

Short Communication

Temporal and spatial distribution of American tegumentary leishmaniasis in north Paraná: 2010–2015

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Abstract

Introduction: Describing the general aspects of American tegumentary leishmaniasis enables the identification of the epidemiological scenario of the disease and the development of preventive actions. **Methods:** We analyzed the records of patients with American tegumentary leishmaniasis in north Paraná between 2010 and 2015. **Results:** We identified 108 cases (mostly in 2014) with the following characteristics: male individuals, rural workers, and ages averaging 56.8 years. Isolated ulcerated lesions were predominant, and Glucantime® was the most frequently used drug. **Conclusions:** American tegumentary leishmaniasis remains endemic and affects mostly men found in areas surrounded by woods; its treatment is partially efficient considering its side effects and incidence of recurrences.

Keywords: Cutaneous leishmaniasis. Epidemiology. Spatial analysis. Surveillance.

American tegumentary leishmaniasis (ATL), a zoonotic disease caused by protozoa of the genus *Leishmania*, is one of the most important infectious diseases worldwide that causes the attacked patients to develop deformations, hence compromising their personal and social routine. Throughout the world, roughly 200,000 cases occur on a yearly basis, out of which 70–75% are recorded specifically in 10 countries, including Brazil. Constant records of the disease have appeared worldwide during the past few years and represented a source of concern for public administrators as well as the Brazilian government. In 2015, 493 new cases of ATL were recorded in the south region of Brazil, out of which 478 occurred exclusively in the state of Paraná¹.

ATL can manifest through different clinical conditions developed according to either the parasite species or the host's immunogenetic factors, and therefore, is classified as a polymorphic illness appearing in cutaneous, cutaneous diffuse, and cutaneous-mucous forms². Its diagnosis can be clinical when based on the aspects of the patient's lesion or medical history combined with laboratory tests, such as Montenegro's intradermal test reaction, serological diagnostic methods, and direct search. Treatment of ATL includes administration of pentavalent antimonial, which is the first drug of choice, such as N-methylglucamine (Glucantime®) or amphotericin B and pentamidine, alternatively, in cases of resistance. However, issues like drug's high cost, difficult administration, long treatment periods, and drug's toxicity restrict this drug for leishmaniasis treatment².

Descriptive studies aim to understand and describe the behavior of diseases in certain regions contributing to health sciences and encouraging administrative actions, such as the implementation of new control measures. In this context, our

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study aimed to describe the general aspects of ATL occurrence in north Paraná between 2010 and 2015. It is relevant to understand the ATL epidemiology considering its endemic and neglected nature in the country, which affects mainly disadvantaged populations and implies difficult psychosocial and economic factors because of the deformities involved, in addition to the therapeutic inefficiency and lack of data on the disease in the state.

For this purpose, we performed a descriptive epidemiological study of medical records at the university hospital (UH) of the State University of Londrina, located in the City of Londrina, a unit of reference for patients suspected with leishmaniasis, which serves 21 cities belonging to the 17th Regional Health Administration of Paraná and comprises a population of 950,821 inhabitants, an estimation for 2017³.

The population investigated was composed of all patients diagnosed with ATL between the years 2010 and 2015. The inclusion criterion was positive ATL diagnosis obtained through serological diagnostic methods, Montenegro’s intradermal test reaction, or direct search. Unconfirmed ATL cases, patients diagnosed with visceral leishmaniasis, and those whose testing results were unavailable were excluded.

The medical records were analyzed using an information collection instrument that is composed of five parts: I) epidemiological aspects (sex, age, date of the first medical checkup, color/race, occupation, origin, previous skin diseases, and family history of ATL), II) clinical aspects (time elapsed since the lesion’s appearance and form and area of the lesion), III) laboratory aspects (performance and result of serological diagnostic methods, Montenegro’s intradermal test reaction, direct search [biopsy and histopathology examination]), IV) treatment aspects (prescription of previous treatment, medications in use, prescribed drugs related to ATL [doses and period of treatment], and adverse events), and V) evolutionary aspects (information on the healing of the lesion, recurrences, and treatment prescribed during the relapse).

The instrument was built and applied to analyze the medical records using the Open Data Kit (ODK) suite of applications. We used two out of the three software programs included in the ODK: XLSForm (form preparation) and ODK Collect (data collection), in which the latter allows to navigate, edit, and store the information collected off-line using an equipment with Android system. Subsequently, the information was sent to an online server (Ona platform) for data storage and was exported to a Microsoft Excel worksheet.

Data analysis was performed using absolute and relative frequencies with measures of central tendency (mean and median) as well as dispersion (standard deviation, minimum and maximum values, and interquartile range) using the software programs Microsoft Excel and SPSS version 19.0. Software QGIS 2.14.11 (www.qgis.org/pt_BR/site/) was used to engineer the images by building heat maps (kernel) to identify areas with higher density of cases. The kernel intensity estimator allows to estimate the number of events per unit area in each cell of a regular grid comprising the study region. To calculate the ATL incidence kernel, this analysis had a grid defined over the region with 250 columns; algorithmic function was composed of a quartic with a bandwidth of 500 meters. The proximity of ATL cases with vegetation areas was identified by satellite image Landsat 8, OLI sensor, on October 14, 2015 (source: earthexplorer.usgs.gov/), using normalized difference vegetation index, varying between -1 (lower amount of vegetation) and +1 (greater amount of vegetation).

Additionally, our project was approved by the Ethics Research Committee of the State University of Londrina according to the resolution 466/12 by the National Health Council.

Our data identified and revealed 108 ATL cases from 2010 to 2015, in which most patients were diagnosed through serological diagnostic methods and Montenegro’s intradermal test reaction (Figure 1A). Despite not being positive for serology – the only

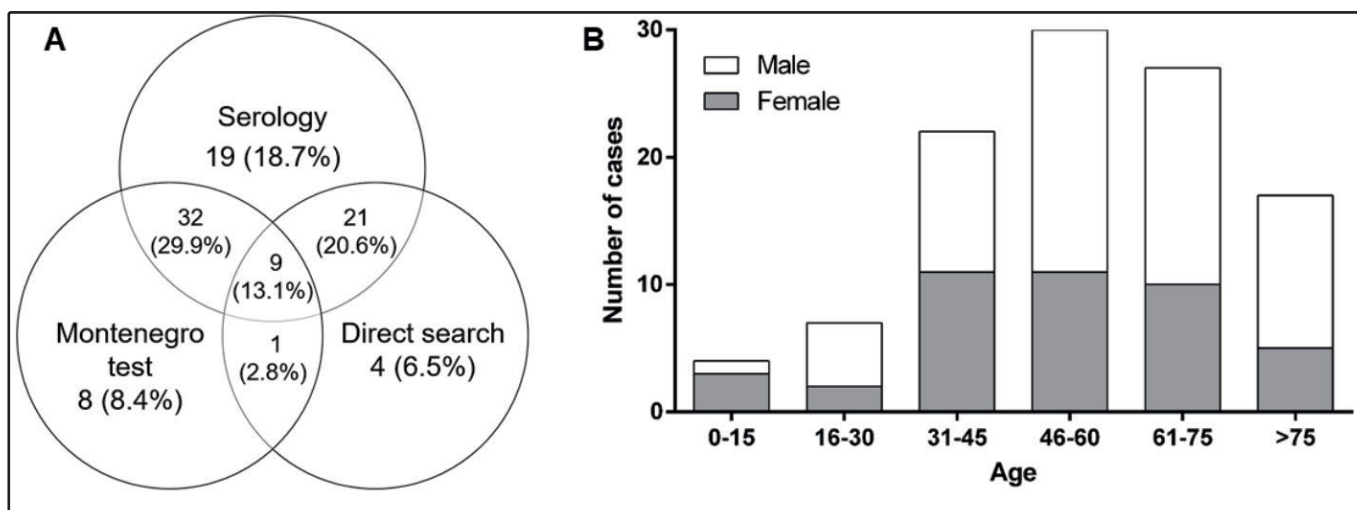


FIGURE 1: ATL-positive cases in north Paraná, Brazil, between 2010 and 2015. (A) Venn's diagram of ATL diagnostic tests in patients of north Paraná, Brazil (n=107); (B) Number of ATL-positive cases in north Paraná, Brazil, between 2010 and 2015 by sex and age group.

diagnosis test conducted – one case was included in the study for having presented classical signs of ATL and medical decision for diagnostic confirmation.

The average age involved in the diagnosis is 56.79 years (interquartile of 24 years), with a minimum of 3 and a maximum of 94 years or more. The most affected age group of people ranges from 31 to 75 years old (73.8%) with a predominance of men (59.5%) (**Figure 1B**). Furthermore, throughout the study period, the year 2014 had the highest number of positive cases for ATL (28.7%), predominantly in male individuals (60.2%). In **Figure 2**, the behavior of the disease in the region by the year studied can be observed. Additionally, the spatial distribution showed that most cases of ATL are concentrated in the urban area (**Figure 3**).

Regarding ethnicity, 29.6% were caucasian, 5.5% black or brown, 1.9% indigenous, and 0.9% asiatic; however, in 67 cases (62.0%) race/color could not be identified. The most frequent occupations were rural workers (17.6%), which comprised the population who worked with primary activities such as plantations and ploughing, and retired workers (12.0%). Other occupations, such as student, housewife, seamstress, bricklayer, contractor, joiner, and mechanic, were also mentioned.

With respect to the clinical record, 24 (22.2%) patients had previous skin diseases, such as leprosy (16.7%) and skin cancer (8.3%). Seven patients (29.2%) had developed leishmaniasis before, and 13 (12.0%) patients presented with a family history of ATL. The skin lesions were clinically manifested as predominantly isolated lesion, which were presented in 84.3% of the patients, with 37.2% of the lesions being located in the lower limbs, 21.7% in the upper limbs, 20.2% in the oronasal region, 8.5% in the trunk region, 7.0% in the facial region, and 1.6% in other parts of the body. In these patients, the size of the lesion varied from 0.5 to 10 cm, with an average size of 3.1 cm (± 1.80 cm).

Additionally, data on the shape of the lesion indicated that 59.9% of the patients had ulcerated/crusted lesions, 11.5% ulceration or absence of the septum, 7.0% erythematous plaque, 5.1% papules, and 8.9% other forms of lesion, like pustule, pediculosis, or tumor. The mean period of time between the appearance of the lesion and the date of the first medical checkup was 16.1 months (± 43.6 months).

Table 1 shows that 81.5% of the patients received Glucantime® treatment, out of which 23.1% discontinued

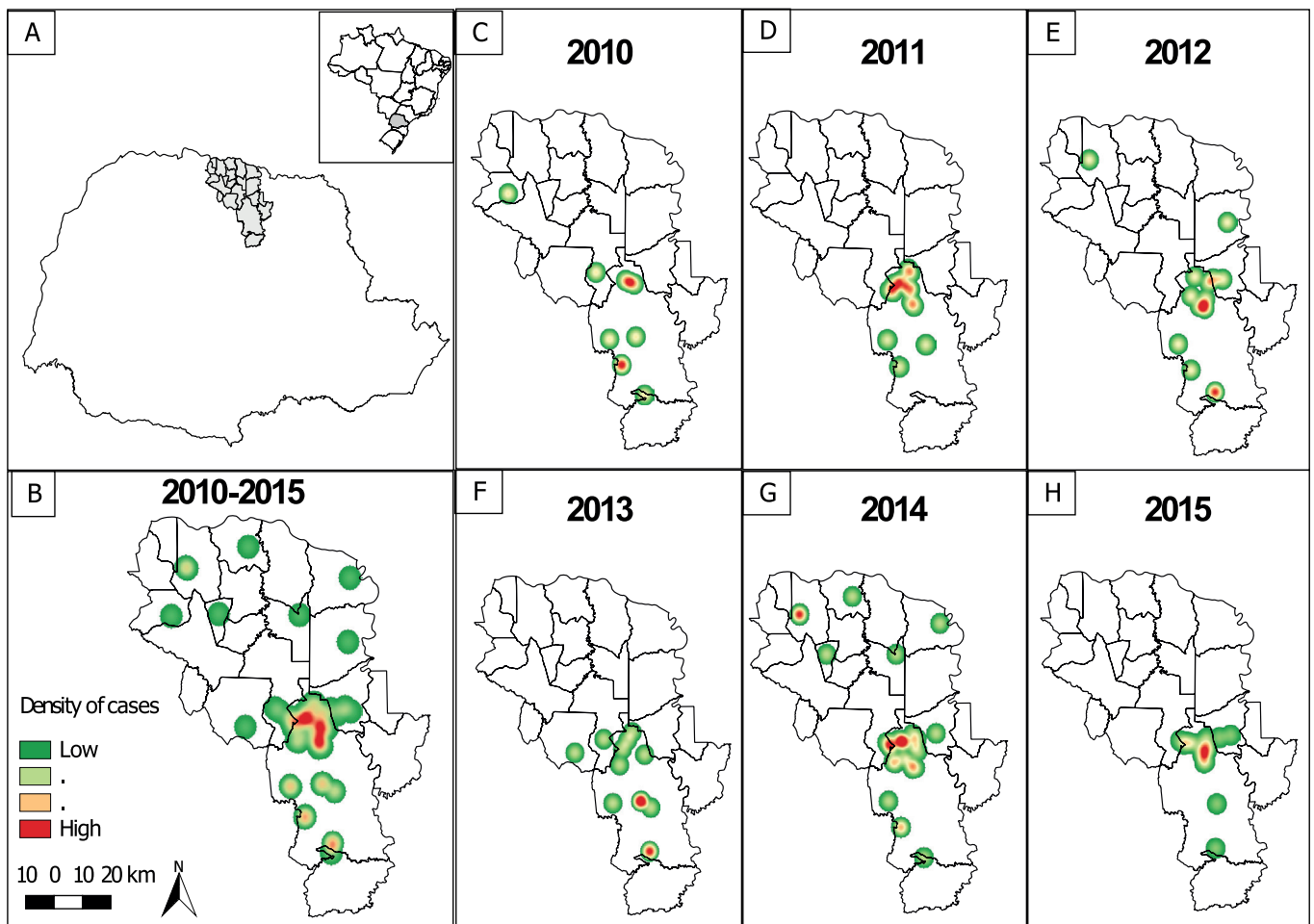


FIGURE 2: Spatial distribution of ATL-positive cases in north Paraná, Brazil, between 2010 and 2015. (A) Location of the 17th Regional Health Administration in the map of Paraná. (B) Density of cases from 2010 to 2015; (C) Distribution of cases in 2010; (D) 2011; (E) 2012; (F) 2013; (G) 2014; and (H) 2015.

TABLE 1: Medications used in ATL treatment associated with relapsed lesion condition.

Type of Medication	First Treatment		Relapse		Second Treatment		
	n	%	n	%	Medication	n	%
Glucantime®	88	68.8	6	6.8	Glucantime®	2	33.3
					Topical use	1	16.7
					Not informed	3	50.0
Amphotericin B	11	8.6	0	0.0	–	–	–
Topical use	17	13.3	3	17.6	Amphotericin	1	33.3
					Topical use	2	66.7
					Not informed	1	33.3
Others	4	3.1	1	25.0	Topical use	1	100.0
Not informed	8	6.3	–	–	–	–	–

n: number of patients who adhered to the treatment, %: percentage of patients who adhered to the treatment, –: absence of the variable on the report form.

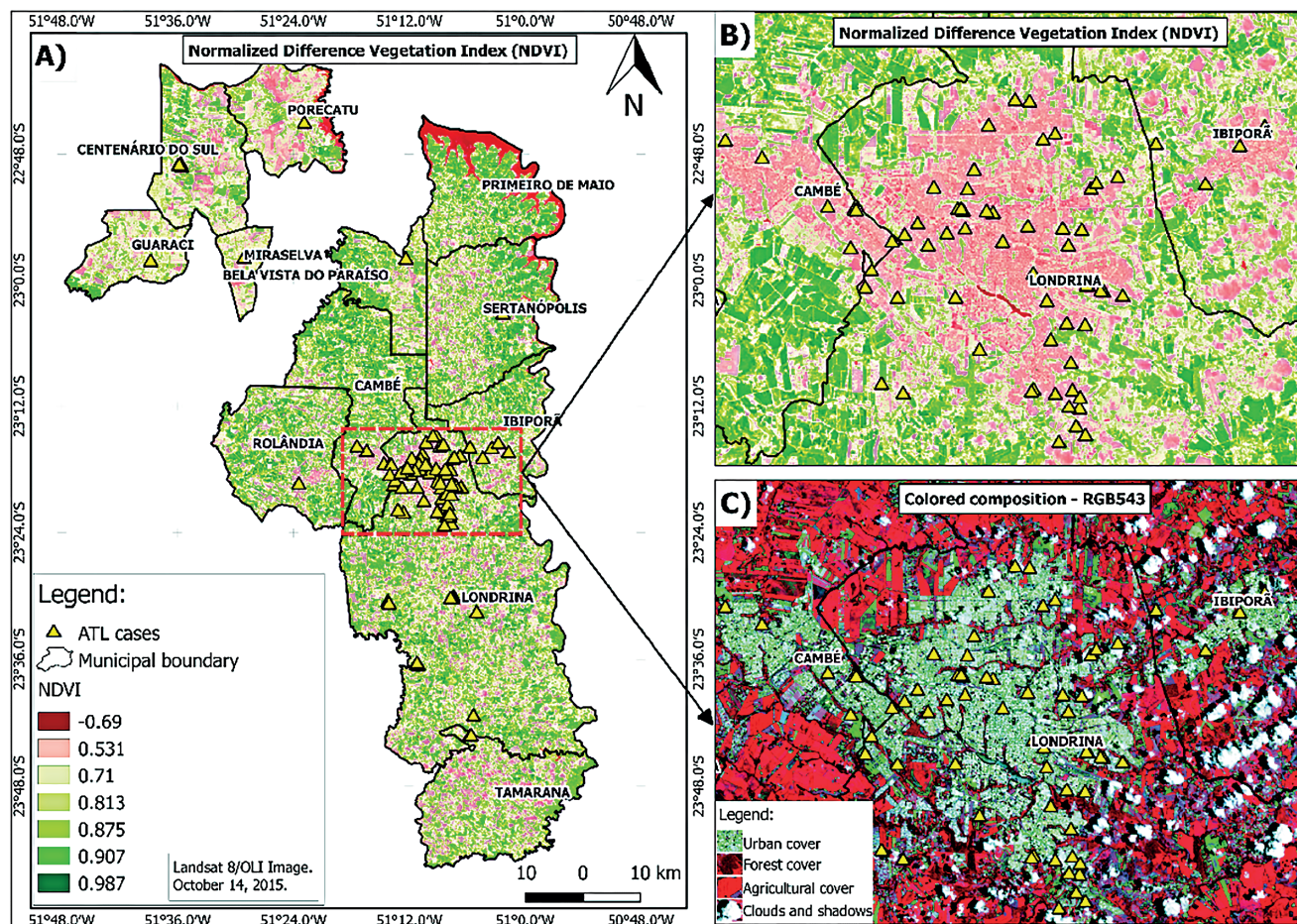


FIGURE 3: Remote sensing of vegetation areas coinciding with cases of ATL. (A) Occurrence of ATL cases and normalized difference vegetation index where red tones (-1) correspond to areas with lower vegetation index and green tones (+1) to areas with higher vegetation index; (B) Area with the highest density of case magnification; (C) False-color composition RGB543, where red corresponds to vegetation areas and shades of blue correspond to soil and urban areas.

the treatment because they experienced the drug's side effects such as body aches, poor appetite, dizziness, nausea, and pruritus. Some patients did not receive the drug because of venous insufficiency and electrocardiogram alterations. Amphotericin B was also prescribed and was administered in 10.2% of the patients, out of which 2.8% had experienced the drug's side effects, which include renal failure and myalgia. Additionally, half of the patients received other medications as treatments, including cefalexin, Bactrim® (sulfamethoxazole and trimethoprim), metformin, dipyrone, omeprazole, and amoxicillin and topical medications (ointment, cream, gel, oil).

Data on the evolutionary aspects reveal that 75.0% of the patients had the lesion healed; however, 7.4% of the patients had relapsed lesions during the assessment period, with mainly isolated (87.5%) lesions.

Our goal was to describe the general aspects of ATL cases in north Paraná. The study identified 108 ATL cases with the highest occurrence rate in the year 2014, possibly due to the high temperature incidence in the state of Paraná, which was regarded as one of the hottest years in the recent decades⁴. High temperature values have a profound effect on the development of the life cycle of *Leishmania* promastigotes in sandflies, allowing for the development of the parasites in areas that were not previously endemic of the disease^{5,6}. Furthermore, the disease has a cyclical pattern in Brazil, with a peak incidence every 5 years related to changes in the rainfall and humidity affecting the ecology of vectors and reservoir hosts and altering the distribution, survival, and population density^{5,7}.

We also found a predominance of male individuals in a working age group, described by many authors as the most vulnerable group in Brazil, which actually leads to a negative impact on the economy of the country^{8,9}. Our findings on the age group (predominance between 31 and 75 years old) differ from the numbers reached by Pontello et al.⁸, who reported the highest occurrence rate among young adults from 21 to 40 years old (from 1998 to 2009) in the region of Londrina. Occupational changes and mobility of the young population to urban centers over the last decade may have contributed to such divergence.

According to *Instituto Brasileiro de Geografia e Estatística* (IBGE) (2016)³, around 3.99% of the total population of the 17th Regional Health Administration of Paraná is composed of rural workers; therefore, the predominance of the group in the results may imply that a significant percentage is affected by the disease. Additionally, the concentration of cases in urban areas, despite the absence of observing patterns of proximity cases with vegetation areas or surroundings, signifies that these areas are at risk and the population of these areas is vulnerable to the disease.

In this regard, some authors have identified the possible risks involved in the developed activities performed close to the forests and rivers due to the presence of phlebotomine^{10,11}. In contrast, intradomicile and peridomicile cases occurred in urban areas because of the accumulation of decaying organic matter caused by incorrect waste disposal, which enables the vector to develop, and the presence of domestic animals that serve as the parasite's secondary reservoirs^{12,13}. The disease relapse in seven cases and the family history of ATL demonstrate the

relationship between the environment and frequent exposure to infection in those locations as well.

In relation to the previous studies, most patients presented isolated lesions^{8,9}. Lesions in the lower limbs were more frequent, which is similar to the findings of Brito et al.⁹ and Name et al.¹⁴; however, Pontello et al.⁸ found higher frequency of lesions in the upper limbs for patients situated in the metropolitan region of Londrina, which occurred because both the lower and upper limbs are more exposed to the insect vector's bite. Furthermore, the gap between the emergence of the lesion and the date of the first medical checkup may indicate issues related to lack of information and difficulty in accessing medical care, aggravating factors that may lead to severe and potentially life-threatening cases.

The laboratory tests performed to diagnose the disease revealed that a serological diagnostic method detected a higher number of cases in relation to the other. It is important to emphasize that in the absence of a gold standard test, combining different laboratory tests and in-depth medical knowledge allows an accurate diagnosis of ATL¹⁵. The treatment followed a proposed therapeutic scheme¹⁶. As expected, the main medications had important side effects in some patients, leading them to discontinue the treatment. Additionally, we verified recurrences and lesions without healing, demonstrating that the therapeutic scheme fails in many cases.

Additionally, half of the patients had prescriptions to nonspecific medications for leishmaniasis, especially topical medications, which are used in isolation or coadministered with specific drugs; however, little is known about the effect of these medications on the lesions, making it necessary to develop further investigations. A limiting factor to our study was the lack of available information on some variables of interest in the medical records studied if we are highlighting that the quality of the information obtained may compromise the application of public policies involving both the control and the treatment of leishmaniasis.

In conclusion, ATL is endemic to the central north region of Paraná attacking mainly male farm workers living in regions close to the woods. Considering that the presence of leishmaniasis results in a negative impact on the public health and economy of the region, it is crucial to emphasize the importance of developing epidemiological studies that reflect on the reality of the local community and creating and developing effective treatment and measures that control and prevent the development of the disease.

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Conflict of Interest: We declare that there is no conflict of interest.

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