Clinical, biological, and anthropological aspects of leishmaniasis in Suriname - report of the final meeting of the Integrated Program

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Abstract

The parasitic disease cutaneous leishmaniasis is an increasing health problem in many countries including the Republic of Suriname. Diagnosis is difficult and treatment options are few, while the side-effects are serious and treatment failure is not uncommon. Insight into the epidemiology and biology of the disease in Suriname is scant. Cutaneous leishmaniasis also puts a significant economic burden on affected individuals and may have a substantial social impact on quality of life as patients can be mutilated and may suffer stigmatization. Nevertheless, a control program for the disease is lacking in Suriname. For these reasons, a comprehensive collaborative effort among stakeholders in Suriname and The Netherlands has been initiated to assess the problem of cutaneous leishmaniasis in Suriname in an integrated manner. This Integrated Program has established diagnostic algorithms to assess and improve the efficacy of current treatment options of cutaneous leishmaniasis in Suriname; has contributed to our understanding of the Leishmania parasite(s), vector(s), and reservoir(s) involved in the transmission of the disease; and has provided more insight into the factors related to treatment seeking behavior, risk factors, and disease perception. This paper reports on these advances.

Key words: Cutaneous leishmaniasis, clinical aspects, biological aspects, anthropological aspects, Integrated Program, Suriname, The Netherlands

Introduction

Leishmaniasis is caused by intracellular protozoan Leishmania parasites (Figure 1) and transmitted via infected female sandflies which are about one-third to half the size of a mosquito (Figure 2), and human or animal reservoir hosts (Saliba and Oumeish, 1999; Desjeux, 2004). This disease is endemic in at least eighty-eight countries throughout the world with a staggering 350 million individuals at risk to get infected (World Health Organization, 2010). This holds particularly true for poor populations in developing countries in tropical and subtropical regions (Ashford, 2000; Alvar et al, 2006; Hotez et al., 2006), as well as war-torn countries such as Afghanistan (Reithinger et al., 2003), Sudan (Seaman et al., 1996), and Iraq (Weina et al., 2004; Korzeniewski and Pieniut, 2011).

Figure 1. Leishmania parasites in the lower center of the image (Moiz et al., 2010)

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Available on-line April 25, 2014
The global prevalence of leishmaniasis exceeds 12 million cases, each year more than 2.5 million new cases are diagnosed (World Health Organization, 2010), and the estimated disease burden is 2.4 million disability-adjusted life years (Murray et al., 2005; World Health Organization, 2010). As a result, the World Health Organization has classified leishmaniasis as a category 1 disease - an emerging and/or uncontrolled disease - acknowledging it as a severely neglected condition and urging the establishment of intensified research programs to improve vector control, diagnostics, and therapeutic arsenal to contain further morbidity and mortality (Murray et al., 2005; World Health Organization, 2010).

Leishmania infection gives rise to several distinct clinical manifestations, ranging from localized single to multiple cutaneous ulcers, satellite lesions, or nodular lymphangitis, to disease forms with mucosal and even potentially fatal systemic visceral involvement (Desjeux, 2004; Reithinger et al., 2007; Romero and Boelaert, 2010). The vast majority of cutaneous leishmaniasis cases occurs in Afghanistan, Algeria, Brazil, Peru, Iran, Iraq, Syria, and Saudi Arabia, whereas most cases of visceral leishmaniasis are seen in India, Bangladesh, Nepal, Brazil, and Sudan (Alvar et al., 2012). Laboratory diagnosis of leishmaniasis is complicated, requiring sophisticated techniques such as analysis of skin scrapings or biopsy specimens; direct visualization of the infecting organism; immunodiagnostic serologic tests; in vitro culturing, and polymerase chain reaction assays, the latter considered the golden standard for diagnosis (Schönian et al., 2003; van der Meide et al., 2005). Unfortunately, such tests are often beyond the reach of communities with limited resources or where species identification is required.

Leishmaniasis can be caused by many species or subspecies of Leishmania (for instance, L. (L.) major, L. (L.) aethiopica, L. (V.) venezuelensis, L. (L.) amazonensis, L. (V.) peruviana, L. (L.) mexicana, L.(V.) panamensis, L. (V.) guyanensis, L. (V.) brasiliensis, L. (L.) infantum, L. (S.) senegalensis, and L.(L.) tropica), all of which have different degrees of virulence and cause distinctive clinical courses (Lainson and Shaw, 1987). This makes the choice of treatment regimen difficult, because different Leishmania (sub-)species respond differently to selected therapies (Lainson and Shaw, 1987). Furthermore, certain forms of treatment are associated with significant toxicity, while the emergence of drug resistance is an additional reason for concern (Croft et al., 2002, 2006).

Mammalian reservoirs for Leishmania parasites include a number of wild and domestic animals (Yoshida et al., 1993; Lainson, 1997; Falquetto et al., 1998; Silva et al., 2000; Travi et al., 1994; Rotureau, 2006; Dantas-Torres, 2007; Schallig et al., 2007; Cardoso et al., 2010, Lopes et al., 2013) as well as humans (Reithinger et al., 2003; Aflatoonian et al., 2013; Noazin et al., 2013). In all these hosts, the parasite exists as a non-flagellated amastigote made up of a large nucleus and a kinetoplast that resides inside a macrophage (Vannier-Santos et al., 2002; Kamhawi, 2006; Dostálková and Volf, 2012). Sandfly vectors of the genus Phlebotomus in the Old World and of the genus Lutzomyia in the New World ingest the amastigotes when drawing a blood meal from an infected host (Vannier-Santos et al., 2002; Kamhawi, 2006; Dostálková and Volf, 2012). At least ninety-three sandfly species are proven or probable vectors of Leishmania worldwide (Killick-Kendrick, 1999; Rotureau, 2006). The amastigotes transform to flagellated promastigotes in the gut of the sandfly, multiply, then migrate to the proboscis of the sandfly, and are inoculated into a naive host during the sandfly’s next blood meal (Vannier-Santos et al., 2002; Kamhawi, 2006; Dostálková and Volf, 2012). The promastigotes then enter into or are ingested by the new host’s macrophages where they transform back to amastigotes, multiply, and eventually spread throughout the reticulo-endothelial system (Vannier-Santos et al., 2002; Kamhawi, 2006; Dostálková and Volf, 2012). Clinical disease becomes apparent within weeks to months after infection, depending on the (sub-)species of parasite and the host’s immune status (Vannier-Santos et al., 2002; Kamhawi, 2006; Dostálková and Volf, 2012).

The Republic of Suriname is situated on the north coast of South America, borders the Atlantic Ocean to the north, French Guiana to the east, Brazil to the south, and Guyana to the west. Suriname’s surface area of 163,820 km² can be distinguished into a narrow lowland urban-coastal area, a rural-coastal area, and a southern rural-interior. Cutaneous leishmaniasis is the most common form of leishmaniasis in Suriname where it is endemic and known as bosjaws or busiayasi (Flu., 1911; van der Meide et al., 2008c). The disease is particularly widespread in the forested interior where it mainly affects individuals involved in gold mining, bauxite mining, and logging, as well as eco-tourists and recreational fishers and hunters (van der Meide et al., 2008c). Cutaneous leishmaniasis occurs predominantly in the rainy seasons, i.e., from May to August and from November to March (Flu., 1911; van der Meide et al., 2008c).
An integrated assessment of cutaneous leishmaniasis in Suriname

The first cases of cutaneous leishmaniasis in Suriname (Figure 3) were reported in 1911 (Flu, 1911). There are no updated numbers available on the occurrence of this disease in Suriname. An annual detection rate of 5.32 to 6.13 per 1,000 inhabitants has been reported for the forested interior, and of 0.64 to 0.74 per 1,000 for the entire country (van der Meide et al., 2008c). The actual number of infections is most likely higher, as certain risk groups - such as infected Brazilian garimpeiros who work (illegally) in southern parts of Suriname, as well as infected Indigenous and Maroon people who treat themselves - are not included in these records (unpublished observations).

Until the Integrated Program on ‘Leishmaniasis in Suriname’ described in this paper was carried out, L. (V.) guyanensis was considered the principal species causing the cutaneous form of this disease in the country (Lai A Fat et al., 2002; van der Meide et al., 2008c). However, patients with diverse clinical forms of cutaneous leishmaniasis had been encountered, suggesting that other Leishmania species were also active in Suriname. This was consistent with the identification of L. (L.) amazonensis (van der Meide et al., 2008a), L. (V.) lainsoni (van der Meide et al., 2008b), and L. (V.) naiffi (van Thiel et al., 2010) in the country. In addition, the illegal workforce in the hinterland might have introduced other Leishmania species such as L. (V.) braziliensis in Suriname (Jones et al., 1987; Grimaldi Jr and Mahan-Pratt, 1991; Rotureau, 2006). Furthermore, cutaneous leishmaniasis is zoonotic in Suriname (Rotureau, 2006), but the vectors involved in its transmission were not exactly known, and animal reservoirs had not been identified.

Pentamidine isethionate is the first-line drug and the only treatment option for cutaneous leishmaniasis caused by L. (V.) guyanensis in Suriname (Lai A Fat et al., 2002). However, dermatologists in Paramaribo had observed increasing numbers of patients who responded inadequately to this treatment (unpublished observations). This might be attributable to several factors including the emergence of drug resistance (Croft et al., 2002, 2006), but this had to be verified. If true, this would obviously have important consequences for the efficacy of this therapeutic modality (Andersen et al., 2005; Machado et al., 2010; World Health Organization, 2010). Also, many patients from the interior receive pentamidine isethionate in Suriname’s capital city Paramaribo but treat themselves in the forest without medical supervision (unpublished observations). This may result in incomplete therapy and sub-therapeutic drug blood levels, contributing to the development of drug-tolerant parasites (Croft et al., 2002, 2006).

Notably, expenses for the treatment of cutaneous leishmaniasis and for transportation to health centers are considerable, while loss of income due to the inability to work often impact substantially on welfare of affected individuals. These factors, together with the lack of resources and health education (Moreira et al., 2002) make compliance to treatment rather poor, representing an additional reason for the apparently increasing unresponsiveness of the infecting parasites to the first-line therapy. For the same reasons, patients tend to attempt self-cure, using, among others, local herbal remedies or household and other chemicals, and seek treatment only in advanced stages of the disease (Rawlins et al., 2001). To which extent this occurs was not known, but also needed to be investigated. It was also not exactly known whether and to which extent the extensive ulceration and disfiguring scar formation (Bailey and Lockwood, 2007) affect patients’ body satisfaction and quality of life as reported for other countries (Yanik et al., 2004), and whether and to which extent these individuals may face social stigmatization (Yanik et al., 2004; Kassi et al., 2008). Clearly, these issues had to be investigated as well.

The Integrated Program

Cutaneous leishmaniasis is an important health problem in Suriname, but many aspects of this disease are not well understood and/or studied. A control program is lacking, and as mentioned above, disease incidence is rising and treatment is becoming complicated, indicating an evident need for further studies. For this reason, a comprehensive Integrated Program on ‘Leishmaniasis in Suriname’ has been conceived that was funded by the Netherlands Organization for Scientific Research / Foundation for the Advancement of Tropical Research – Science for Development. More specifically, this program aimed to introduce diagnostic algorithms, evaluate, and improve the efficacy of current treatment options; gain insight into the biology of the parasite and the disease; and advance our understanding of treatment-seeking behavior and disease perception of (ex-)patients, thereby increasing awareness and acceptance of cutaneous leishmaniasis and improving its management and control in Suriname. These issues have been addressed through three sub-projects which were under
combined supervision from Suriname and The Netherlands, formulated as three research projects, and concluded with three PhD theses.

The first project, ‘Cutaneous leishmaniasis in Suriname: improved diagnosis, assessment of treatment efficacy and patient care’ has studied clinical aspects of the disease with the ultimate goal to improve diagnosis, treatment, and patient compliance. The latter aspect might be accomplished by introducing a shorter but more dose-intensive treatment regimen. This study was carried out by Ricardo V.P.F. Hu, MD, from the Dermatology Services (a division of Suriname’s Ministry of Health), and lasted from January 2009 to December 2012. It was supervised by prof. dr. Rudy F.M. Lai A Fat, Anton de Kom University of Suriname (AdekUS) and the Academic Hospital Paramaribo; Leslie O.A. Sabajo, MD, MPH, from the Dermatology Services in Paramaribo; and prof. dr. Henry J.C. de Vries from the Department of Tropical Dermatology of the Academic Medical Centre in Amsterdam. Dr. Hu defended his PhD thesis on these topics successfully in November 2013.

The second project was carried out by Alida D. Kent, MSc, from the Faculty of Medical Sciences of the AdeKUS, and was about ‘The biology and epidemiology of cutaneous leishmaniasis in Suriname’. The supervisors were prof. dr. Dennis R.A. Mans from the Faculty of Medical Sciences of the AdeKUS, and Henk D.F.H. Schallig, PhD, from the Royal Tropical Institute (KIT) in Amsterdam. This project started in April 2009 and was concluded in May 2013. Mrs. Kent received her PhD diploma in December 2013 with a thesis on these aspects of cutaneous leishmaniasis.

The third project, ‘Social and cultural aspects related to the perception and treatment of cutaneous leishmaniasis in Suriname’ was the responsibility of Sahienshadebe Ramdas, MA, from the Amsterdam Institute for Social Science Research (AISSR), University of Amsterdam (UvA). Mrs. Ramdas was supervised by prof. dr. Sjaak van der Geest from the UvA and prof. dr. Ria Reis from the UvA and the Department of Public Health and Primary Care, Leiden University Medical Centre, as well as dr. Schallig. This project started in November 2008 and was finished in November 2012. Mrs. Ramdas is anticipated to defend her PhD thesis on these issues in June 2014.

The principal stakeholders involved in the execution and dissemination of the Integrated Program were the Academic Hospital Paramaribo, Paramaribo, Suriname; the Academic Medical Centre, Amsterdam, The Netherlands; the Amazon Conservation Team, Paramaribo, Suriname; the Anton de Kom University of Suriname, Paramaribo, Suriname; the Dermatology Services, Paramaribo, Suriname; the University of Amsterdam, Amsterdam, The Netherlands; the Ministry of Health, Paramaribo, Suriname; the Primary Health Care Suriname - Medical Mission, Paramaribo, Suriname; the Bureau for Public Health, Paramaribo, Suriname; and the Royal Tropical Institute, Amsterdam, The Netherlands.

The clinical component – ‘Cutaneous leishmaniasis in Suriname: improved diagnosis, assessment of treatment efficacy, and patient care’

Cutaneous leishmaniasis is treated in Suriname since 1994 with pentamidine isethionate given as 3 intramuscular injections of 300 mg in 7 days (Lai A Fat et al., 2002). As mentioned earlier, this treatment is not always effective, which suggests that the infecting parasite species - mostly L. (V.) guyanensis - does not always respond to pentamidine isethionate. It is also possible that the infections are caused by unresponsive Leishmania species other than L. (V.) guyanensis (van der Meide et al., 2008a, b; van Thiel et al., 2010), and/or to poor therapy compliance (Moreira et al., 2002). Obviously, these factors may lead to incomplete healing, the emergence of drug resistance, and therapy failure.

To assess these possibilities, the clinical trial ‘PEntamidine for cutaneous Leishmaniasis in Suriname’ (the PELESU study) was designed, a non-inferiority study aimed at the evaluation of the efficacy and toxicity of the standard 7-day regimen with respect to an experimental 3-day, more dose-intensive treatment regimen. The PELESU study also compared the cost-effectiveness of both regimens, and evaluated the effects of the body location of the lesions on quality of life of the patients in collaboration with the anthropological part of the program. And together with the biological part of the Integrated Program, this study identified the Leishmania species present in patient samples using molecular tools (see below and Hu et al., 2012). As mentioned above, these aspects of the Integrated Program were described in dr. Hu’s PhD thesis entitled ‘Cutaneous leishmaniasis in Suriname: improved diagnosis, assessment of treatment efficacy and improved patient care’.

The Director of the Ministry of Health in Suriname granted ethical clearance to carry out these studies after approving a mandatory clinical research protocol, a clinical research form, an informed consent form, and a patient information leaflet. Other essential elements of the study were a questionnaire for the cost-effectiveness analysis, an application for the clinical trials.gov database, a randomization algorithm and software program, and a clinical research database in EPIDATA. Dr. Hu received support with the data analysis from the staff of the Biomedical Research - Epidemiology Unit of the Royal Tropical Institute in Amsterdam.

A total of 163 patients was accrued for the clinical trial, 84 of whom received the standard treatment of 4 mg/kg pentamidine isethionate on days 1, 4, and 7, and 79 the experimental treatment of 7 mg/kg of the drug on days 1 and 3. Clinical cure was assessed at 6 and 12 weeks follow-up visit, parasitological cure at 6 and 12 weeks follow-up visit (Figure 4), adverse and drug-related toxicity events at 1 week follow-up visit, and quality of life before treatment and at 6 weeks follow-up visit.
Figure 4. During each evaluation (before treatment as well as 6 and 12 weeks after treatment) a 2-mm skin biopsy was taken from the active margin of a lesion (image by R. Hu, 2012)

Although losses to follow-up were substantial in both treatment arms (around 30%), the 3-day regimen was not non-inferior to the 7-day regimen. The proportions of clinical cures at 6 and 12 weeks follow-up in the 3-day arm were 39 and 47%, respectively, and in the 7-day arm 49 and 54%, respectively. Therapy failure at 6 and 12 weeks follow-up was observed in 28 and 15% of patients, respectively, in the 3-day arm, and in 33 and 17%, respectively, of patients in the 7-day arm. Evaluation of parasitological cures showed comparable numbers.

Adverse events of both arms were also comparable, although the shorter, more dose-intensive regimen produced more toxicity, in particular to liver and kidneys. Furthermore, taking into consideration the medical expenses and loss of income of the patients in both treatment arms, the 3-day regimen was 20 to 25% more cost-effective than the 7-day arm when expressed as cost per patient treated and cured at 6 and 12 weeks. Still, dr. Hu’s recommendation on the basis of these findings was to maintain the 7-day treatment regimen because of its lesser toxicity when compared to the 3-day regimen.

The Skindex-29 symptoms scale and the EQ-5D measure of health were employed to assess quality of life of 46 patients with cutaneous leishmaniasis in relation to the location of lesions on certain parts of their body. These evaluations revealed that patients with lesions on the lower limbs had significantly higher scores – thus, lower quality of life - when compared to those with lesions on head and or face, upper limbs, and/or trunk. Furthermore, the former group was more likely to experience problems regarding self-care, mobility, and day-to-day activities, as well as pain and discomfort. Notably, social stigma was not a major issue.

The biological component – ‘Studies toward an improved understanding of the biology of the Leishmania parasite in Suriname’

As mentioned above, the Leishmania species identified in Suriname before this study were L. (V.) guyanensis (Lai A Fat et al., 2002), L. (L.) amazonensis (van der Meide et al., 2008a), L. (V.) lainsoni (van der Meide et al., 2008b), and L. (V.) naiffi (van Thiel et al., 2010). Whether other Leishmania species can cause the disease in Suriname was not known. It was also not certain which vectors and reservoirs are involved in the transmission of leishmaniasis in Suriname. Suspected vectors were female phlebotomine sandflies (Diptera: Psychodidae) belonging to the species Lutzomyia umbratilis, Lu. flaviscutellata, and Lu. whitmani (Hudson and Young, 1985; Burgos and Hudson, 1994; Rotureau, 2006; Fouque et al., 2007; Maroli et al., 2013). Candidates for the role as reservoir were wild animals (Yoshida et al., 1993; Lainson, 1997; Falqueto et al., 1998; Silva et al., 2000; Travi et al., 1994; Schallig et al., 2007) but also domestic animals such as cats (Cardoso et al., 2010), horses (Lopes et al., 2013), and dogs (Rotureau, 2006; Dantas-Torres, 2007).

For these reasons, this part of the Integrated Program was dedicated to the characterization of Leishmania species and strains in lesions of patients from different parts of the country by molecular methods: the identification of the sandfly vector(s) that may transmit the parasites; and the identification of possible vertebrate reservoirs in the transmission cycle. In addition, in collaboration with the clinical part of the program (see above), patients were monitored for their response to pentamidine isethionate by comparing their parasite loads before and after the start of the treatment using molecular methods (Figure 4). For these purposes, the PhD student on the project, mrs. A. Kent, MSc, followed a course in molecular biology at the Parasitology Unit of the Biomedical Research Department of the Royal Tropical Institute in Amsterdam, The Netherlands, as well as a training on the capture, identification, mounting on microscopic slides, and dissecting and identifying phlebotomine sandflies at the Evandro Chagas Institute in Belém, Brazil.

Assessment of Leishmania-specific DNA sequences in the lesions of patients by quantitative real-time PCR (q-PCR); van der Meide et al, 2008b) and a PCR restriction fragment length polymorphism assay (PCR-RFLP; Marfurt et al., 2003) showed that almost 90% of infections was caused by L. (V.) guyanensis, but that there were also a few infections by L. (L.) amazonensis and L. (V.) braziliensis. In fact, these studies were the first to establish the presence of the latter species of parasite in Suriname (Hu et al., 2012), warranting health care professionals of the possible presence in the country of parasites that may cause mucocutaneous leishmaniasis (Jones et al., 1987; Lessa et al., 2007).

Pentamidine isethionate treatment led to cures in more than 70% of infections with L. (V.) guyanensis but
was without effect in almost one-quarter of patients infected with this species, suggesting that unresponsive variants of this species are active in Suriname. Determination of parasite loads in the lesions of patients before as well as at 6 and 12 weeks after the start of pentamidine isethionate treatment by qPCR showed that median parasite counts in cured patients had dropped to zero on week 6 after treatment and remained zero on week 12 after treatment in cured patients. However, this was not the case in patients who were not cured. These findings indicate that qPCR is a useful molecular tool for monitoring patients during treatment, warranting its implementation to improve diagnosis and treatment of patients with cutaneous leishmaniasis.

To establish which sandfly vector(s) may be responsible for the transmission of leishmaniasis in Suriname, sandflies were captured in several gold mining areas and Maroon villages in the hinterland selected on the basis of cases of cutaneous leishmaniasis reported by the Dermatology Services and the Medical Mission (Figure 5).

Female sandflies were assessed for the presence of *Leishmania* sp. using qPCR, and *Leishmania* species were identified using mini-exon PCR-RFLP. The total catch of more than 2,500 sandfly specimens comprised thirty-four different species including four new records for Suriname, viz. *Lu. aragaoi*, *Lu. damascenoi*, *Lu. ayrozai*, and *Lu. sordellii* (Kent et al., 2013a). More importantly, there were six proven vectors of leishmaniasis (Kent et al., 2013a), viz. *Lu. squamiventris sensulato*, *Lu. umbratilis*, *Lu. flaviscutellata*, *Lu. whitmani*, *Lu. ayrrozai*, and *Lu. ubiquitalis*, proven vectors for *L. (V.) naiiffi*, *L. (V.) guyanensis*, *L. (L.) amazonensis*, *L. (V.) braziliensis*, and *L. (V.) lainsoni* (Le Pont et al., 1980; Naiff, 1989; Rotureau, 2006; Fouque et al., 2007; Ferreira-Rangel and Lainson, 2009; Maroli et al., 2013).

To investigate whether the dog could represent a reservoir of cutaneous leishmaniasis in Suriname, blood was collected from dogs from the animal shelter of Paramaribo, dogs from locations around Paramaribo, dogs brought to hunting trips in the hinterland, and animals from foci of cutaneous leishmaniasis in Afohaka en Witagron located in the interior of Suriname. Assessing *Leishmania*-specific antibodies and *Leishmania*-specific DNA in the blood samples using the direct agglutination test (DAT; Oskam et al., 1996; Schallig et al., 2003) and qPCR (van der Meide et al., 2008b), respectively, five dogs appeared seropositive for canine leishmaniasis, and *Leishmania* DNA was detected in one dog, albeit at relatively low quantities (Kent et al., 2013b). Thus, although not proven conclusively, the dog may play a role in the transmission of cutaneous leishmaniasis by acting as a reservoir for the parasites.

The anthropological component – ‘Social and cultural aspects related to the perception and treatment of cutaneous leishmaniasis in Suriname’

As cutaneous leishmaniasis can lead to extensive ulceration and disfiguring scar formation, this part of the Integrated Program was dedicated to perceptions of the disease and treatment-seeking behavior; aspects regarding self-treatment and treatment by traditional healers in the context of local social and cultural beliefs about the disease; as well as the possibility of stigmatization of patients. This study was performed by the PhD candidate Mrs. S. Ramdas, MA, in collaboration with the Dermatology Services, the Medical Mission, the Bureau of Public Health, and the Amazon Conservation Team. The research took place at the Dermatology Services in Paramaribo as well as in several rural communities in the hinterland, namely that of the Ndyuka Maroons from Godo-olo along the Tapanahony river; those of the Saramaka Maroons from Brokopondo Centrum along the Suriname river; those of the Caraim Amerindians from Donderskamp located in the coastal area of Suriname along the Wayambo river; and those of the Trio Amerindians from Tepu in the south of Suriname close to the border with Brazil. Fieldwork took also place at Benzdorp, a Brazilian gold diggers village.

Data were collected through qualitative research methods using questionnaires, in-depth interviews, focus group discussions, open-non structured interviews with community members and key informants (e.g., family heads, teachers, community leaders, health professionals); open interviews with local traditional practitioners; observations of patients and informal conversations in family homes; and observations at the Dermatology Services where patients suffering from cutaneous leishmaniasis were treated.

A total of 205 individuals has been approached. Cutaneous leishmaniasis was a well-known disease in all communities visited, as indicated by its many
different names in local populations. Examples are azo in Aucan, kaaso in Trio, matuyasi, tatayasa, and a leishmania in Saramakan, dalasoro and krabuyasi in Surinamese, and leisha, leishomajosu, uma ferida brava, leisho seco, and leisho chorao in Portuguese. The infection was often recognized and diagnosed by lay people based on the appearance and the progression of the sores.

Still, many aspects of cutaneous leishmaniasis were unknown. Etiological explanations ranged from ‘flies and all kinds of insects’ or ‘something from the nature’ to ‘something supernaturally’ and ‘some kind of bacteria’ (Ramdas, 2012). This unfamiliarity with the exact cause of cutaneous leishmaniasis resulted in (unnecessary) concerns, reflected in the perception of a disease that, although curable, was regarded as a ‘difficult’, ‘evil’, ‘cruel’, ‘horrible’, ‘stubborn’, ‘dangerous’, ‘serious’, ‘filthy’, ‘uncontrollable’, ‘contagious’, and/or ‘expensive’ condition (Ramdas, 2012).

Self-treatment was common, and the majority of the substances employed were painful and aggressive; indeed, an ‘evil’, ‘cruel’, ‘horrible’, ‘stubborn’, and ‘dangerous’ disease was believed to require treatment with harsh remedies (Ramdas, 2012). Examples of such remedies are hot botanical oils, hot herbal water, burning with gunpowder, the skin fluid of the blue poison dart frog Dendrobatus azureus (Dendrobatidae), and horse feces (Ramdas, 2012). Gendered ideologies of masculinity may also play a role in the decision to use aggressive medicines (Ramdas, 2012).

Ramdas further found ‘western’ medications to be used in self-treatment such as antibiotics and muscle pain relievers, but also household chemicals, insecticides and mosquito repellents, herbicides, insecticides and larvicides for veterinary use (Figure 6), and chemical (industrial) products (Ramdas, 2012). Traditional ‘bush’ medicines were also frequently used (Ramdas, 2012). Examples are fresh or processed plants or plant parts and extracts from certain plant parts (such as Aloe vera gel or coconut oil). These substances were used either alone or combined with other materials such as lemon mixed with salt and vinegar or a mix of garlic and camphor (Ramdas, 2012).

More than three-quarters of patients with cutaneous leishmaniasis had attempted self-treatment prior to visiting the Dermatology Services. However, medical treatment was only sought after all attempts at self-treatment had failed. Notably, almost 90% of patients had leishmanial lesions for one to three months (in one case for even three years) before visiting the Dermatology Services. Only a relatively small segment of patients (about 20%) exclusively sought medical help. These individuals belonged in general to the younger generations, had a higher education, and lived in or close to more urbanized areas. Nevertheless, almost one-third of overall patients did not adhere to the medical treatment because of the risk of loss of income, the relatively high costs of the medical treatment, fear of the painful injections with pentamidine isethionate and the side-effects of this treatment, and lack of information about the efficacy of the medication.

Despite the ulceration and disfiguring scar formation characteristic of cutaneous leishmaniasis, this study – similarly to the clinical part of the Integrated Program - also did not find strong stigmatization of patients in Suriname as reported in other societies (Yanik et al., 2004; Kassi et al., 2008). Cutaneous leishmaniasis did not seem a high-priority disease as, for instance, malaria, snakebites, or HIV/AIDS, and patients were not socially excluded. However, patients tended to be shielded from food and were treated with extra caution, while some were confronted with open disgust and fear, and a few tried to conceal their lesions. Apparently, there was a limited degree of enacted, perceived, or felt stigma and internalized stigma towards patients.

**Future directions**

The Integrated Program ‘Leishmaniasis in Suriname’ has compared the efficacy, side-effects, and cost-effectiveness of the current treatment with pentamidine isethionate with an experimental regimen, and has shown the usefulness of the current regimen against infection with L. (V.) guyanensis. However, evidence regarding the emergence of drug insensitivity has been obtained, which could be related to the presence of unresponsive strains of L. (V.) guyanensis but also that of L. (V.) brasilienesis, as well as poor therapy compliance. Notably, responses to pentamidine isethionate could be more accurately monitored on the basis of parasite loads at week 6 after the treatment using qPCR. Furthermore, the sandfly species involved in the infection cycle in Suriname have been updated.
and indications have been obtained to regard the dog as a potential reservoir for cutaneous leishmaniasis. Importantly, the program has provided more insight into the factors related to the perception of cutaneous leishmaniasis and treatment-seeking behavior in Suriname, and has shown that stigmatization hardly occurs in the country. More comprehensive reviews on these findings are in preparation and are anticipated to be published soon.

The challenge now is to use this information to develop, implement, and evaluate future control, treatment, and prevention programs of cutaneous leishmaniasis in Suriname. One way to go forward is through programs aimed at the discovery and development of novel, more efficacious anti-leishmanials. For this purpose, the Surinamese and Dutch stakeholders involved in the program are now developing a high-throughput in vitro test system to evaluate drug-sensitive and possibly drug-resistant strains isolated from patients for their response to different anti-leishmanial drugs (see for instance Mikus and Steverding, 2000; Davis et al., 2004; Sereno et al., 2007). The same technology is being used to evaluate a number of the above-mentioned traditional (plant-based) forms of treatment for their potential efficacy against cutaneous leishmaniasis. It is hoped that these preclinical studies will lead to the identification of novel pharmaceuticals and promising candidate substances to manage the disease more efficaciously.

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