherited from both parents, while the trait presented when sickle cells were transmitted by only one of them (Neel, 1947). That same year, physician Jessé Accioly, professor at the Bahia Faculty of Medicine (Faculdade de Medicina da Bahia), raised the same hypothesis as Neel. Accioly received no support from those who published on the disease in the 1940s, even though his hypothesis was presented two other times, once in a

journal and once as a paper in the annals of the Second Brazilian Congress of Hematology and Hemotherapy (Accioly, 1947).

In 1949, the world's understanding of sickle cell anemia changed yet again, when Pauling and collaborators (1949) defined it as a molecular disease. Although Pauling's role in this new discovery is a matter of controversy (Feldman, Tauber, 1997), his study was a milestone in representations of sickle cell anemia and carriers of sickle cells (Wailoo, 1997).

This article has endeavored to show that we must view the naturalization of disease concepts within the framework of a set of presumptions characteristic of the context where these concepts take shape and that this naturalization will thus vary according to time and place. In Brazil in the 1930s and 1940s, scientists worked with the idea that sickle cell anemia might not be racial in origin, since doubts remained about its racial specificity and the impact of miscegenation on its epidemiology. At the close of the 1940s, hematological studies in Africa would confirm the racial origin of sickle cells. But at the start of the following decade, new ideas from the fields of molecular biology, the social sciences, and the genetics of populations once again put the question of race back on the agenda, with debate turning to the validity of 'race' as a way of differentiating between individuals.

NOTES

* This article is based on Juliana Manzoni Cavalcanti's thesis, presented at the Graduate Program in the History of the Sciences and of Health (Programa de Pós-graduação em História das Ciências e da Saúde), Casa de Oswaldo Cruz, Oswaldo Cruz Foundation, in 2007, under the supervision of Professor Marcos Chor Maio (Cavalcanti, 2007).

¹ This resistance stems from a more efficacious immune reaction, as the immune system quickly identifies and ingests sickle cells. When the malaria parasite infects erythrocytes, it consumes the oxygen inside them and prompts their 'sickling.' The body's immune system detects the structure as a foreign element and therefore eliminates it. Even with this advantage, the health of a carrier of sickle cell anemia is already jeopardized and he readily succumbs to infection (Torres, Bonini-Domingos, 2005).

² In 1947, based on clinical research, James Neel asserted that sickle cell anemia was a pathologically permanent condition, that is, it did not shift from a latent to an active phase or vice versa, and it was inherited from both parents, while the sickle cell trait was inherited from only one parent and did not cause any disease (Neel, 1947). Using electrophoresis, Linus Pauling and collaborators (1949, p.543) declared that the abnormal morphology of sickle cells derived from a change in the hemoglobin molecule and that the disease manifested when a person acquired the characteristic sickle-shaped red blood cells from both parents through gene transmission. Relying on concepts from natural selection, A.C. Allison (1954) later suggested that healthy carriers of sickle cells resisted malaria infection, as they were always found in regions with high malaria rates.

³ Our study was inspired by the method devised by Charles Rosenberg (1992), which construes the definition of a disease as a frame that varies according to time and context. This frame is shaped by concepts derived from different fields of human knowledge. On the use of this method in the historical analysis of Chagas disease in Brazil, see Kropf, 2009.

⁴ Distortions of erythrocytes were already associated with diseases at that time, whether caused by infections or hereditary in nature (Ehrlich, Lazarus, 1898; Löwit, 1905).

⁵ Eosinophilia is an increase in eosinophils, the healthy white blood cells whose main role is played during allergic reactions and infection by helminthes (Janeway et al., 2000).

⁶ James Herrick, Victor Emmel, and W.A. Mulherin took part in this debate (Sydenstricker, 1924, p.16-17).

⁷ Papers that were published after James Herrick's and prior to the AMA debate paid special attention to the specificity of sickle cells, varied symptoms, and black heritage; they did not assert, but merely presumed,

that it was a specific disease (Washburn, 1911, cited in Cook, Meyer, 1915; Cook, Meyer, 1915; Emmel, 1917; Manson, 1922; Huck, 1923; Taliaferro, Huck, 1923; Sydenstricker, Mulherin, Houseal, 1923).

⁸ According to Savitt (1981, p.743), during the first half of the twentieth century, U.S. physicians were especially ignorant about sickle cell anemia because high rates of infectious diseases like malaria and ancylostomiasis confined sickle cell anemia to the shadows.

⁹ The first study to suggest a link between sickle cells and the black race was conducted by Jerome Cook and Jerome Meyer (1915, p.650): "It will be seen that there is a striking similarity in both the blood picture and the clinical history of our case with those of Washburn and Herrick. *All three of the patients were of negro blood*; all three suffered from peculiar, indolent, recurring leg ulcer; in all three the anemia was sufficiently severe to cause dyspnea on exertion, and in all of the cases there was a peculiar discoloration of the sclerae" (emphasis added).

¹⁰ A study published in the French journal *Anthropologie* in 1919 proposed a "biochemical race index" based on the incidence of A and B blood groups. Conducted by the couple Ludwik Hirszfeld and Hanna Hirszfeld during World War I, this research analyzed thousands of blood samples from allied soldiers camped at a Greek port. We will not delve into a discussion of anthropology's use of blood groups as racial markers, yet we would like to point out that these criteria did not alter the era's predominant form of racial classification, but stood as only one more physical element used to distinguish human races. The use of blood groups as racial markers did, however, take different form in different countries. In the United States, for instance, there was a debate over the efficacy of using blood groups as racial markers (Marks, 1996) while interest in blood groups was widespread in Germany from the 1920s through the mid-1940s (Mazumdar, 1990).

¹¹ Sickle cell anemia was classified as a group of anemias typical of Africans. On the topic, see Foy, Kondi, Hargreaves, 1952.

¹² Álvaro Serra de Castro (1911-1970) graduated from the National Faculty of Medicine (Faculdade Nacional de Medicina – FNM) in Rio de Janeiro in 1933. In 1944 he defended a medical thesis entitled *Eritrofalçemia* (Sickle cell anemia) as part of the qualifying exam to become a *livre-docente*, or full professor, of Medical Pediatric Practice at FNM; after ten years as a professor he took over the Chair. As a member of the Brazilian Society of Pediatrics, the Société de Pédiatrie de Paris, and the American Academy of Pediatrics, he attended a number of scientific events, such as the Fourth International Pediatric Congress in 1950. Serra de Castro served as federal deputy for the state of Maranhão from 1954 to 1958 and directed several projects in the area of pediatrics. He published papers on blood disorders and congenital syphilis and, together with Martinho da Rocha, wrote *Tratados de pediatria*. In a posthumous tribute, physician José Martinho da Rocha (1970, p.177) said that Serra de Castro had been a pioneer "in the realm of children's hematology among us ... both because he was the first to observe sickle cell anemia in South America and because he published a leading manual: 'Doenças do sangue na infância e na adolescência' [Blood disorders in childhood and adolescence]." Much of this information was obtained from Castro's son, Rogério Álvaro Serra de Castro.

¹³ In *A Folha Médica* in 1933, Coutinho (1933, p.449) stated that sickle cell anemia had been described for the first time in Brazil on June 27 of that year by physician Álvaro Serra de Castro at a session of the Rio de Janeiro Society of Medicine and Surgery (Sociedade de Medicina e Cirurgia do Rio de Janeiro). Serra de Castro's contemporaries considered him the first professional in Brazil to identify a case of the disease (Araújo, 1961).

¹⁴ A 1946 article by physician Maria Clara Mariano da Rocha, from the state of Rio Grande do Sul, reports on the challenge of diagnosing sickle cell anemia: "The hematological test, which informed all of our diagnoses, showed our small patient to be a carrier of a nosological entity of which we had no clinical knowledge: SICKLE CELL ANEMIA ... Our case, which would have been labeled as rheumatism without the information from the hematologist, was clinically identical to that of a boy who was hospitalized in 1939 ... and whose comparison had led us to diagnose the current [case] as ACUTE ARTICULAR RHEUMATISM OF THE SPINE" (Rocha, 1946, p.61; capital letters from the original).

¹⁵ Carlos Estevão Frimm (1916-) was born in Budapest, Hungary. He immigrated to Brazil in 1936, where he graduated from the Porto Alegre Faculty of Medicine (Faculdade de Medicina de Porto Alegre) in 1946. His interest in hematology was sparked during his 1944-1946 internship at an infirmary headed by Doctor Saint Pastous de Freitas, where he began the research on sickle cell anemia that grounded his medical thesis "A drepanocitose: clínica e patologia da anemia drepanocítica e da drepanocitemia" (Drepanocytosis: the clinical profile and pathology of drepanocytic anemia and drepanocytemia), defended on Dec. 15, 1947, and awarded the Miguel Couto Prize by the National Academy of Medicine

(Academia Nacional de Medicina) in late 1948. Frimm worked in the city of Bossoroca, Rio Grande do Sul as the region's only doctor until 1950. That same year, at the invitation of hematologist Michel Jamra, he attended the First Brazilian Congress on Hematology and Hemotherapy, serving as rapporteur on the topic Treatment of Anemia (Frimm, 2000).

¹⁶ In this text, drepanocytosis refers to a syndrome whose phases consisted of drepanocytic anemia (i.e., the presence of varied symptoms and abundant sickle cells in the blood) and drepanocytemia (in which there were no symptoms and very few sickle cells were present). As mentioned earlier, uncertainty surrounding the clinical presentation of sickle cell anemia made it a syndrome whose symptoms could be divided into two phases, latent and active. It was known by many names. In Portuguese, the terms *meniscocitemia*, *eritrofalçemia*, and *siclemia* indicated that sickle cells were found in the blood, while *anemia meniscocítica* and *anemia de células falcêmicas* were the terms used in cases of pathological manifestations of the syndrome. See Table 1 for a complete picture of the terms then in use.

¹⁷ Ernani Martins da Silva was born on Mar. 3, 1914 in Diamantina, Minas Gerais. He graduated from the Rio de Janeiro Faculty of Medicine (Faculdade de Medicina do Rio de Janeiro) and in the late 1930s he took the Oswaldo Cruz Institute's program of specialization courses (Curso de Aplicação). In the early 1940s, he went to work with Walter Oswaldo Cruz at the Institute's Hematology Section (Cruz, 1949).

¹⁸ Son of Oswaldo Gonçalves Cruz and Emilia Fonseca da Cruz, Walter Oswaldo Cruz (1910-1967) graduated in 1930 from the former University of Brazil's National Faculty of Medicine (Faculdade Nacional de Medicina da Universidade do Brasil; now the Universidade Federal do Rio de Janeiro). Two years before graduating, he went to work at Carlos Chagas's laboratory at the Oswaldo Cruz Institute, where he became familiar with hematological studies, particularly on the causes of anemia in ancylostomiasis. Between 1931 and 1932 he took the Institute's Curso de Aplicação. Starting in 1936, he made several trips to Germany and the United States to do internships at hematological research laboratories (Lent, 1967; Silva, 1967).

¹⁹ Fritz Ottensooser was born in Nuremberg, Germany, on July 19, 1891. He graduated in medicine from the University of Munich in 1912 and received the title of doctor of medicine from Heidelberg University in 1915, defending a medical thesis on malformation. He worked as a military doctor during the four years of World War I. In 1924, he received the title of doctor of chemistry for his work on serum proteins. He worked at the Paul Ehrlich Institute from 1926 to 1930; the following ten years, he was at the Bern Hygiene Institute in Switzerland, conducting studies on determining paternity through the use of blood groups. In 1932, he finished his thesis on agglutininogen A, which earned him a full professorship. In 1941, Ottensooser immigrated to Brazil and began working at the Paulista Biology Laboratory, where he remained active until his death at the age of 83, on Dec. 24, 1974 (Wiener, 1975; Leon, 1975).

²⁰ Ettore Biocca was born in Rome in 1912; he graduated from the University of Rome's Faculty of Medicine in 1935. He first began studying pathological hematology and then focused on tropical medicine, bacteriology, anthropology, genetics, and virology. Biocca made two scientific trips to regions of the Amazon. In 1959, he helped found the Italian Society of Parasitology and the journal *Parassitologia*. For more on this physician and anthropologist, see Coluzzi, 2002.

²¹ William Boyd was a professor of immunochemistry at Boston University's School of Medicine, a member of the American Anthropological Association, and editor of the *American Journal of Physical Anthropology* (Boyd, 1949, 1950).

²² In 1949, only two Brazilian studies on sickle cell anemia suggested enforcing rigorous reproductive control among individuals presenting sickle-shaped cells (Nunan Filho, 1949; Carvalho, 1949). For Carvalho (1949, p.256), every member of the black race presenting varied and serious clinical symptoms should be blood tested for sickle cells, while Nunan Filho (1949, p.101) asserted that "prevention [of sickle cell anemia] entails questions of eugenics – negative or restrictive eugenics – whose importance it is unnecessary to emphasize, most particularly in countries like Brazil, whose population has been influenced by the black race."

²³ In 1945, Ernani Silva released an article on hereditary diseases in which he highlighted sickle cell anemia and stressed the need to identify 'sickleemics', comparing them to other carriers of hereditary diseases. Dividing hereditary diseases into five groups (diseases of the hematic system, of the nervous system, skin diseases, abnormal skeletal development, and cancer) and placing special emphasis on blood diseases, he constantly reiterated that although 'sickleemics' might be healthy, they were disease carriers. Referring yet again to the need for 'prevention,' Ernani Silva (1945b) asserted that his quest to identify carriers in his research was justified by the need to understand the passage from latent to active phase.

²⁴ The idea of pre-nuptial testing and other control measures did not come only from Carlos Estevão Frimm and Ernani Silva. Expositions about the need to identify carriers of sickle cells and to forestall the appearance of the disease can be found mainly in discussions of forms of treatment and prevention (Castro, 1934; Carvalho, 1949; Nunan Filho, 1949).

²⁵ Mendonça also stated that he was re-editing the 1933 issue of *A Folha Médica* devoted to hematology; according to his mentor, Oscar Clark, the purpose of that issue had been to glorify the period known as the Renaissance of Hematology, which saw hematological research gain new impetus with studies on the role of iron and the liver in anemias. Mendonça had likewise taken part in the older collection with his paper “Valor do exame de sangue em cirurgia” (The value of blood tests in surgery), about the blood tests needed to prepare a patient for surgery (Mendonça, 1933).

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