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REVIEW ARTICLE

Neglected Tropical Diseases key aspects for the rheumatologist

Le Goueff Anouk*[1], Martin Charlotte[3], Jayne David[2], Hachulla Eric[1], Vandergheynst Frederic[4], Longley Nicky[5,6]

[1] Department of Internal Medicine and Clinical Immunology, Referral Centre for Centre for rare systemic autoimmune diseases North and North-West of France (CeRAINO), CHU Lille, Univ. Lille, Inserm, U1286 - INFINITE - Institute for Translational Research in Inflammation, F-59000 Lille, France
[2] Vasculitis and Lupus Unit, Department of Medicine, University of Cambridge, UK
[3] Infectious Diseases Department, CHU Saint-Pierre, ULB, Brussels
[4] Hôpital Erasme, Internal Medicine Department, 808 route le Lennik, 1070 Brussels, Belgium
[5] Hospital for tropical diseases, UCLH, Mortimer Market Capper St, WC1e 6JB London, UK
[6] London School of Hygiene and Tropical medicine, Keppel St, WC1E 7HT London, UK

***Corresponding author:** Anouk@legoueff.com

ABSTRACT

Neglected tropical diseases (NTDs) are a group of 20 infectious diseases that are no longer restricted to tropical regions and that will be increasingly encountered by physicians of the Northern hemisphere.

In this article, we review key aspects of tropical medicine relevant for rheumatologists or doctors working with autoimmune diseases or immunosuppressive drugs in order to be aware of NTDs, look out for them and prevent their complications.

The article addresses four main topics:

(i) eosinophilia workup,
(ii) rheumatic presentations of NTDs, such as myositis or arthritis
(iii) lupus, granulomatosis with polyangiitis or vasculitis mimickers, such Leishmaniasis, Leprosy or Human African Trypanosomiasis and
(iv) screening before starting immunosuppression, including Strongyloidiasis and Chagas disease

NTDs should be considered and excluded in patients with relevant travel history or exposure in following situations:

i. during the differential diagnosis of a suspected new autoimmune condition,
ii. in case of poor response or flare of symptoms on initiating immunosuppressive therapy,
iii. during systematic screening prior to starting immunosuppressive medication, along with blood born viruses and tuberculosis.

Introduction

Neglected tropical diseases (NTDs) are a group of diseases that affect people living in or travelling to tropical and subtropical countries (Figure 1). Presentation, epidemiology, work-up and treatment of NTDs reviewed in this article are summarized in Table 1 and their geographical distribution is depicted in Figure 2. Raising awareness for these diseases is important because they may affect over a billion people whilst, if recognized, they are preventable and sometimes easily treatable. 1,2,3

Figure 1: Neglected Tropical Diseases

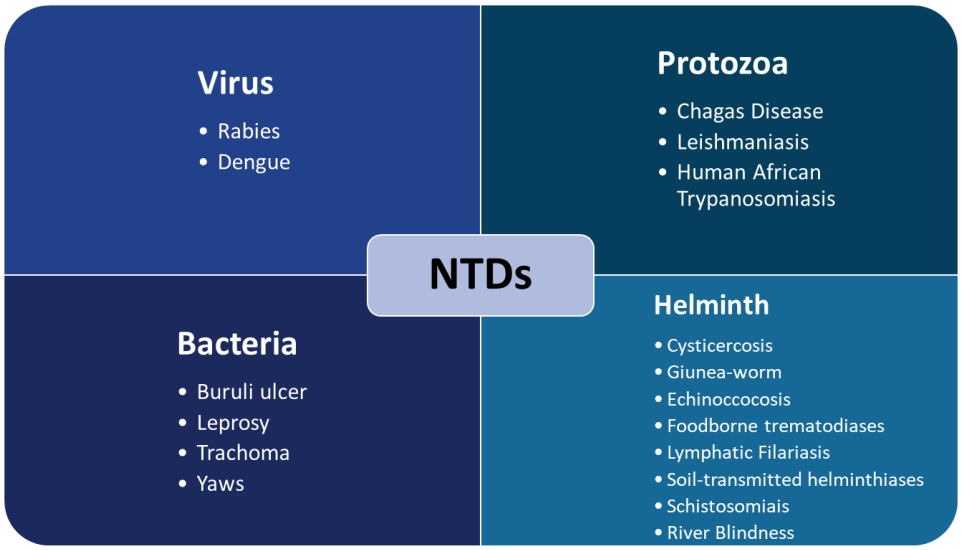

Figure 1: Neglected Tropical Diseases (NTDs). Of note, snake bite is an additional NTD that is not listed above.

Figure 2: World map of Neglected Tropical Diseases

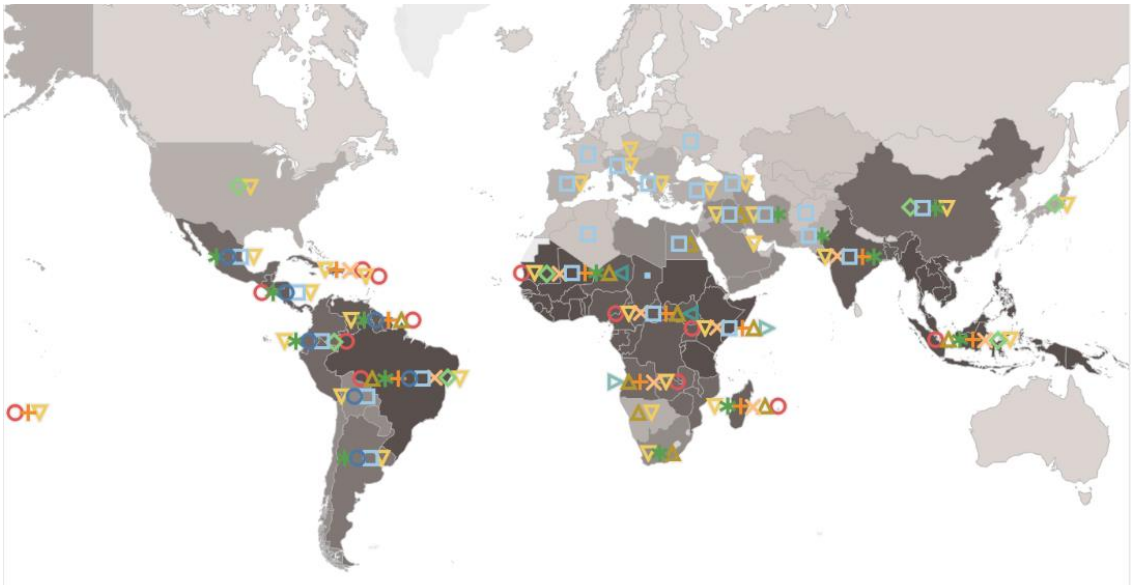

Figure 2: Worldmap of major NTD distribution. ○ : Chagas, □ : Leishmania, ✚ : Leprosy, ✖ : Lymphatic filariasis, ✸ : Melioidosis, ◇ : Paragonimus, △ : Schistosomiasis, ▽ : Strongyloides, ◁ : Trypanosoma gambiense, ▷ : Trypanosoma rhodiense, ○ : Yaws. Grey intensity darkening with raising prevalence of NTDs.

Table 1 : NTDs

Disease	Pathogen	Vector transmission	Epidemiology	Acute symptoms	Chronic manifestation	Diagnosis	Treatment
Leprosy	Mycobacterium leprae	Respiratory	**India, Brazil, Nepal, Ethiopia, Congo,** Afr, S Am, SEA, Oceania	/	Hypopigmented skin patch, thickened nerve, ENT destruction	Skin smear positive for AFB	Rifampicin +Clofazimin +Dapsone 6-12m
Yaws	Trepnoma pallidum pertenue	Skin	**SEA** SSA	Ulcer chancre	Arthralgia, destructive bone + nasopharynx lesions	TPHA, VDRL	Penicillin, Azithromycin
Melioidosis	Burkholderia pseudomallei	water inhalation ingestion skin contact	**SEA N Austalia** C Afr S+C Am	/	pneumonia abscesses osteomyelitis septic arthritis	Blood culture	Ceftazidim 2w then TMP-SMX 12-20w
Chagas Diasease	Trypanosoma cruzi	Triatomine vertical transplant	C+S Am	Chancre Chagoma Romania sign	Heart, CNS megacolon megaoesophagus myocarditis meningo encephalitis	Serology PCR Blood cultures	Nifurtimox Benznidazole 2m
Leishmaniasis	L. donovani L. infantum L. major L. tropica	Sandflies	**VL: Sudan India Bengladesh Nepal Brazil CL: Afghanistan Iran, Saudi Arabia Syria, Brazi Peru** E Afr, S Am, S As, S Eur	CL: non-healing ulcer VL: kala-azar	VL: kala-azar HSM pancytopenia LAD CL: oral/nasal lesions	Serology histology PCR spleen bone marrow aspirates skin biopsy	VL/MCL: Amphotericin B Pentostam 30d CL: intralesions Pentavalent Antimony 4-6w
Human African Trypanosomiasis	Trypanosoma gambiense T. rhodiense	Tsetse fly	Africa	fever chancre LAD	Encephalitis sleep disorder	Thick blood film Serum + CSF IgM CATT, CIATT	Pentamidine Nifurtimox Eflornithine Suramin Melasoprol
Paragonimiasis	Paragonimus spp.	raw fish/**crab**	**China** SEA S Am	Persistent cough brown sputum chest pain night sweats	Persistent cough brown sputum chest pain night sweats	feces ova skin test serology	Preaziquantel 2-3d
Lymphatic filariases	Loa loa Brugia malayi Wucheria bancrofti	Loasis: Chrysops flies Others: any mosquitoes	Loasis: C+W Afr Others: SSA, Asia Pacific	Loasis: urticaria Calabar swelling eye worm Others: acute lymphangitis	tropical pulmonary eosinophilia meningoencephalitis lymphangitis endomyocardial fibrosis, arthritis	Serology night blood cultures PCR	Pred + Albendazol /doxycyclin 4w then DEC/Ivermectin
Schistosomiasis	Schistosoma mansoni S. haematobium S. japonicum	Snails water	SEA SSA S Am	Dermatitis Katayama fever	Liver/uro-genital /endomyocardial fibrosis	Serology urine Ag	Praziquantel

Disease	Pathogen	Vector transmission	Epidemiology	Acute symptoms	Chronic manifestation	Diagnosis	Treatment
Stongyloides	Strongyloides stercoralis	Soil	S+C Am SSA, SEA E Eur	Larva currens Loefller, GI	Malabsorption hyperinfestation syndrome	Serology, stool O&P string test	Ivermectin

Table 1: NTD characteristics. S Am: South America, SEA: Southeast Asia, SSA: Sub-Saharan Africa, Afr: Africa, Eur: Europe, S: South, E: East, W: West, N: North, C: central, w: week, m: month, d: day, ENT: Ear-Nose-Throat, CNS: central nervous system, HSM: hepatosplenomegaly, LAD: lymphadenopathy, , CSF: cerebrospinal fluid, GI: gastro-intestinal, AFB: acid-fast bacilli, PCR: polymerase chain reaction, L: Leishmania, VL: Visceral Leishmania, CL: Cutaneous Leishmania, MCL: muco-cutaneous Leishmania Pred: prednisone, Ag: antigen, TPHA: Treponema Pallidum Particle Agglutination Test, VDRL: Veneral Disease Research Laboratory, TMP-SMX: Trimethoprim-sulfamethoxazole, CATT: Card Agglutination Test for Trypanosomiasis, CIATT: Card Indirect Agglutination Trypanosomiasis Test, DEC: Diethylcarbamazine, O&P: ova and parasites

Epidemiology

Until recently, NTDs were thought to be restricted to low-income countries, as industrialized nations had eliminated them by water sanitation, vector control and public health infrastructures. 3,4 However, NTD incidence is now rising in the Northern hemisphere due to climate change, migration and travel. 4,5,6,7 Currently, it is estimated that more than 10 million Americans are infected with at least one NTD. 4 Due to climate change, many tropical species have shifted their geographic range towards Northern latitudes and higher altitudes. 5,8,9,10 As such, locally transmitted outbreaks of dengue or leishmaniasis have recently occurred in Europe and the USA after decades of absence. 4,11 Moreover, the biggest drivers of infectious disease events remain international trade and travel that has expanded dramatically over the last decades and with patterns that have changed: increase of migration to the USA from Asia and Latin America instead of Europe and increase of immigrants from non-EU countries to Europe. 5,12,15,16,17 Infection was detected in 3.7% of migrants [range: 0.00 – 95.16] arriving in Europe, with latent tuberculosis having the highest prevalence. 18 As a result of travel and migration, diseases can be encountered in areas where their vector is not located: Chagas disease that was once confined to Latin America, is now reported in North America and Europe. 4,22,23

Internists and rheumatologists working in high income countries are regularly taking care of patients with diagnostic challenges or at increased risk of infection and pathogen reactivation due to iatrogenic immunosuppression for their underlying disease. This review aims to inform them of the key elements to bear in mind when taking care of a patient who has travelled or lived in low- or middle-income countries in terms of eosinophilia workup, differential diagnosis and screening before starting immunosuppressive therapy.

1. EOSINOPHILIA WORKUP

Eosinophilia is defined by an eosinophil count above 500/µL and is most frequently associated with drug allergy, neoplasia, helminth infection and non-infectious eosinophilic inflammatory disease, such as eosinophilic asthma and eosinophilic granulomatosis with polyangiitis (EGPA). 3,24,25 Infrequently, non-helminthic infections, such as human immunodeficiency virus (HIV), human T-cell lymphotropic virus type 1 or 2 (HTLV1/2), Isospora *belli*, Aspergillus *spp*, Coccidiodes *spp*, Paracoccidioides *spp*, Histoplasma *spp* and Cryptococcus *spp* can cause eosinophilia. 24 In developed countries, allergy is the first aetiology for eosinophilia, while in tropical regions, helminth infection represents the main diagnosis. 24 Even in a patient without travel history, *Ascaris, Toxocara, Strongyloides* and *Trichinella* infection should be evoked. 27 Prevalence of eosinophilia varies between 8-28.5% amongst migrants and travellers and a helminthic cause is found in 17-76%; migrants being more frequently affected than travellers. 24,26 *Strongyloides stercoralis* is the most common helminthic cause of eosinophilia in Spain and in the UK, regardless of the country of origin, and its rate has been increasing over the last years. 24,26

Investigation of eosinophilia relies on the personal history and clinical presentation (table 2). Work-up should include basic laboratory studies as well as three stool samples looking for ova, cysts and parasites. In 25-30% of travellers and migrants, eosinophilia remains idiopathic after investigation. In such patients, empiric treatment with ivermectin 200µg/kg/d for 2 days, albendazole 400mg BID/day for 15 days and praziquantel 40mg/kg/d once achieves a cure rate of over 90%, shown by a disappearance of eosinophilia at 3 months. 24,28

Table 2 : Eosinophilia workup

Disease	Distribution	Transmission	Symptoms	Diagnosis	Treatment
Without travel history					
Toxocara canis/cati	Worldwide	Dog/cat feces	VLM encephalitis myocarditis OLM	Serology	Albendazole +/- CS for VLM/OLM
Fasciola hepatica	Worldwide	Ingestion of water plants	Hepatomegaly urticaria abdo pain	Serology stool ova	Triclabendazole
Trichinella spiralis	Worldwide	Undercooked meat	Myalgia, myositis, edema, myocarditis, meningitis, vasculitis	Serology, stool larvae	Albendazole Mebendazole +/- CS
Anisakis spp.	Worldwide	Raw fish	Acute GIS, chronic sensitization	Endoscopy visualization	Self-limited, Albendazole?
Ascaris spp.	Worldwide	Feco-oral	Loeffler, GIS, malabsorption, malnutrition, obstruction	Stool ova	Benznidazole + piperazine
Echinococcus spp	Worldwide, mostly pastural communities	Ingestion of dog feces	Slowly growing mass/syptoms; abrupt symptoms if rupture	Serology imaging	Albendazole, Praziquantel, PAIR procedure, surgery
Strongyloides	worldwide; mostly sub/tropics	Barefoot walking	larva currens, Loeffler, GIS malabsorption	Serology, stool larvae	Ivermectin
With travel history to LIC/tropical country					
<2 years					
Paragonimus spp.	SEA, S Am, Pacific	Raw crab/crayfish	Persistent cough brown sputum chest pain night sweats	feces ova skin test serology	Praziquantel 2-3d
Angiostrongylus cantonensis	SEA, Pacific, Africa, S Am	Raw snails	eosinophilic meningitis	Larvae in CSF	Supportive
<2 years or >2 years					
Schistosoma spp.	Africa, Asia, S am	Snails/water	dermatitis, Katayama fever, GI/urogenital inflammation/fibrosis	Serology urine Ag	Praziquantel
Strongyloides	worldwide, mostly sub/tropics	Barefoot walking	larva currens, Loeffler, GIS, malabsorption	Serology, stool larvae	Ivermectin
Cysticerca	C+S Am, SSA, SEA	feco-oral	epilepsy, ocular/muscle nodules	Serology	Albendazole + Praziquantel + CS 2-4w
Filariasis	Loasis: C+W Afr Others: SSA, Asia Pacific	Mosquito/flies	TPE meningoencephalitis lymphangitis endomyocardial fibrosis, arthritis	Serology night blood cultures PCR	Pred + Albendazole/ doxycyclin 4w then DEC/Ivermectin
Ankylostomiasis	tropics/coal mines	Skin	Loeffler, anaemia, malabsorption edema	Stool ova	Benznidazole
Gnathostoma spingerum	SEA	Raw fish	GIS, VLM, eosinophilic meningitis	Serology	Albendazole/ Ivermectin >21d

Table 2: Eosinophilia work-up. CS: cortico-steroids, OLM: ocular larva migrans, VLM: visceral larva migrans, GIS: gastro-intestinal symptoms, SEA: Southeast Asia, S Am: South America, C+S Am: Central and South America, SSA: Sub-Saharan Africa, C+W Afr: Central and West Africa, d: day, CSF: cerebrospinal fluid, Ag: antigen, TPE: Tropical Pulmonary Eosinophilia, PCR: polymerase chain reaction, DEC: Diethylcarbamazine

2. RHEUMATOLOGIC MANIFESTATIONS OF TROPICAL DISEASES

Presentation with arthralgia, myalgia, fatigue, weight loss, fever or rash may be presenting features of immune-mediated inflammatory diseases (IMID), such as, rheumatoid arthritis, ankylosing spondylarthritis, psoriatic arthritis, vasculitis or connective tissue disorders or they may have an infective, post-infective or reactive aetiology. 30,31 Parvovirus B19, Rubella, hepatitis B and C virus, HIV, tuberculosis and toxoplasmosis can present as IMID-mimickers regardless of travel history, whilst dengue, Chikungunya, Brucella, leprosy, fungi, parasites and helminths must be ruled out in a returning traveller or a migrant. 29,32,33,34,35,36,37 There have also been

reports of inflammatory diseases that had been misdiagnosed as infectious diseases. For example, in the Byzantine era, some individuals were exiled into the Judean desert with Leprosy. Excavations, millennials later, have revealed that they had psoriatic arthropathy and not Leprosy. 38 Specific features of rheumatological presentations of tropical diseases are summarized in Table 3.

Table 3: Rheumatological presentations of NTDs

Arthritis	
Large joint monoarthritis	
Dracunculosis	Destructive arthritis Patient well
Filariasis	Chylous arthritis Febrile patient Myalgia
Psoriasic-like: large joint oligoarthritis, enthesopathy, sacroileitis	
Schistosoma	Pruritic papular erythema Glomerulonephritis Vasculitis
Strongyloides	
Brucellosis	Fever Malaise Pruritic papular erythema Glomerulonephritis Vasculitis Spondylitis Bursitis Uveitis
Rheumatoid arthritis-like : symmetrical arthritis, enthesitis and tenosynovitis of small joints +/- mono/oligoarthritis NB: Patients may have raised rheumatoid factor and fulfill ACR criteria for rheumatoid arthritis	
Giardiasis	Urticaria Erythema nodosum
Onchocerciasis	Itchy dermatitis Subcutaneous nodules Keratitis Myositis Glomerulonephritis
Leprae	Mononeuritis multiplex Thickened nerves Hypopigmented skin patches
Chikungunya	Mostly triad: rash + fever + arthritis Persistent invalidating polyarthritis can last for years in 10-20%
Other arthritis	
Anisakiasis	Symmetrical arthritis of ankles, knees, elbows
Toxocariasis	Monoarthritis or oligoarthritis Vasculitis Myositis
Amoebiasis	Arthralgia Back pain
Loasis	Calabar swelling: transient migrating swelling
Histoplasmosis Cryptococcosis Paracoccidoidosis Sporotrichosis Blastomycosis Penicilliosis	Chronic low-grade arthralgia or arthritis Osteomyelitis Bony destructions Subcutaneous abscesses Lung involvement

Myositis		
Invasion of the muscle cell		
Toxoplasma	Unwell patient Generalized myalgia Pyrexia Cough Headache Abdominal tenderness Urticaria Lymphadenopathy	If immunosuppressed: possible neurological, ophtalmological, pulmonary involvement, polymyositis
Trichinella		Periorbital oedema Eosinophilia Polymyositis/ Dermatomyositis /PAN-like vasculitis
Toxocara		Visceral larva migrans: fever, HSM, wheezing, transient myositis Ocular larva migrans
American Trypanosomiasis		During acute or chronic stages
Schistosomiasis		Katayama fever: fever + malaise + urticarial rash Sometimes myositis
Taenia	Usually asymptomatic muscle involvement	Well patient 1st cause of epilepsy worldwide
Echinococciasis	Local symptoms	
Amoebiasis	Gastro-intestinal symptoms	
Immune-mediated myositis during migration phase		
Dracunculus medinensis	Patient well	
Toxocara	Monoarthritis or oligoarthritis Vasculitis	

Table 3: Rheumatological presentations of NTDs. ACR: American College of Rheumatology, PAN: Polyarteritis Nodosa

3. TROPICAL DISEASES MIMICKING AUTOIMMUNE CONDITIONS

In addition to the rheumatological presentations of NTDs, some NTDs can mimic autoimmune conditions. They have to be ruled out in a patient with travel history to tropical or subtropical regions –including the Mediterranean basin, presenting with symptoms compatible with an autoimmune condition or a flare-up of a known rheumatological condition.

3.a. Lupus-mimickers

In 2019, the European League Against Rheumatism (EULAR) and the American College of Rheumatology (ACR) developed new classification criteria for systemic lupus erythematosus (SLE) with

a sensitivity of 96.1% and a specificity of 93.4%. These diagnostic criteria are based on positive antinuclear antibodies (≥ 1:80 on Hep-2 cells) followed by additive weighted criteria such as arthritis, rash, serous effusion, nephritis, cytopenia, autoimmune haemolysis, anti-double-stranded DNA (dsDNA), antiphospholipid antibodies and low complement proteins. 41,42 Visceral leishmaniasis, *Mycobacterium leprae*, and African Trypanosomiasis can fulfil the 2019 EULAR/ACR criteria hence presenting as SLE mimickers. 41,43,44,45

Leishmaniasis is caused by different species of Leishmania protozoa transmitted by phlebotomine sandflies. Leishmania is an obligate intracellular parasite of lymphoid organs that can cause 3 distinct clinical pictures: visceral leishmaniasis (VL) when the parasite disseminates to the spleen, lymph nodes, bone marrow and liver; cutaneous leishmaniasis (CL) when it is limited to phagocytes of the skin, or mucocutaneous leishmaniasis (MCL) when spreading from the skin to nasal or oro-pharyngeal mucosa. 11,20,43,46 VL affects 50.000-400.000 people annually, mainly in Brazil, Bangladesh, India, Nepal and Sudan; France, Italy, Spain and the USA are endemic countries. Almost 2000 cases are reported annually in Europe, mostly in people living or travelling to the Mediterranean Basin with some kind of underlying immunosuppression. 46 VL is fatal in 95% of cases if left untreated and is characterized by chronic fever, weight loss, pancytopenia, polyclonal hypergammaglobulinemia, hepatosplenomegaly and anaemia. 11,20,43 One study reported that 80% of VL patients had ANAs >1/80, 4% had raised dsDNA and 27% raised rheumatoid factor (RF). Other reports have shown that VL patients can harbour anti-Sm, anti-cardiolipin antibodies or complement activation. 43,44,47 A case series from Santana *et al*. reported 18 cases of VL leading to an inappropriate suspicion of SLE and 10 cases of SLE with VL mimicking a lupus flare. 47 Massive splenomegaly and high CRP were more common in VL, whereas arthritis and low complement were more common with SLE diagnosis. 47,50

Leprosy is a chronic granulomatous disease caused by *Mycobacterium leprae* (ML). Although ML cases have diminished drastically over the last decades, its prevalence remains stable since 2005, with 200.000 cases reported annually, mainly in India, Brazil, Indonesia, Bangladesh, Ethiopia, Nigeria and Tanzania. 21,48,49,50 As incubation may be as long as 20 years, travel may have occurred a long time before diagnosis and in some cases, treatment with Tumour Necrosis Factor inhibitors unravels a dormant disease. 21,48,49,51 In 2018, 50 new cases were diagnosed in Europe and 185 in the USA. 21 Patients typically present with hypopigmented hypaesthesic skin patches and thickened peripheral nerves that can lead to paresis or paraesthesia. 48,49 However, leprosy can also present with Rheumatoid-like arthritis or spondylarthropathy-like arthritis (25-62%), a rash (72%), malar rash (44%), photosensitivity (29%), positive ANA >1/80 (30%), antiphospholipids (98%) or lymphopenia (19%) and thus be misdiagnosed as SLE or as lupus flare. 45,51,52,53,54,55,56 Other features that can be seen are oral ulcers, orchitis, mononeuritis multiplex, erythema nodosum, lymphadenopathy, uveitis, necrotizing vasculitis, haemolytic anaemia, glomerulonephritis, RF, ANCA, dsDNA, anti-CCP, or anti-Sm. 45,48,56,59 Numerous cases are reported where patients were misdiagnosed as lupus and leprosy diagnosis was finally made after clinical worsening under steroid, hydroxychloroquine or mycophenolate mofetil treatment. 57,58,59,60

Human African Trypanosomiasis (HAT) is a sub-acute protozoan illness caused by Trypanosoma brucei *spp*. that is transmitted mainly by tse-tse flies and is endemic in Africa only. 61 Between 2000 and 2010, 94 HAT cases were reported in non-endemic countries, 72% from *T.b. rhodiense*, usually in travelers infected while doing Safari tourism in Tanzania, Kenya or Malawi and 28% from *T.b. gambiense*, usually in migrants or long-term travelers from Democratic Republic of Congo (DRC). 62,63 HAT is characterized first by a haemo-lymphatic stage, with fever, headaches, lymphadenopathy, chancre, arthralgia and pruritus that last from months to years depending on the species. Secondly, it will convert to the meningo-encephalitic stage, characterized by behavioral changes, confusion, sensory disturbances, ataxia and sleep cycle disturbances, which is almost always fatal without treatment. 61 Case reports of misdiagnosis with SLE or neurolupus have been published, where patients presented with persistent fever, malaise, headaches, pancytopenia, rash, serositis and arthralgia. 62,63,64,65 In those patients, ANA were raised (>1/80) in up to 84%, sometimes with polyclonal hypergammaglobulinemia, anti-Sm or anti-cardiolipin antibodies. Important symptoms and signs suggesting HAT over SLE are the presence of severe headache, a chancre, a travel history to Africa, and large cervical lymphadenopathy (Winterbottom sign). 63

3.b. Localized Granulomatosis with Polyangiitis (GPA)-mimickers

Ear-Nose-Throat (ENT)-limited GPA is suspected when a patient presents with chronic inflammatory lesions of the sino-nasal tract, with rhinorrhea,

hyposmia, nasal bleeding, crusting, obstruction, nasal septum perforation or saddle-nose deformity. 66 ANCA, mainly of proteinase 3 (PR3), but sometimes of myeloperoxidase (MPO) specificity are present in 90% of generalized GPA patients, but can be rarely detected in RA, SLE, Crohn's disease, HIV and cocaine-abuse. New ACR/EULAR classification criteria for ANCA vasculitis have been published in 2022 combining clinical, laboratory, imaging and biopsy criteria. 67 To be used as diagnostic criteria on an individual level, alternate diagnoses mimicking vasculitis should be excluded. Differential diagnoses include chronic rhinosinusitis, cocaine-abuse and extranodal natural killer or T-cell lymphoma (NKTL). More rarely, infectious diseases, such as HIV, TB, Syphilis, Klebsiella or Histoplasma infection or autoimmune affections, such as EGPA, sarcoidosis, relapsing polychondritis, SLE and Crohn's disease have to be excluded. 68,69,70,71 Leprosy and cutaneous or mucocutaneous leishmaniasis are NTDs that can cause chronic inflammatory lesions of the sinonasal tract and thus should be considered in patients presenting with symptoms of limited GPA and having a migratory or travel history from the South of France southward. Furthermore, these NTDs are characterized by granuloma on histology and they can present with raised ANCA levels, thus easily fulfilling ACR criteria for limited GPA. 66,67,69,70,71,72,73,74,75

In leprosy, the nasal cavity is usually the initial and most frequent site of involvement, with more than 95% of the patients presenting with symptoms of chronic rhinosinusitis. 69,70,71,73,75,76,77,78,76 oreover, 36-48% of lepromatous patients display external nasal deformities and 9-34% develop septum perforations. 71,75,77 Furthermore, leprosy can lead to ear deformities in 38-73%, involve paranasal sinuses, the larynx or the oral cavity in 19-60% and can cause eye deformities in 22-48%, facial nerve palsy in 10-25 % or facial hypopigmentation. 75,79,80 ANCA, being mostly p-ANCA, can be raised in up to 28-62% of leprosy patients. 73 Canacho *et al*. reported a case of a Colombian patient living for 10 years in the US who was diagnosed with leprosy after years of unsuccessful treatment for resistant chronic rhinitis. Lockwood *et al*. also reported various leprosy patients misdiagnosed as GPA, vasculitis, sarcoidosis or cutaneous TB in the UK. 74,81

Cutaneous Leishmaniasis (CL) is the most common form of leishmaniasis, affecting 1.5 million people worldwide annually. More than 90% of CL cases occur in Iran, India, Pakistan, Afghanistan, Syria, Saudi Arabia and Algeria. In Europe, Spain and Portugal are endemic countries. 82 It presents as a slowly evolving chancre that will heal spontaneously within a year. Mucocutaneous leishmaniasis (MCL) can complicate CL in Central and South America (essentially Bolivia, Brazil and Peru) and lead to chronic nasal inflammation, stuffiness, septum ulceration and perforation. 68,69,70,72,76,82 Travel, migration and climate change are spreading these diseases to non-endemic countries such as Northern America, the North of Italy, the Jura region in France and Central Europe. 76,83 In Europe, imported cases are increasing and originate mainly from backpackers to Central and South America and tourists to the Mediterranean region. Two patients, one from Bolivia and one from Germany with a travel history to Panama, were reported in Spain, and one Brazilian patient was reported in the US, with chronic rhinorrhea, bleeding, crusting and necrotic areas that were misdiagnosed and treated as GPA or NKTL. Diagnosis of MCL was made after treatment failure and disease progression despite prednisone, cyclophosphamide, methotrexate, azathioprine or CHOP chemotherapy. 76 All cases mentioned above were ANCA negative and eventually achieved remission with IV liposomal amphotericin B. 76

3.c. Vasculitis-mimickers

Vasculitis has been reported with leishmaniasis, angiostrongyliasis, Chagas' disease, amoebiasis, ascariasis, leprosy and toxocariasis. Leishmaniasis can manifest as cutaneous vasculitis with dermatomyositis-like eruption, accompanied by myositis, glomerulonephritis or interstitial nephritis.35 Angiostrongyliasis can cause pulmonary and intestinal vasculitis on top of the eosinophilic meningitis, which is its core manifestation35. Chagas' disease can generate central nervous system vasculitis35. Amoebiasis has been associated with intestinal, central nervous system, cutaneous or renal vasculitis and ascariasis with aortitis or EGPA-like vasculitis. 35,84,85 Leprosy can present with almost any rash, diverse musculoskeletal symptoms, and a clinical picture resembling scleroderma, polyarteritis nodosa (PAN), Guillain-Barre syndrome, RS3PE syndrome or relapsing polychondritis. 86,87,88,89,90,91, 92,93,94 Although toxocariasis is caused by a cosmopolite helminth, typically presenting with asthenia, pruritus, abdominal pain and hypereosinophilia in a patient having contact with cats or dogs, its presentation can be challenging. The subacute form is called visceral larva migrans (VLM), caused by hypersensitivity and sometimes vasculitis triggered by the migration of the larvae through inner organs. 95,96 VLM manifests with asthenia, fever, migrating oedema, hepatosplenomegaly and sometimes with

cutaneous, pulmonary, gastrointestinal or neurological symptoms. ANA, dsDNA and other antibodies can be elevated and the condition can be misdiagnosed for SLE. 95,96

4. SCREENING BEFORE IMMUNOSUPPRESSION

Chronic immune-mediated inflammatory diseases (IMID), connective tissue diseases and vasculitis affect up to 8% of the world population. Affected patients are more likely to present with severe infections and hospitalisation, due to the disease itself as well as by the immunosuppressive therapy used to treat it. 32,97 Inflammatory diseases were previously thought to be rare amongst people living in low- and middle-income countries (LMIC) but a similar prevalence is now reported globally. 33 As such, tropical diseases may put at risk people receiving immunosuppressant agents that are living in these areas as well as those traveling to or migrating from them. 32,98

Screening before immunosuppression aims to detect patients at risk of reactivation of chronic/latent infection before initiating treatment.

Guidelines for screening before immunosuppression of the native population are widespread in high income countries (HIC) 14,28,99,100 and recommend testing for HIV, hepatitis B and C and latent tuberculosis infection. 27 However, specific recommendations for screening of immunosuppressed individuals who travel or migrate from LMIC to HIC or *vice versa* are lacking. Although most NTDs are symptomatic in the acute phase and self-limited, some, such as *Strongyloides stercoralis and Trypanosoma cruzi* usually cause a silent infection for years to decades. However, they can provoke life-threatening complications after immunosuppression if not detected and treated beforehand. 6,22,101,107

Strongyloides stercoralis and Trypanosoma cruzi

Strongyloides stercoralis is a soil-transmitted helminth living in a broad geographical range of tropical and subtropical regions. 101 This NTD affects globally 30-100 million people 101,102 and Strongyloidiasis has been detected in up to 75% of refugees arriving to Europe 103 and North America. 13,102 While presenting with mild gastrointestinal symptoms or being asymptomatic in immunocompetent hosts, immunosuppression, especially high dose glucocorticoids put patients at risk for Strongyloides hyperinfection syndrome (lethality of 85-100%). 32,101,102,103 Screening or systematic preemptive treatment with a single dose of Ivermectin in migrants or travellers from South-East Asia (SEA), South and Central America, Sub-Saharan Africa (SSA) or for any patient with eosinophilia is recommended (grade of evidence Ia). 28,102,103

Chagas disease is a vector-borne disease, caused by the parasite *Trypanosoma cruzi* and is endemic to Central and South America. In 2010, over 5 million persons were infected worldwide, of which 120,000 living in Europe. 105,106 Spain accounts for 75% of European cases, but Italy, the Netherlands, UK, Germany and France also report a prevalence of approximately 6% in Latin American migrants. 32,105 While asymptomatic in the vast majority of cases, the parasite persists in the human body for a lifetime and can provoke cardiac, gastrointestinal and neurologic complications in 30-40% of patients, 10 to 30 years after infection. 22,23,105 In cases of immunosuppression, especially in HIV and transplant recipients, the disease can reactivate mostly with meningo-encephalitis, sometimes with subcutaneous nodules (chagoma), panniculitis and myocarditis. 23,28 Italian and Spanish guidelines now recommend screening for Chagas disease before immunosuppression, for people who lived, or whose mother lived, in Latin America for more than 3 months or who received a blood transfusion in these countries (grade of evidence III). 27,105

Other tropical diseases may also be considered for screening before immunosuppression in special circumstances and are summarized in Table 4. 27,32

Table 4 : Screening before immunosuppression

Disease	Criteria	Screening method	Treatment if screening positive
Always screen for			
Tuberculosis, HIV, Hepatitis B&C			
Strongyloides	If travel to the Southern hemisphere or Meditarranean basin OR if eosinophilia	Serology	Ivermectin 1x repeat if needed NB: if travel to W/C Afr: thin + thick blood film for loasis
Chagas	If lived/his mother lived in C/S Am for >3m or if transplant/transfusion in C/S Am	Serology	Benznidazole/nifurtimox

Disease	Criteria	Screening method	Treatment if screening positive
Schistosomiasis	If travel to Africa, Asia or South America	Serology Urine or Stool microscopy	Praziquantel
Salmonellosis	If Asia/Africa/CS Am, Oceania AND cholelithiasis or urinary tract defect	Stool or urine culture	Ampicillin Amoxycillin TMP-SMX
If symptomatic, rule out before starting biologics			
If respiratory symptoms, bronchiectasis, lung alterations			
Non-Tuberculosis Mycobacterium	Regardless of the country of origin	Sputum/blood culture	Macrolide + Ethambutol + Rifamycin +/- Aminoglycoside
Histoplasmosis Coccidioido mycosis Paracoccidio idomycosis	Americas AND pneumonia history or abnormal CXR	Serology	Itraconazole Fluconazole Amphotericin B
In febrile patients			
Brucella	If coming from a Mediterranean country/NE Afr, Middle East, SEA, Americas AND exposed to unpasteurized milk/cattle	Serology	Streptomycin 2-3w or gentamycin 5-7d + Doxycyclin 8w
Leishmaniasis	If HSM/pancytopenia AND travel southwards from the South of the US or of Europe on	Serology PCR of spleen/bone marrow aspirates/skin biopsy	Amphotericin B or Pentostam 30d
Babesiosis	If tick bite in Europe/USA/Australia/Taiwan/Japan/ Korea	Blood smear Serology PCR	Atovaquone + Azithromycin or Clindamycin + quinine 7-10d
Others			
Mycobacterium leprae	If coming from Africa, SEA, Americas, W Pacific, Mediterranean AND unexplained cutaneous lesions or peripheral neuropathy	Skin smear positive for AFB	Rifampicin +Clofazimin +Dapsone 6-12m
Cysticercosis	If epilepsy in an adult with travel history to a LIC	Serology	Albendazole + Praziquantel + CS 2-4w
Hepatitis E	In migrants with unexplained liver enzyme abnormalities	Serology PCR	Delay immunosuppression
General recommendations for patients on biologics: hand hygiene, use bottled water, avoid unpasteurized milk and uncooked shellfish/fruits/vegetables			

Table 4: Screening before immunosuppression. W/C Afr: West or Central Africa, C/S Am: Central or South America, NE Afr: North-East Africa, SEA: Southeast Asia, US: United States of America, d: day, m: months, w: week, TMP-SMX: Trimethoprim-sulfamethoxazole, CXR: chest X-ray, HSM: hepatosplenomegaly, PCR: polymerase chain reaction, LIC: low-income country, CS: cortico-steroids

Strengths and limitations

This review has collated local guidelines, case reports and expert recommendations in order to give an overview of NTDs to internists and rheumatologists working in high income countries (HIC). Thereby a wide range of diseases and of clinical pictures have been covered. However, we have not attempted to put together a systematic review of NTDs nor of autoimmune disease management; the PRISMA or STROBE guidelines are thus not applicable to this work. No clear guidelines can be elaborated from this article as epidemiology and health care systems may change from one HIC to another. Moreover, many case reports have been included in this literature review

and the quality and methodology could vary considerably amongst them.

Conclusion

With global international travel and climate change, NTDs are no longer restricted to tropical regions and should be considered in high income countries in patients presenting with non-specific symptoms of autoimmune disease, especially in atypical or treatment-resistant cases. NTDs can be misdiagnosed as autoimmune diseases or inversely and immunosuppression increases the risk of NTD infection or reactivation. Neglected Tropical Diseases are particularly misdiagnosed when (i) the infection is chronic, (ii) the incubation period is long and the travel history is old, (iii) their geographical range is progressing northward and reaching the South of Europe or of the USA, (iv) they present with positive auto-antibodies and (v) their diagnosis is arduous.

More work is needed (i) to assess the changing epidemiology of NTDs in HIC, (ii) to investigate the infectious burden of latent infections and the percentage of mimickers and (iii) to pull together unified guidelines and cost-effective strategies for screening of NTDs in the population of patients receiving immunosuppressive therapy in order to avoid unnecessary morbidity and mortality.

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References

1. The Lancet. Neglected tropical diseases: becoming less neglected. *Lancet* 2014;383(9925):1269.
2. Holmes P. Neglected tropical diseases in the post-2015 health agenda. *Lancet* 2014;383(9925):1803.
3. O'Connell EM, Nutman TB. Eosinophilia in Infectious Diseases. *Immunol Allergy Clin North Am* 2015;35(3):493–522.
4. Neglected tropical diseases: no longer someone else's problem. *Lancet Infect Dis.* 2014;14(10):899.
5. Seventh Meeting of the Working Group on Health in Climat Change (HIC) of the European Environment and Health Task Force. Bonn: World Health Organization; 2019 (https://www.euro.who.int/ data/assets/pdf file/0004/440338/7th-meeting-Health-in-Climate-Change-HIC.pdf).
6. Fabiani S, Bruschi F. Rheumatological patients undergoing immunosuppressive treatments and parasitic diseases: A review of the literature of clinical cases and perspectives to screen and follow-up active and latent chronic infections. *Clin Exp Rheumatol* 2014;32 :587-596.
7. Zammarchi L, Gobbi F, Bartoloni A *et al.* Schistosomiasis, strongyloidiasis and Chagas disease: the leading imported neglected tropical diseases in Italy. *J Travel Med* 2020;27(1):taz100
8. Public health and climate change adaptation policies in the European Union – final report. Geneva: World Health Organization; 2018 (https://www.euro.who.int/ data/assets/pdf file/0010/386965/Pagoda-REPORT-final-published-2.pdf).
9. Climate change data and statistics. Geneva: World Health Organization (http://www.euro.who.int/en/health-topics/environment-and-health/Climate-change/data-and-statistics, accessed 09 August 2020)
10. Climate change and health. Geneva: World Health Organization; 2017 (https://www.who.int/mediacentre/factsheets/fs266/en/, accessed 09 August 2020).
11. Manual on management and surveillance of the leishmaniases in the WHO European Region. Geneva: World Health Organization; 2017 (https://www.who.int/leishmaniasis/resources/EURO WHO Leish manual on case management and surveillance 9789289052511 2017.pdf?ua=1).
12. Romero Alegría A, Hernández Cabrera, Pérez Arellano JL, *et al.* Fake imported tropical diseases: A retrospective study. *Rev Esp Quimioter* 2018;31(6):528-531.
13. Statistics Canada. Table 17-10-0008-01 Estimates of the components of demographic growth, annual ; 2021 (https://www150.statcan.gc.ca/t1/tbl1/en/tv.action?pid=1710000801, accessed 13 September 2021).
14. U.S. Department of Homeland Security. Table 20. Petitions for Naturalization Filed, Persons Naturalized, and Petitions for Naturalization Denied: Fiscal Years 1908 to 2019; 2020 (https://www.dhs.gov/immigration-statistics/yearbook/2019/table20, accessed 13 September 2021).
15. Migration and migrant population statistics. Eurostat 2020 (https://ec.europa.eu/eurostat/statistics-explained/index.php/Migration and migrant population statistics#Acquisitions of citizenship: EU-27 Member States granted citizenship to 672 thousand persons in 2018, accessed 09 August 2020).
16. Keystone JS. Chapter 9 - Visiting Friends & Relatives. Centers for Disease Control and Prevention; 2020 (https://wwwnc.cdc.gov/travel/yellowbook/2020/travel-for-work-other-reasons/visiting-friends-and-relatives-vfr-travel, accessed 09 August 2020)
17. Migration Data Portal. (https://migrationdataportal.org/?i=stock abs &t=2019, accessed 09 August 2020).
18. Seedat F, Hargreaves S, Friedland JS, *et al.* How effective are approaches to migrant screening for infectious diseases in Europe? A systematic review. *Lancet Infect Dis* 2018;18:259–271.
19. Cinardo P, Farrant O, Gunn K, Ward A, Eisen S, Longley N. Screening for neglected tropical diseases and other infections in refugee and asylum-seeker populations in the United Kingdom. *Ther Adv Infect Dis* 2022 ;9:20499361221116680.
20. Leishmaniasis. Geneva: World Health Organization; 2020 (https://www.who.int/health-topics/leishmaniasis, accessed 09 August 2020).
21. Leprosy (Hansen's disease. Geneva: World Health Organization; 2020 (https://www.who.int/health-topics/leprosy, accessed 09 august 2020).
22. Chagas disease (also known as American trypanosomiasis. Geneva: World Health Organization; 2020 (https://www.who.int/en/news-room/fact-

sheets/detail/chagas-disease-(american-trypanosomiasis), accessed 09 august 2020).
23. Salvador F, Sánchez-Montalvá A, Valerio L, Molina I, *et al*. Immunosuppression and Chagas disease; experience from a non-endemic country. *Clin Microbiol Infect* 2015;21(9):854-860.
24. Salas-Coronas J, Ramírez-Olivencia G, Muñoz J, *et al*. Diagnosis and treatment of imported eosinophilia in travellers and immigrants: Recommendations of the Spanish Society of Tropical Medicine and International Health (SEMTSI). *Rev Esp Quimioter* 2016; 30(1):62-78.
25. Valent P, Klion AD, Gleich GJ, *et al*. Contemporary consensus proposal on criteria and classification of eosinophilic disorders and related syndromes. *J Allergy Clin Immunol* 2012;130(3):607-612.
26. Barrett J, Warrell CE, Whitty CJM, *et al*. The changing aetiology of eosinophilia in migrants and returning travellers in the Hospital for Tropical Diseases, London 2002-2015: An observational study. *J Infect* 2017;*75*(4):301-308.
27. Bartalesi F, Scirè C, Requena-Méndez A, *et al*. Recommendations for infectious disease screening in migrants to Western Europe with inflammatory arthropathies before starting biologic agents. Results from a multidisciplinary task force of four European societies (SIR, SER, SIMET, SEMTSI) facing the largest impact of the flow of migrants today. *Clin Exp Rheumatol*. 2017;35(*5*):*752*-765.
28. Fairley JK. Chapter 11 – General approach to the returned traveller. Centers for Disease Control and Prevention; 2020 (https://wwwnc.cdc.gov/travel/yellowbook/2020/posttravel-evaluation/general-approach-to-the-returned-traveler, accessed 09 August 2020).
29. Misra DP, Sharma A, Agarwal V. Rheumatology science and practice in India. *Rheumatol Int*. 2018;38(9):1587-1600.
30. Alpay-Kanıtez N, Çelik S, Bes C. Polyarthritis and its differential diagnosis. *Eur J Rheumatol* 2018;6(4):167-173.
31. Mathew AJ, Ravindran V. Infections and arthritis. *Best Pract Res Clin Rheumatol* 2014;28(6):935-959.
32. Shu Kurizky P, Dos Santos Neto LL, Martins Gomes C, *et al*. Opportunistic tropical infections in immunosuppressed patients. *Best Pract Res Clin Rheumatol* 2020;101509.
33. Adizie T, Adebajo AO. Travel- and immigration-related problems in rheumatology. *Best Pract Res Clin Rheumatol* 2014;28(6):973-985.
34. Sixdorf U, Märker-Hermann E. Viral Arthritis and vasculitis. *Z Rheumatol 2016;75(9):878-884*.
35. Peng S. Rheumatic manifestations of parasitic diseases. Semin Arthritis Rheum 2002;31:228-47.
36. Amaral JK, Bilsborrow JB, Schoen RT. Chronic Chikungunya Arthritis and Rheumatoid Arthritis: What They Have in Common. *Am J Med* 2020;133(3):e91-e97.
37. Pathak H, Mohan MC, Ravindran V. Chikungunya arthritis. *Clin Med (Lond)* 2019;19(5):381-385.
38. Zias J, Mitchell P. Psoriatic arthritis in a fifth-century Judean Desert monastery. *Am J Phys Anthropol* 1996;101(4):49-502.
39. El-Beshbishi S, Bardicy S, Taman A, *et al*. Parasitic infections and myositis. *Parasitol Res* 2012;110:1–18.
40. Molina B, Pogossian A, Le Berre R, *et al*. Infectious myositis. *Rev Med Interne* 2020;41(4):241-249.
41. Aringer M. EULAR/ACR classification criteria for SLE. *Semin Arthritis Rheum* 2019;49(3S):14-17.
42. Tsokos GC. Systemic Lupus Erythematosus. *N Engl J Med* 2011; 365:2110-2121.
43. Van Griensven J, Carrillo E, Moreno J, *et al*. Leishmaniasis in immunosuppressed individuals. *Clin Microbiol Infect* 2014;20(4):286-299.
44. Illescas-Montes R, Corona-Castro CC, Costela-Ruiz VJ, *et al*. Infectious processes and systemic lupus erythematosus. *Immunology* 2019;158(3):153-160.
45. Chauhan S, Wakhlu A, Agarwal V. Arthritis in leprosy. *Rheumatology* (Oxford, England);49:2237-42.
46. Fletcher K, Issa R, Lockwood DN. Visceral leishmaniasis and immunocompromise as a risk factor for the development of visceral leishmaniasis: a changing pattern at the hospital for tropical diseases, London. *PLoS One* 2015;10:e0121418.
47. Santana IU, Dias B, Santiago MB, *et al*. Visceral leishmaniasis mimicking systemic lupus erythematosus: case series and a systematic literature review. *Semin Arthritis Rheum* 2015; 44:658–65.
48. WHO guidelines for diagnosis, treatment and prevention of leprosy. Geneva: World Health Organization; 2018 (http://apps.who.int/iris/bitstream/handle/10665/274127/9789290226383-eng.pdf).
49. Reibel F, Chauffour A, Aubry A, *et al*. New Insights into the Geographic Distribution of Mycobacterium leprae SNP Genotypes Determined for Isolates from Leprosy Cases Diagnosed in Metropolitan France and French

Territories. *PLoS Negl Trop Dis* 2015;9(10):e0004141.
50. Norman F, Fanciulli C, López-Vélez R, *et al*. Imported and autochthonous leprosy presenting in Madrid (1989-2015): A case series and review of the literature. *Travel Med Infect Dis* 2016;14:331-349.
51. Prasad S, Misra R, Aggarwal A, *et al*. Leprosy revealed in a rheumatology clinic: a case series. *Int J Rheum Dis* 2013;16:129–133.
52. Baharuddin H, Taib T, Zain MM, Ch'ng S. Leprae reaction resembling rheumatologic disease as presenting feature of leprosy. *Int J Rheum Dis* 2016;19(10):1035-1038.
53. Ribeiro FM, Gomez VE, Shoenfeld Y, *et al*. Lupus and leprosy: beyond the coincidence. *Immunol Res* 2015;61(1-2):160-163.
54. Junior G, Elis E, Magalhães V. Application of the diagnostic criteria for systemic lupus erythematosus to patients with multibacillary leprosy. *Rev Soc Bras Med Trop* 2011;44:85-90.
55. Horta-Baas G, Hernandez-Cabrera MF, Arenas-Guzman R, *et al*. Multibacillary leprosy mimicking systemic lupus erythematosus: case report and literature review. *Lupus* 2015;24(10):1095–102.
56. Labuda SM, Schieffelin JS, Shaffer JG, Stryjewska BM. Hansen's Disease and Rheumatoid Arthritis Crossover of Clinical Symptoms: A Case Series of 18 Patients in the United States. *Am J Trop Med Hyg* 2017;97(6):1726-1730.
57. Hsieh TT, Wu YH. Leprosy mimicking lupus erythematosus. *Dermatol Sin* 2014:32(1):47-50.
58. Karadeniz A, Lally L, Lockshin MD, *et al*. Lepromatous Leprosy Mimicking Systemic Lupus Erythematosus. *HSS J* 2014;10(3):286-291.
59. Garg G, Gogia A, Kakar A. Leprosy: A Great Mimicking Disease. *Indian J Lepr* 2016;88(2):123-127
60. Kusumaningrum N, Purnamawati S, Soebono H, *et al*. Lepromatous leprosy mimicking systemic lupus erythematosus: a case report. *Med J Indones* 2019;28(1):77-1.
61. African Trypanosomiasis. Geneva: World Health Organization; 2020 (http://www.who.int/topics/trypanosomiasis_african/en, accessed 09 August 2020).
62. Meltzer E, Leshem E, Steinlauf S, *et al*. Human African trypanosomiasis in a traveler: diagnostic pitfalls. *Am J Trop Med Hyg* 2012;87(2):264-266.
63. Sudarshi D, Brown M. Human African trypanosomiasis in non-endemic countries. *Clin Med* 2015;15(1):70-73.
64. Guillaume MP, Hermanus N, Karmali R, *et al*. Specific autoantibodies of SLE, such as anti-Ku, anti-ribosome Po and anti-membrane DNA autoantibodies, in a case of human African trypanosomiasis. *Rheumatology* 2003 ;42(12) :1568–1569.
65. Kirrstetter M, Lerin-Lozano C, Lamprecht P, *et al*. Trypanosomiasis in a woman from Cameroon mimicking systemic lupus erythematosus]. *Dtsch Med Wochenschr* 2004;129(23):1315-1317.
66. Leavitt RY, Fauci AS, Lightfoot RW, *et al*. The American College of Rheumatology 1990 criteria for the classification of Wegener's granulomatosis. *Arthritis Rheum* 1990;33(8):1101.
67. Robson JC, Grayson PC, Ponte C, DCVAS Investigators, *et al*. 2022 American College of Rheumatology/European Alliance of Associations for Rheumatology classification criteria for granulomatosis with polyangiitis. *Ann Rheum Dis* 2022;81(3):315-320.
68. Guntupalli L, Patel K, Faraji F, Brunworth JD. Autoimmune-related nasal septum perforation: A case report and systematic review. *Allergy Rhinol* 2017;8(1):40-44.
69. Montone KT. The molecular genetics of inflammatory, autoimmune, and infectious diseases of the sinonasal tract: a review. *Arch Pathol Lab Med* 2014;138(6):745-753.
70. Laudien M. Orphan diseases of the nose and paranasal sinuses: Pathogenesis - clinic - therapy. *GMS Curr Top Otorhinolaryngol Head Neck Surg* 2015;14:Doc04.
71. Sachse F, Stoll W. Nasal surgery in patients with systemic disorders. *GMS Curr Top Otorhinolaryngol Head Neck Surg*. 2010;9:Doc02.
72. Alam E, Abbas O, Moukarbel R, Khalifeh I. Cutaneous Leishmaniasis: An Overlooked Etiology of Midfacial Destructive Lesions. *PLoS Negl Trop Dis* 2016;10(2):e0004426.
73. Edington FL, Bacellar MO, Machado PR, *et al*. Anti-neutrophil cytoplasmic antibodies in leprosy. *Clin Rheumatol* 2007;26(2):208-210.
74. Camacho ID, Burdick A, Benjamin L, Casiano R. Chronic rhinitis: a manifestation of leprosy. *Ear Nose Throat J* 2011;90(9):E1-E3.
75. Kim JH, Lee OJ, Lee JJ, Park CH. Analysis of facial deformities in korean leprosy. *Clin Exp Otorhinolaryngol* 2013;6(2):78-81.
76. Crovetto-Martínez, R, Aguirre-Urizar JM, Torre CD, *et al*. Mucocutaneous leishmaniasis must be included in the differential diagnosis of midline destructive disease: Two case reports. *OOOO Journal* 2014;119(1):20-26.
77. Bhat R, Sharma VK, Deka RC. Otorhinolaryngologic manifestations of leprosy. *Int J Dermatol* 2007;46(6):600-606.

78. Martins AC, Castro JC, Moreira JS. A ten-year historic study of paranasal cavity endoscopy in patients with Leprosy. *Braz J Otorhinolaryngol* 2005;71(5):609-615.
79. Taheri JB, Mortazavi H, Moshfeghi M, *et al*. Oro-facial manifestations of 100 leprosy patients. *Med Oral Patol Oral Cir Bucal*. 2012;17(5):728-732.
80. Pooja VK, Vanishree M, Surekha R, *et al*. Evaluation of the orofacial lesions in treated leprosy patients. *J Oral Maxillofac Pathol* 2014;18(3):386-389.
81. Lockwood D. Recognizing Leprosy: Pointers for the Busy Rheumatologist. *Rheumatology* 2014;53:i12.
82. Wall EC, Watson J, Lockwood DN, *et al*. Epidemiology of imported cutaneous leishmaniasis at the Hospital for Tropical Diseases, London, United Kingdom: use of polymerase chain reaction to identify the species. *Am J Trop Med Hyg* 2012;86(1):115-8.
83. Bart A, Thiel PP, Van Gool T, *et al*. Imported leishmaniasis in the Netherlands from 2005 to 2012: epidemiology, diagnostic techniques and sequence-based species typing from 195 patients. *Euro Surveill* 2013;18(30)205-44.
84. Antunes ML, Cabral G, Araújo J, *et al*. Going Round in Circles with a Multisystemic Disease: A Unique Case of Parasitic Aortitis. *Eur J Case Rep Intern Med* 2017;4(6):000601.
85. Chauhan A, Scott DGI, Neuberger J, *et al*. Churg–Strauss vasculitis and ascaris infection. *Ann Rheum Dis* 1990;49:320–322.
86. Pandey S, Nayak R, Mehndiratta MM. Hansen's disease manifesting as acute distal symmetric microvasculitic polyneuropathy. *Clin Neurol Neurosurg* 2013;115(10):2223-2225.
87. Sampaio L, Silva L, Terroso G, et al. Hansen's disease mimicking a systemic vasculitis. *Acta Reumatol Port* 2011;36(1):61-64.
88. Sadeghinia A, Azizzadeh-Roodpishi S, Mahmoudi H, *et al*. A Case of Lepromatous Leprosy Clinically Masquerading as Vasculitis. *Dermatol Pract Concept* 2019;9(3):222-224.
89. Pawar M, Zawar V. Mid-borderline leprosy masquerading as an overlap syndrome. *Rheumatology* 2018 ;57(9):1686–1688.
90. Gupta L, Zanwar A, Wakhlu A, Agarwal V. Leprosy in the rheumatology clinic: an update on this great mimic. *Int J Rheum Dis* 2016;19(10):941–5.
91. Lee JY, Park SE, Kim SS, *et al*. Case of lepromatous leprosy misdiagnosed as systemic sclerosis. *J Dermatol* 2014;41(4):343–5.
92. Pruthi P, Munganda H, Brajpuriya S, *et al*. Case Report Leprosy with Atypical Skin Lesions Masquerading as Relapsing Polychondritis. *Case Rep Infect Dis* 2016;2016:7802423.
93. Yusuf SYM, Ismail IA, Yasin MM, *et al*. Isolated Bilateral Pinna Swelling: A Rare Initial Presentation of Leprosy. *Open Access Maced J Med Sci* 2019;7(11):1815-1817.
94. Deligny C, Arfi S. Images in clinical tropical medicine. Pseudochondritis in leprosy. *Am J Trop Med Hyg* 2010;83(6):1175.
95. Levy M, Bourrat E, Fila M, *et al*. Toxocara canis infection: Unusual trigger of systemic lupus erythematosus. *Ped Intern* 2015;57(4):785-788.
96. De Boysson H, *et al*. Vasculitis Secondary to anti-C1q Antibodies Induced By Toxocariasis. *Infection* 2015 ;43(6) :755-8.
97. Kotton CN. Chapter 5 - Immunocompromised travellers. Centers for Disease Control and Prevention; 2019 (https://wwwnc.cdc.gov/travel/yellowbook/2020/travelers-with-additional-considerations/immunocompromised-travelers, accessed 09 August 2020).
98. Braz AS, de Andrade CA, Da Mota LM, Lima CM. Recommendations from the Brazilian Society of Rheumatology on the diagnosis and treatment of intestinal parasitic infections in patients with autoimmune rheumatic disorders. *Rev Bras Reumatol* 2015;55:368-80.
99. Libman L, Barkati S. Chapter 11 – Screening asymptomatic returned travellers. Centers for Disease Control and Prevention ; 2019 (https://wwwnc.cdc.gov/travel/yellowbook/2020/posttravel-evaluation/screening-asymptomatic-returned-travelers, accessed 09 August 2020).
100. Refugee Health guidelines. Centers for Disease Control and Prevention; 2020 (https://www.cdc.gov/immigrantrefugeehealth/guidelines/refugee-guidelines.html, accessed 09 August 2020).
101. Krolewiecki A, Nutman TB. Strongyloidiasis: A Neglected Tropical Disease. *Infect Dis Clin North Am* 2019;33(1):135-151.
102. Requena-Méndez A, Buonfrate D, Muñoz J, *et al*. Evidence-Based Guidelines for Screening and Management of Strongyloidiasis in Non-Endemic Countries. *Am J Trop Med Hyg* 2017;97(3):645-652.
103. Boggild AK, Libman M, Greenaway C, McCarthy AE. CATMAT statement on disseminated strongyloidiasis: prevention, assessment and management guidelines. *Can Commun Dis Rep* 2016;42:12-19
104. Agbata EN, Morton RL, Bisoffi Z, *et al*. Effectiveness of Screening and Treatment

Approaches for Schistosomiasis and Strongyloidiasis in Newly-Arrived Migrants from Endemic Countries in the EU/EEA: A Systematic Review. *Int J Environ Res Public Health* 2018;16(1):11.

105. Velasco M, Gimeno-Feliú LA, Molina I, *et al.* Screening for *Trypanosoma cruzi* infection in immigrants and refugees: Systematic review and recommendations from the Spanish Society of Infectious Diseases and Clinical Microbiology. *Euro Surveill* 2020;25(8):1900393.
106. Salvador F, Sánchez-Montalvá A, Sulleiro E, *et al.* Prevalence of Chagas Disease among Solid Organ-Transplanted Patients in a Nonendemic Country. *Am J Trop Med Hyg* 2018;98(3):742-746.
107. Pinazo MJ, Espinosa G, Cortes-Lletget C, *et al.* Immunosuppression and Chagas disease: a management challenge. *PLoS Negl Dis* 2013;7:e1965.