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Cutaneous leishmaniasis: Literature review and report of two cases from communities devastated by insurgency in North-East Nigeria

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INTRODUCTION

Leishmaniasis is a parasitic disease most often as result of bite by infected female phelobotomine sandflies. Various species of sand flies are potential vectors and some 100 species of wild and domestic animals including humans could serve as reservoir hosts.[1] The causative agents are blood and tissue dwelling intracellular protozoan parasite species belonging to the genus *Leishmania*. Infection with leishmania specie could result in disease condition ranging from chronic but often self-healing skin lesions, cutaneous leishmaniasis (CL), to erosive mucosal membrane destruction of the nasopharynx known as mucocutaneous leishmaniasis, and a life-threatening systemic infection with hepato-spleenomegly in visceral leishmaniasis. The nature and extent of the disease is determined by complex interactions between the infecting species of *Leishmania* and the immunological status of the host.[1, 2]

Although the disease has been described from parts of 88 countries in the tropics and sub-tropics where some 350 million are at risk of infection, over 12million affected with some 1.5–2million new cases each year, there is dearth of studies on leishmaniasis in West Africa where the disease is estimated to be endemic, arguably it is a less recognized or under-reported parasitic infections in this region.[3-6] The risk of acquisition of leishmaniasis has been reported to increase considerably with human activity; the disease gets into the human population when man, flies and the animal reservoirs coexist in the same environment.[7] Cutaneous form is the most common presentation of leishmaniasis, its epidemic has been associated with deforestation, road construction, wars, or other activities where humans intrude the habitat of the vector.[6,7] Northeastern Nigeria has been ravaged by the activities of insurgency in the last six years. This has resulted in internal displacement of people from their homes, distortion of ecosystem and increased interaction between humans and vectors. In the light of the above we report two cases of cutaneous leismaniasis. To the best of our knowledge this report is the first documented cases from our environment.

CASE REPORT 1

A 38yr old military personal deployed to fight insurgency in Mallum Fatori, a Village boardering Niger Republic where the first case of leishmaniasis was detected West Africa in 1915. He presented with ulcerated multiple nodular swelling on the right upper limb and right elbow, the swelling were notice one month prior to presentation and had ulcerated a week before coming to hospital. The ulcer has sloping edge and necrotic floor they measures 4x3 cm and 3x3 cm respectively. Proposed diagnosis of Kaposi sarcoma was made and biopsy of edge of an

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ulcer was taken for histology. Diagnosis of cutaneous leishmaniasis was made based on the histology result. He was given caps fluconazole 200mg for six weeks and he responded well. The skin lesion healed completely after six weeks of therapy leaving a tiny scar.

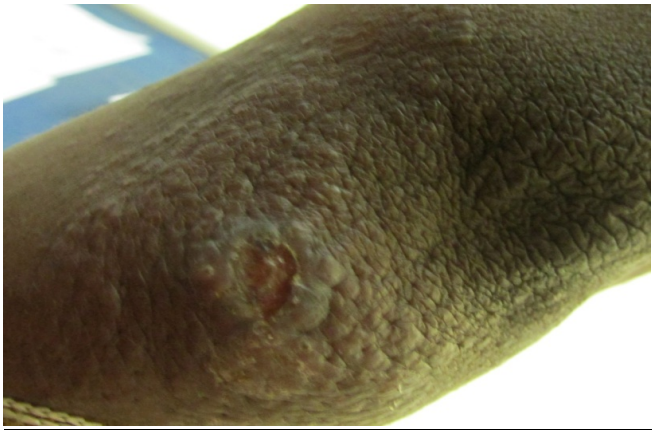

Fig 1: Show cutaneous ulcer at the elbow joint that has rolled edge and necrotic floor

Histology report of case 1

The sections show an ulcerated skin tissue composed of hyperkeratotic, acanthotic and parakeratotic epidermis overlying dense fibrocollageneous dermis with marked chronic inflammatory cells infiltrates. Focal areas of microabscesses and necrosis at the edge of the ulcer are also noted. Giemsa stain shows numerous histiocytes with intracytoplasmic Donovani bodies.

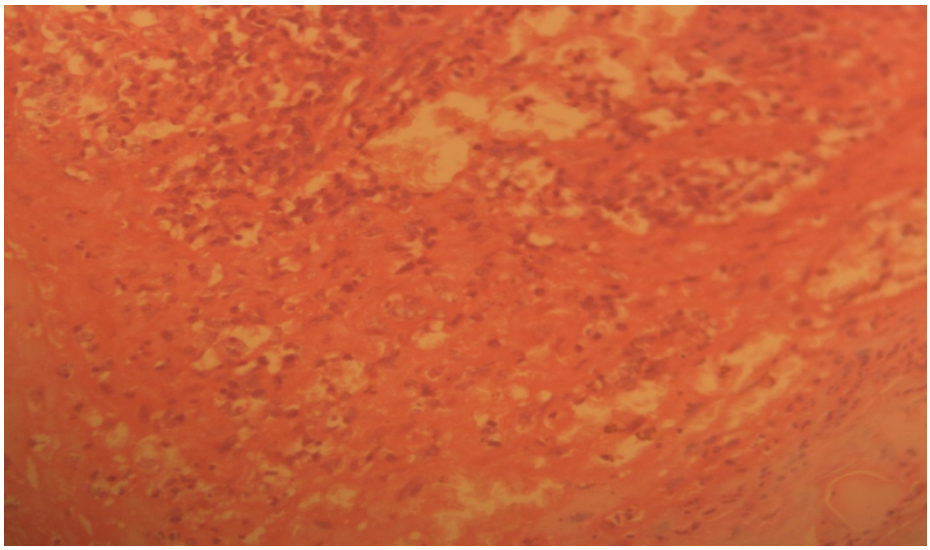

Fig: 2 Photomicrograph of tissue biopsy; show micro-abscess with focal areas of necrosis. H&E (x10)

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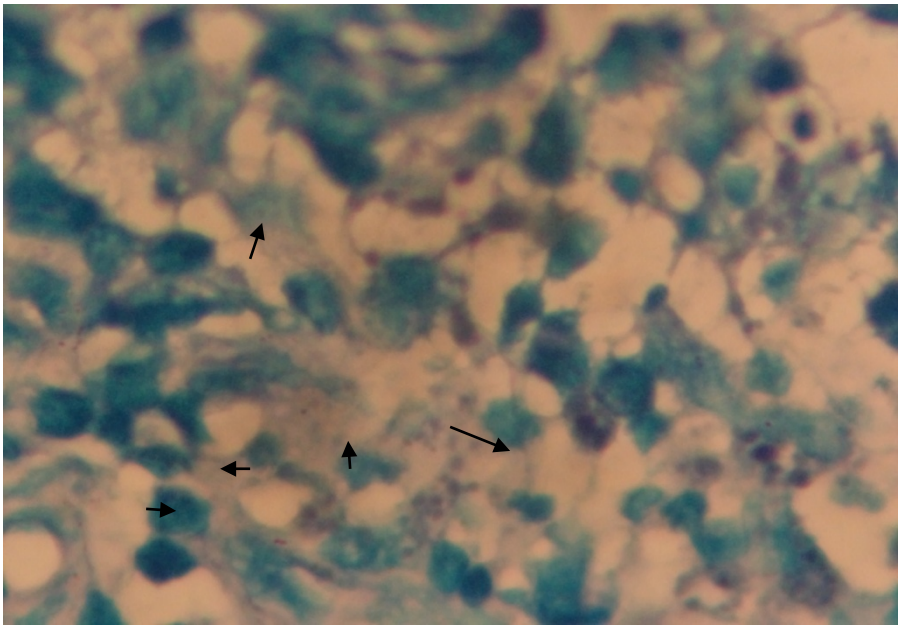

Fig: 3 Giemsa stain, showing histiocytes with numerous intra-cytoplasmic donovani bodies, indicated by blank arrow. (x100)

CASE REPORT 2

27yr old female, who came from a village near Konduga local government of Borno state, Nigeria, the village was ravaged by activities of Boko Haram insurgency that lead all the inhabitant to flee. She presented with three months history of multiple nodular skin lesions on the right thigh and right elbow. There was history of similar cutaneous lesion in the community but we were unable to trace the other suspected cases due to internal displacement. Patient was seen in Microbiology clinic and suspected parasitic infection was made, biopsy from the wound edge was then taken for histology. The result was in keeping with cutaneous leishmaniasis. She responded well had six month therapy with caps fluconazole 200mg given daily.

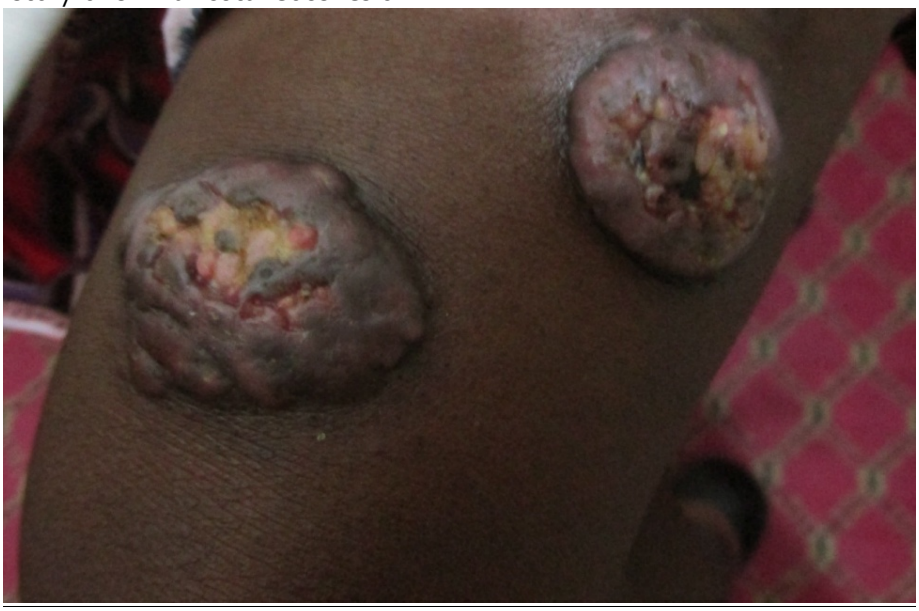

Fig 4: Shows two cutaneous nodules with ulceration on the surface, from the right thigh of a 27yr old female

Histology report of case 2

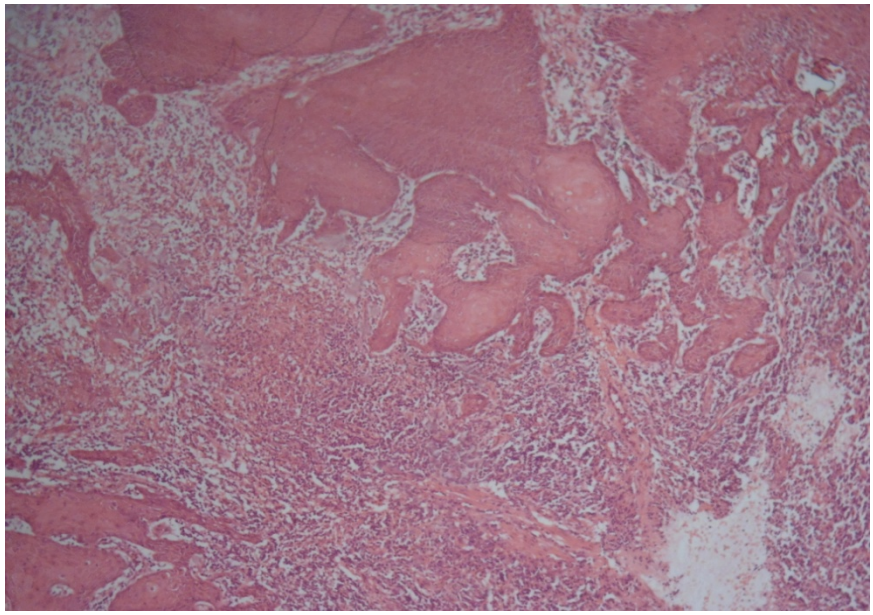

Fig 5: Photomicrograph of ulcerated skin tissue composed of acanthotic epidermis overlying chronically inflamed dermis with focal area of necrosis. H& E x 10

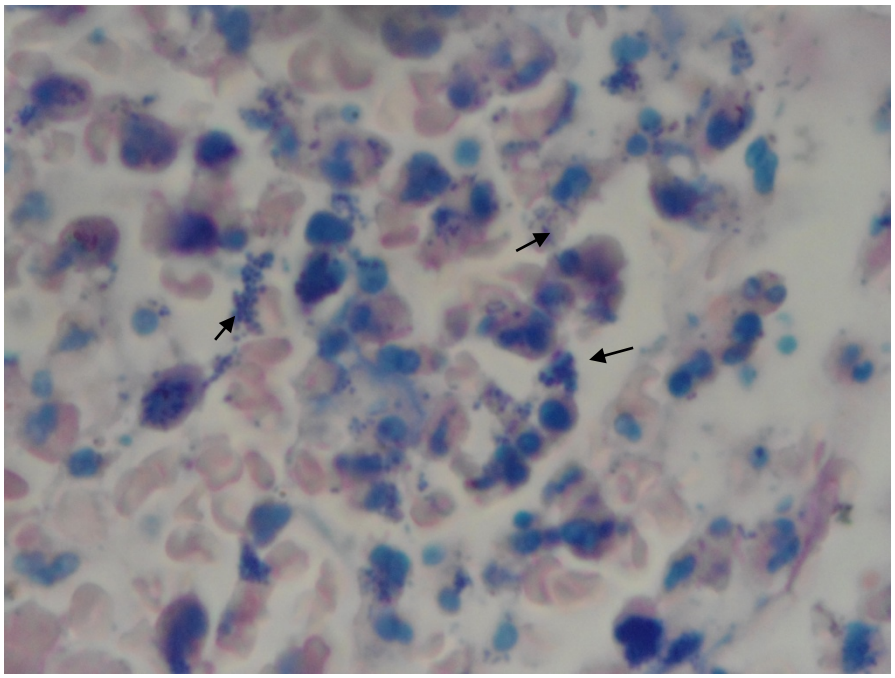

Fig 6: Giemsa stain show abundant histiocytes composed of intracytoplasmic amastigote indicated by black arrow. X 100

DISCUSSION

Leishman and Donovan working separately in 1903 first described leishmaniasis.[7] Since then it has been characterized into complex species, at least 20 of which has been demonstrated to cause disease in humans. Some species exclusively causes cutaneous, others visceral leishmaniasis, and some both.[7] Cutaneous forms result from infection of macrophages in the dermis, involvement of reticuloendothelial system result in visceral leishmaniasis, a fatal disease condition if left untreated. A third uncommon mucoccutaneous

leishmaniasis exist; when the macrophages in naso-pharangeal mucosa is involved. This report focuses on cutaneous leishmaniasis, the most common form of the disease.[5-7]

The incidence of leishmaniasis is usually associated with rural areas and poverty, it has also adapted to the urban environment. Tropical medicine clinicians are often baffled by the complexities of leishmaniasis by the apparently innumerable possible combinations of different leishmanial syndromes, species, and geographical areas of acquisition of infection, each combination varying by clinical presentation, ease of diagnosis, natural history, and response to therapy. The geographical distribution of leishmaniasis is determined by the species of sand fly vectors, their feeding preferences and capacity to support internal development of specific species of leishmania. Human activities such as deforestation, road construction, wars and other activities that enhances interaction and proximity with the vector has been associated with CL.[8, 9] The global burden of leishmaniasis is enormous, it has remained stable in the last decade, causing a morbidity and mortality loss of 2.4 million disability adjusted life-years (DALYs) and approximately 70,000 deaths, a significantly high rank among communicable diseases.[3,10,11]

The first established case of leishmaniasis in West Africa was reported in Niger in 1911[12], since then cases have been reported in several nations in the region mostly from Mali[13], Nigeria[14], Senegal[15], Cameroun[16] and Gambia.[17] Although the disease is also reported to be endemic in West Africa, there is dearth of studies on its incidence, presentation and management. Neither the reservoir animals nor the vectors are well characterized, arguably it is a less recognized or under-reported parasitic infections in this region.[14-17] Another contributing factor for under reporting is lack of facility for case identification and self healing nature of CL. However, sporadic reports of CL in epidemiological proportion has increases in the region. Leishmania major has been identified from Mauritania, Senegal, Mali and Burkina Faso. Three zymodermes (MON-26, MON-117, and MON-74, the most frequent) have been found.[5]

CL is an infection caused by various species of leishmania protozoa. The parasite is transmitted by the bite of phlebotamine sandflies. Sand flies belongs to insect order Diptera (true flies) in the family Psychodidae, two main genera found in West Africa include Phebatomus and Sergentomyia. Anthropophilic West Africa identified sandflies includes P. duboscqi and P. rhodaini in Ghana[18,19],P. duboscqi in Senegal[20], P. duboscqi in the Gambia[17]. Different leishmania species cause Old World versus New World (American) cutaneous leishmaniasis. In the Old World (the Eastern Hemisphere), the etiologic agents include leishmania tropica, L. major, and L. aethiopica, as well as L. infantum and L. donovani. The main species in the New World (the Western Hemisphere) are either in the L. Mexicana species complex (L.mexicana, L. amazonensis and L. venezuelensis) or the subgenus Viannia also refered to as L. (V.) braziliensis specie complex. In West Africa Leishmania major has been reported from reverviour hosts, vectors and human patients in studies from Gambia, Senegal, Burkina Faso and Mali.[21-24] This distribution of leishmaniasis correlates with appropriate vector species, even within a year, reports from studies conducted in West Africa shows that the highest number of cases occur during the raining season implying that transmission may occur at least two months before the rainfall.[25-27]

The incubation period is two to eight weeks, although longer periods have been noted. CL causes skin lesion begins as an erythematous papule at the site of the sandfly bite on exposed parts of the body. The papule increases in size and becomes a nodule. It eventually ulcerates and crusts over. The border is usually raised and distinct. There may be multiple lesions, especially when the patient has encountered a nest of sandflies. The ulcer is typically large but painless unless there is secondary bacterial or fungal infection.[28]

Diagnosis of CL depends on the clinical signs, epidemiological information, PCR and culture of infected tissue, or finding the intracellular parasite in biopsy material from the periphery of the lesion. It is not always possible to culture the parasite (gold standard method) since other microorganisms from the wound may infect the culture material and stop

Leishmania growth. Various laboratory methods exist for diagnosis of leishmaniasis-to detect the parasite and identify the leishmania species. Cutaneous leishmaniasis is diagnosed by direct visualization of amastigotes (Leishman- Donovan bodies) from biopsy of suspicious lesion. Invasive laboratory methods specialized culture techniques and molecular methods are available in reference laboratory.[28-31]

Treatment for CL depends on the Leishmania species involved [32] and the means available to the hospital. Not all patients require treatment since lesions may heal spontaneously, after approximately 1 year, leaving a skin scar.[32] However therapy may be indicated to reduce the risk for mucosal dissemination, accelerate healing of skin lesion, decrease risk for relapse, decrease local morbidity caused by large or persistent skin lesions, decrease reservoir of infection in a locality. Leishmania lesions appear to respond well to local treatment using cryotherapy, thermotherapy or surgical removal, in combination with chemical treatment; mainly meglumine antimoniate or amphotericin B but pentamidine isethionate, paromomycin, and antifungals are also used.[33-40] Pentavalent antimony remains the treatment of choice. It is thought to work by inhibition of adenosine triphosphate synthesis. However, antimonials have a high incidence of reversible adverse effects.[33] Furthermore, resistance to meglumine antimoniate has been reported in some areas[41,42] and it should be used with caution. Certain azole antifungal drugs have activity against leishmania in vitro.[43-48] They inhibit the growth of leishmania in culture systems by inhibiting the cytochrome P-450–mediated 14 a -demethylation of lanosterol, blocking ergosterol synthesis, and causing accumulation of 14a -methyl sterols[45-48] In the treatment of cutaneous leishmaniasis caused by various species, the clinical effectiveness of the azole drugs has been varied.[46-48] Data are limited on the clinical efficacy against leishmania of fluconazole, a triazole antifungal agent available for oral and parenteral administration.[47-49] Its excellent safety profile and pharmacokinetic properties make it a suitable alternative therapy for cutaneous leishmaniasis. It has a long half-life, high solubility in water, and a concentration in skin that is 10 times that in plasma. A six-week course of oral fluconazole is a safe and useful treatment for cutaneous leishmaniasis caused by L. major.[48,49]

CONCLUSION AND RECOMMENDATIONS

CL is should be considered as a possibility of cutaneous lesion especially in inhabitants of communities affected by insecurity in Northern Nigeria. Given the good safety profile of azoles in this anedoctal report an unavailability, high cost and toxicities associated with pentavalent antimony compounds, we advocate the use of azole for the treatment of cutaneous leishmaniasis. We advocate further studies on this disease including but not limited to active case management, surveillance within the health system and mapping. Other measures include entomological surveillance and identification of host in domestic animals.

REFERENCES

1. Jeronimo SMB, de Queiroz Sousa A, Pearson RD. Leishmaniasis. In: Guerrant RL, Walker DH, Weller PF, eds. Tropical infectious diseases: principles, pathogens and practice. Edinburgh, Scotland: Churchill Livingstone Elsevier. 2006; 1095–1113.
2. World Health Organization Control of the leishmaniases. Report of a WHO Expert Committee. World Health Organ Tech Rep Ser 1990; 793: 1–158.
3. World Health Organization (2007). Control of leishmaniasis. Sixtieth World Health Assembly WHA 60.13 agenda item 12.3. http://www.who.int/gb/ebwha/pdf_files/WHA60/A60_R13-en.pdf.
4. World Health Organization (2006). Control of leishmaniasis. Report of the secretariat. www.who.int/gb/ebwha/pdf_files/EB118/B118_4-en.pdf
5. Margaret A. Kweku, Shirley Odoom, NaikiPuplampu, Kwame Desewu, Godwin KwakyeNuako, Ben Gyan, Greg Raczniak, Karl C. Kronmann, KwadwoKoram, Silvia Botero, Daniel Boakye and Hannah Akuffo. An outbreak of suspected cutaneous leishmaniasis in Ghana: lessons learnt and preparation for future outbreaks. Global Health Action 2011, 4: 5527 - DOI: 10.3402/gha.v4i0.5527
6. D.A. Boakye, M.D. Wilson and M. Kweku A Review of Leishmaniasis in West Africa . Ghana Med J 2005; September 39(3) 94-97

7. Herwaldt BL. Leishmaniasis. Lancet 1999;354: 1191-9.
8. Roberts, M.T.M. Current understandings on the immunology of leishmaniasis and recent developments in prevention and treatment. Br. Med. Bull 2006; 76: 115– 130.
9. Albert Kimutai, Peter KamauNgure, Willy KiprotichTonui, Michael MuitaGicheru and Lydia BonareriNyamwamuLeishmaniasis in Northern and Western Africa: A review Afr. J. Infect. Dis. 2009; 3(1): 14 – 25
10. Davies, C.R., Kaye, P., Croft, S.L. and Sundar, S. Leishmaniasis: new approaches to disease control. BMJ.2003; 326: 377– 382.
11. Reithinger, R., Dujardin, J-C., Louzir, H., Pirmez, C., Alexander, B. and Brooker, S. Cutaneous leishmaniasis. Lancet. Infect. Dis.2007; 7: 581– 596
12. Stevene L. Les cro-cro de la région de Zinderetleur identification avec l'ucèrephagédé-nique des pays chaude et le boutond'Orient. Bull Soc Path Exot 1911; 4: 180-182.
13. Lefrou G. La leishmaniosecutanée au soudanfrançais. Fréquence de la formesèche a papulo-tuberculeuse. Bull Soc Path Exot 1948; 41: 622-627.
14. Dyce-Shar. Oriental sore in Nigeria. Trans Roy Soc Trop Med Hyg 1924; 18: 336.
15. . Riou M and Advier M. Leishmaniosecutanéecantractée au Sénégal. Bull Soc Path Exot 1933; 26; 254-256
16. . Rageu J. Phlébotomes du Cameroon. Bull Soc Path Exot 1951; 44: 793-800.
17. Greenwood BM, Adjukiewicz AB, Conteh S, Hagan P, Mabey DC and Panton LJ. Leishmaniasis in The Gambia. Is its incidence increasing? Trans Roy Soc Trop Med Hyg 1984; 78: 407-409
18. Seccombe AK, Ready PD and Huddleston. A catalogue of Old World phlebotomine sand-flies (Diptera: Psychodidae, Phlebotominae). Natural History Museum, UK
19. Naing AA, Geofroy B, Angel G, Trouillet J, Killick-Kendrick R, Hervy JP and Brunhes J. Les phlebotomesd'Afrique de l'Ouest. Centre IRD, Montpellier, France.
20. Dedet JP, Desjeux P, and Derouin F. Ecology of a focus of cutaneous leishmaniasis in the Thies region (Senegal, West Africa). Sponta-neous infestation and biology of PhlebotomusduboscqiNeveu-Lemaire 1906. Bull Soc Path ExotFiliales 1982a; 75: 588-598.
21. Dedet JP, Hubert B, desjeux F and Derouin F. Ecology of a cutaneous leishmaniasis focus in the Thies region (Senegal, West Africa). Spontaneous infection and disease reservoir role of various wild rodent species. Bull Soc Path ExotFiliales 1981; 74:71-77.
22. Dedet JP, Saf' Janova VM, Desjeux P, Emel-vanova LP, Schnur LF and Chance ML. Ecology of a reservoir of cutaneous leishmaniasis in the region of Thies (Senegal, West Africa). Characterization and types of isolates Leishmania strains. Bull Soc Path ExotFiliales 1982c; 75: 155-168.
23. Harrat Z, Pratlong F, Benikhlef R, Lami P, Belkaid M and Dedet JP. Leishmania major MON-74 as a causative agent of cutaneous leishmaniasis in Burkina Faso. Trans Roy Soc Trop Med Hyg 1998; 92: 355
24. Izri MA, Doumbo O, Belazzoug S and Prat-long F. Presence de Leishmaniasis major MON-26 au Mali. Ann Parasitol Hum Comp 1989; 64: 510-511.
25. Traoré KS, Sawadogo AS, Traoré A, Ouedraogo JB, Traoré TR and Guiguimdé TR. Étudepreliminairedelaleishmaniosecutanéedans la ville de Ouagadougou de 1996-1998. Bull Soc Path Exot 2001; 94: 52-55.
26. Dedet JP, Marchand JP, Strobel M, Derouin F and Pradeau F. Ecology of a focus of cutane-ousleishmaniasis in the Thies region (Sene-gal, West Africa). Epidemiologic and clinical characteristics of the human disease. Bull Soc Path ExotFiliales 1982a; 75: 568-576.
27. Develoux M, Blanc L, Garba S, Mamoudou H, Ravisse P and Cenac A. Etude clinique et épidémiologique de la leishmaniosecutanée au Niger. Cahier Sante 1991; 1: 130-134.
28. Dacie, John V.; Bain, Barbara J.; Imela Bates. Dacie and Lewis practical haematologyPhiledelphia: ChurchhillLivigstone/Elsevier.ppISNN 0-443-06660-4.
29. Centers for Disease Control and Prevention. Parasites home: leishmaniasis. Resources for health professionals. Available at http://www.cdc.gov/parasites/leishmaniasis/health_professionals/. Accessed April 10, 2014.
30. Monno R, Giannelli G, Rizzo C, De Vito D, Fumarola L. Recombinant K39 immunochromatographic test for diagnosis of human leishmaniasis. Future Microbiol. Mar 2009;4(2):159-70.
31. Kubar J, Fragaki K. Recombinant DNA-derived leishmania proteins: from the laboratory to the field. Lancet Infect Dis. Feb 2005;5(2):107-14.

32. William H. Markle, Khaldoun Makhoul. Cutaneous Leishmaniasis: Recognition and Treatment Am Fam Physician 2004;69:455-60.
33. Aronson NE, Wortmann GW, Johnson SC, Jackson JE, Gasser RA Jr, Magill AJ, et al. Safety and efficacy of intravenous sodium stibogluconate in the treatment of leishmaniasis: recent U.S. military experience. Clin Infect Dis 1998;27:1457-64.
34. Martinez S, Marr JJ. Allopurinol in the treatment of American cutaneous leishmaniasis. N Engl J Med1992;326:741-4.
35. Velez I, Agudelo S, Hendrickx E, Puerta J, Grogl M, Modabber F, et al. Inefficacy of allopurinol as monotherapy for Colombian cutaneous leishmaniasis. A randomized, controlled trial. Ann Intern Med 1997;126:232-6.
36. Esfandiarpour I, Alavi A. Evaluating the efficacy of allopurinol and meglumine antimoniate (Glucantime) in the treatment of cutaneous leishmaniasis. Int J Dermatol 2002;41:521-4.
37. Llanos-Cuentas A, Echevarria J, Cruz M, La Rosa A, Campos P, Campos M, et al. Efficacy of sodium stibogluconate alone and in combination with allopurinol for treatment of mucocutaneous leishmaniasis. Clin Infect Dis 1997;25:677-84.
38. Navin TR, Arana BA, Arana FE, de Merida AM, Castillo AL, Pozuelos JL. Placebo-controlled clinical trial of meglumine antimonate (glucantime) vs. localized controlled heat in the treatment of cutaneous leishmaniasis in Guatemala. Am J Trop Med Hyg 1990;42:43-50.
39. Velasco-Castrejon O, Walton BC, Rivas-Sanchez B, Garcia MF, Lazaro GJ, et al. Treatment of cutaneous leishmaniasis with localized current field (radio frequency) in Tabasco, Mexico. Am J Trop Med Hyg 1997;57:309-12.
40. Gurei MS, Tatli N, Ozbilge H, Erel O, Seyrek A, Kocyigit A, et al. Efficacy of cryotherapy and intralesional pentostam in treatment of cutaneous leishmaniasis. J Egypt Soc Parasitol 2000;30:169-76.
41. Soto J, Toledo . J. T. Oral miltefosine to treat American cutaneous leishmaniasis Lancet Infect Dis 2007; 7(1): 7.
42. Arevalo J, Ramirez L, Adaui V, et al. Influence of Leishmania species on the response to antimonial treatment in patients with American tegumentary leishmaniasis. J. Infec. Dis 2007; 195 (12): 1846-51.
43. Berman JD, Gallalee JV. In vitro antileishmanial activity of inhibitors of steroid biosynthesis and combinations of antileishmanial agents. J Parasitol 1987;73:671-3.
44. Berman JD. Activity of imidazoles against Leishmania tropica in human macrophage cultures. Am J Trop Med Hyg 1981;30:566-9.
45. Hart DT, Lauwers WJ, Willemsens G, Vanden Bossche H, Opperdoes FR. Perturbation of sterol biosynthesis by itraconazole and ketoconazole In Leishmania mexicana Mexicana infected macrophages. Mol Biochem Parasitol 1989;33:123-34.
46. Brammer KW, Farrow PR, Faulkner JK. Pharmacokinetics and tissue penetration of fluconazole in humans. Rev Infect Dis 1990;12:Suppl 3: S318-S326.
47. Wildfeuer A, Faergemann J, Laufen H, et al. Bioavailability of fluconazole in the skin after oral medication. Mycoses 1994;37:127-30.
48. Alrajhi AA, Ibrahim EA, De Vol EB, Khairat M, Faris RM, Maguire JH. Fluconazole for the treatment of cutaneous leishmaniasis caused by Leishmania major. N Engl J Med 2002;346:891-5.
49. Emad M, Hayati F, Fallazadeh MK, Namazi MR. Superior efficacy of oral fluconazole 400mg daily versus oral fluconazole 200mg daily in the treatment of cutaneous leishmaniasis major infection: a randomized clinical trial. J Am Acad Dermatol 2011 Mar ; 64 (3): 606-8.