VOL VI

Ciências da Saúde:

Investigação e Prática

Dr. Guillermo Julián González-Pérez
Dra. María Guadalupe Vega-López
(organizadores)

EDITORA ARTEMIS
2026

VOL VI

Ciências da Saúde:

Investigação e Prática

Dr. Guillermo Julián González-Pérez
Dra. María Guadalupe Vega-López
(organizadores)

EDITORA ARTEMIS
2026

Editora Chefe	Profª Drª Antonella Carvalho de Oliveira
Editora Executiva	M.ª Viviane Carvalho Mocellin
Direção de Arte	M.ª Bruna Bejarano
Diagramação	Elisangela Abreu
Organizadores	Prof. Dr. Guillermo Julián González-Pérez
	Profª Drª María Guadalupe Vega-López
Imagem da Capa	peopleimages12/123RF
Bibliotecário	Maurício Amormino Júnior – CRB6/2422

Editora Artemis
Curitiba-PR Brasil
www.editoraartemis.com.br
e-mail:publicar@editoraartemis.com.br

Editora Artemis
Curitiba-PR Brasil
www.editoraartemis.com.br
e-mail:publicar@editoraartemis.com.br

Editora Artemis
Curitiba-PR Brasil
www.editoraartemis.com.br
e-mail:publicar@editoraartemis.com.br

Dados Internacionais de Catalogação na Publicação (CIP)
(eDOC BRASIL, Belo Horizonte/MG)

C569 Ciências da saúde [livro eletrônico] : investigação e prática VI / Organizadores Guillermo Julián González-Pérez, María Guadalupe Vega-López. – 1. ed. – Curitiba, PR: Editora Artemis, 2026.

Formato: PDF
Requisitos de sistema: Adobe Acrobat Reader
Modo de acesso: World Wide Web
Edição bilíngue
Inclui bibliografia.
ISBN 978-65-82858-05-5
DOI 10.37572/EdArt_300626055

1. Ciências da saúde. 2. Saúde – Pesquisa. 3. Prática clínica. I. González-Pérez, Guillermo Julián. II. Vega-López, María Guadalupe.

CDD 610

Elaborado por Maurício Amormino Júnior – CRB6/2422

EDITORA ARTEMIS
2026

Editora Artemis
Curitiba-PR Brasil
www.editoraartemis.com.br
e-mail:publicar@editoraartemis.com.br

PRÓLOGO

La salud contemporánea se configura como un campo de conocimiento, intervención y cuidado atravesado por múltiples dimensiones: biológicas, clínicas, sociales, éticas, tecnológicas, educativas e institucionales. En este sentido, el volumen ***Ciências da Saúde: Investigação e Prática VI*** reúne un conjunto de trabajos que permiten observar la amplitud y la complejidad de los desafíos actuales en el área sanitaria, articulando reflexiones conceptuales, estudios clínicos, análisis de prácticas profesionales y debates sobre la organización del cuidado, así como sobre los desafíos crecientes para la salud pública.

Los capítulos que integran esta obra evidencian que la investigación en ciencias de la salud no puede limitarse a una mirada exclusivamente biomédica. Si bien el diagnóstico, el tratamiento, la prevención y la seguridad terapéutica siguen ocupando un lugar central, los procesos de salud y enfermedad también exigen considerar las trayectorias de vida, la autonomía, los derechos, las condiciones sociales, la formación profesional, la comunicación clínica, la toma de decisiones y la calidad de los sistemas de registro, gestión e investigación. Esta perspectiva amplia permite comprender la salud como una experiencia compleja, situada y profundamente vinculada a los contextos en los que las personas viven, envejecen, enferman, se cuidan y son cuidadas.

La organización del volumen fue pensada a partir de una lógica progresiva, distribuida en tres ejes temáticos. El primero reúne reflexiones que abordan tópicos de salud pública desde una perspectiva integral, humanizada y transdisciplinaria, considerando temas como la violencia como problema de salud pública, el curso de vida, el curso de vida, el envejecimiento saludable, la autonomía, el cuerpo, la educación sexual integral y los derechos. Este conjunto de trabajos invita a pensar la salud más allá de la ausencia de enfermedad, reconociendo su relación con el entorno social, la capacidad funcional, la participación, la subjetividad, las decisiones informadas y las condiciones éticas y sociales que permiten una vida digna.

El segundo eje se aproxima a la práctica clínica, al diagnóstico oportuno y a la seguridad terapéutica. Los trabajos reunidos en esta sección destacan la importancia de la sospecha clínica, de la evaluación integral y de la actualización profesional frente a enfermedades que pueden presentar manifestaciones atípicas, diagnósticos tardíos o desafíos terapéuticos relevantes. Asimismo, se subraya la necesidad de fortalecer prácticas clínicas basadas en evidencia, capaces de reducir riesgos, evitar intervenciones innecesarias y mejorar la seguridad de los pacientes en distintos escenarios asistenciales.

El tercer eje se orienta hacia la investigación clínica, los registros, la gestión del cuidado y la formación profesional en salud. En este bloque, la obra pone de relieve la

importancia de los equipos de investigación, la calidad de los datos, la documentación clínica, los indicadores de desempeño, la profesionalización de funciones estratégicas y el desarrollo del razonamiento clínico en los procesos formativos. Estas discusiones son fundamentales para comprender cómo las instituciones sanitarias producen conocimiento, organizan prácticas, evalúan resultados y forman profesionales capaces de responder a demandas cada vez más complejas.

En conjunto, los trabajos aquí reunidos -de autores tanto europeos como latinoamericanos-muestran que investigar y practicar la salud implica un ejercicio permanente de integración. La atención sanitaria requiere conocimiento científico, sensibilidad ética, competencia técnica, capacidad reflexiva y compromiso con las personas y las comunidades. Al mismo tiempo, exige revisar críticamente los modelos de enseñanza, los sistemas de información, las decisiones clínicas y las políticas institucionales que orientan el cuidado en la vida cotidiana.

De este modo, ***Ciências da Saúde: Investigação e Prática VI*** propone una lectura que avanza desde una comprensión amplia y humanizada de la salud, pasa por los desafíos clínicos y diagnósticos, y culmina en la reflexión sobre las prácticas profesionales, investigativas e institucionales que sostienen la atención sanitaria contemporánea. Esperamos que este volumen contribuya al diálogo entre investigadores, docentes, profesionales y estudiantes del área de la salud, favoreciendo nuevas preguntas, nuevas prácticas y nuevas formas de pensar el cuidado, la formación y la investigación en salud.

Dr. Guillermo Julián González-Pérez
Dra. María Guadalupe Vega-López

SUMÁRIO

SALUD PÚBLICA, VIOLENCIA, CURSO DE VIDA, AUTONOMÍA Y DERECHOS

CAPÍTULO 5

LEPROSY IS EVADING ERADICATION - A REVIEW ARTICLE EVALUATING MISSED DIAGNOSIS AND CLINICAL SENSITISATION

Data de submissão: 14/05/2026
Data de aceite: 29/05/2026

Aidan Baker Johal
University of Warwick
West Midlands- United Kingdom

ABSTRACT: Leprosy remains prevalent in 2026 and continues to cause irreversible disability. This is despite efforts to increase detection rate *of M. Leprae* and *M. lepromatosis*, reduce the social stigma of leprosy, and provide afflicted patients with appropriate therapy at the earliest opportunity. Improvements in the accessibility of technology augmenting our ability to detect pathogens goes some way to improve detection rates. However, clinical suspicion remains the most important factor in increasing the rate of accurate and timely detection. Misdiagnosis of leprosy results from its ability to mimic many disease states and due to the lack of suspicion held by the examining clinician on first and repeated presentations. This project considers the case reports published either side of the start of the most recent leprosy elimination campaign to evaluate the factors which impede progress in reducing the prevalence and burden of leprosy globally. Through a systematic literature review, it is demonstrated that the average duration of disease prior to classic cardinal symptoms is over 18 months, and to accurate diagnosis over 2 years, these are significant results. Not only does this period of disease impact the patient themselves, but this time duration is also a period in which they pose a potential infective reservoir. In addition to this, environmental exposure is a factor which is poorly evaluated and requires additional exploration in the immediate future if we are to reduce the risk of exposure through this route. A gap in the literature exists to convincingly explain autochthonous cases of leprosy in non-endemic regions. A high level of clinical suspicion is required in all territories to better develop our control over leprosy pathogens. Presented within is a novel pre-diagnosis disease timeline, developed through the analysis of included case reports. This timeline will help sensitise clinical suspicion in endemic and non-endemic regions alike.

KEYWORDS: Leprosy; M. Leprae; M. Lepromatosis; Misdiagnosis; Delayed diagnosis.

1. INTRODUCTION

Leprosy, first clinically defined in the 1847 publication “Om Spedalsked” (Danielssen et al., 1847), is a disease of hugely variable clinical characteristics. Presently,

two pathogenic, obligate intracellular, rod-shaped, slow-dividing (12-14 days), acid-fast (AFB) (Fite-Farco and Ziehl-Neelsen staining), parasitic bacilli *Mycobacterium leprae* and *Mycobacterium lepromatosis* – first isolated in 1873 and 2008 – are implicated in lepromatous disease states (Han et al., 2008; Uaska Sartori et al., 2020).

Both *M. leprae* and *M. lepromatosis* have undergone gene decay and genome downsizing since their separation between 10 and 13.9 million years ago(Mark, 2017; Singh et al., 2015). The analysis of micro-polymorphisms within samples of *M. Leprae* demonstrate a distributive pattern which closely resembles historical human migratory routes over 100,000 years (Rinaldi, 2007). Current evidence of the historic distribution of *M. leprae* and *M. lepromatosis* (Donoghue et al., 2019; Krause-Kyora et al., 2018; Pfrengle et al., 2021; Monot et al., 2009) starkly contrast the present global human incidence of leprosy in a way that is not easily explained.

The Global Leprosy Strategy, which aspires to have achieved global eradication by 2030, is progressing slower than anticipated with 182,815 new cases detected in 2023 alone (Global leprosy (Hansen disease) update, 2023), this is 24% higher than the projected 2023 milestone and at least 3 years behind the anticipated schedule of case reduction (Towards zero leprosy, 2021). The SARS-CoV-2 pandemic has undoubtedly contributed to this, although a multitude of factors are likely to be influencing the continued high incidence and detection rate of leprosy across the globe.

The clinical presentation of leprosy is determined by the specifics of bacilli infiltration and the host-pathogen reaction (Mi et al., 2024), as such, leprosy is associated with numerous atypical signs and symptoms and has a firm reputation as a self-disguising disease. Leprosy is a disease of mimicry leading to misdiagnosis or delayed diagnosis, both of which may result in poor patient outcomes, this is increasingly common with respect to autoimmune conditions (Chen et al., 2023). Rheumatic symptoms are the third commonest presentation in leprotic disease (Labuda et al., 2017) and a feature of both autoimmune and functional disease – the detection rate and disproportionately large disease burdens of which are presently unaccounted for (Hedar et al., 2021; Rometsch et al., 2024). Asymptomatic infection is associated with a genetic predisposition to effectively irradicate detected bacilli or an immune response so slight that the typical manifestations are not clinically detectable (Li et al., 2024), another factor linked to asymptomatic infection includes low point or continuously low bacillary loading resulting in subclinical infection (Godal & Negassi, 1973). It is not known what proportion of asymptomatic infection eventually leads to clinical disease. Infected patients without symptoms also represent pre-clinical latent leprosy and whilst these individuals present

a lower risk of transmission prior to clinical manifestation, it is suggested that the reservoir of individuals with latent leprosy might be partly responsible for difficulties in reducing disease prevalence in some areas (da Silva et al., 2021). Latent leprosy can remain hidden or dormant for extensive periods of time with incubation periods generally expected to be measured in years with a suspected 30-year incubation period existing within the literature (Jariyakulwong et al., 2022) and another in excess of 50 years (Taggart et al., 2022).

Presently, the World Health Organisation (2023) identify the diagnostic criteria of leprosy as the identification of at least 1 of 3 cardinal symptoms, including: loss of sensation in a skin patch with deranged pigmentation; thickened peripheral nerve with evidence of loss of function of that same nerve; or an acid-fast bacilli (AFB) positive slit-skin smear. On diagnosis WHO (2018) recommend management with rifampicin, dapsone, and clofazimine for 6 months in patients with paucibacillary leprosy and 12 months for multibacillary leprosy. If treated appropriately and early patient outcomes can be overwhelmingly positive, with total resolution of both signs and symptoms and the cessation of bacillary shedding (Maymone et al., 2020). However, advanced disease states demonstrating extensive damage and deformity to musculoskeletal or nervous structures are less likely to be fully reversed, with disability and disfigurement becoming permanent (Sinha et al., 2024), in some cases disability continues to progress even after the infection itself is cured. Reactional states, including post-treatment reactions are reported by some patients and can be experienced any time during the disease progression or following the initiation of treatment (Nery et al., 2013). They may be triggered without warning, by a period of ill health or, an intervention such as vaccination (Shi et al., 2018; Bhandari et al., 2022). The reactional states are grouped into type 1 and type 2. A type 1 reactional state describes the acute inflammation in one or more of the affected tissue structures (Kahawita et al., 2008). Type 2 reactions are alternatively termed Erythema Nodosum Leprosum and can be acute, subacute, or chronic – these terms describe a typically painful multisystemic condition which may reflect either disseminated systemic infection or a disseminated system-wide immune response (Walker, 2020).

2. OBJECTIVES

This study compares data from before and after the launch of the Global Leprosy Strategy 2021-2030 (World Health Organisation, 2017) by analysing discreet data published between 01/01/2019-31/12/2019 and 01/11/2023-31/10/2024.

The primary study aim is to evaluate the frequency of non-cardinal signs and symptoms reported in leprosy patients and compare the time delay between the first symptom of disease being detected with the delay following the first clinical cardinal signs and the effect this has on time-to-diagnosis and/or delays to accurate diagnosis.

The secondary study aims are to evaluate: reported exposure risk factors; disease time-course and characteristics; response to therapies and management. Additional aims will be to report intermediate misdiagnoses patients may have received and the response to treatments provided for these misdiagnosed conditions.

This study will record:

- individual characteristics of patients diagnosed with leprosy including age, sex, previous leprosy diagnosis, and exposure risk factors to leprosy will be evaluated.
- disease characteristics of patients diagnosed with leprosy including reported signs and symptoms, chronology of signs and symptoms, intermediate misdiagnosis if reported, response to intermediate treatments, delay between being initial symptom presentation and achieving accurate diagnosis, and response to appropriate and definitive MDT.

The methodology of this project is presented in figure 1.

Data analysis consisted of both descriptive analysis of qualitative data and statistical analysis of quantitative data. For statistical analysis the software package GraphPad PRISM 10.4.0 for Windows was utilised. As no interventions were measured in this study, data was assessed for normality using Q-Q plotting and subsequently analysed for statistical significance using an appropriate testing model. For all data statistically analysed in this study, Mann Whitney testing was undertaken.

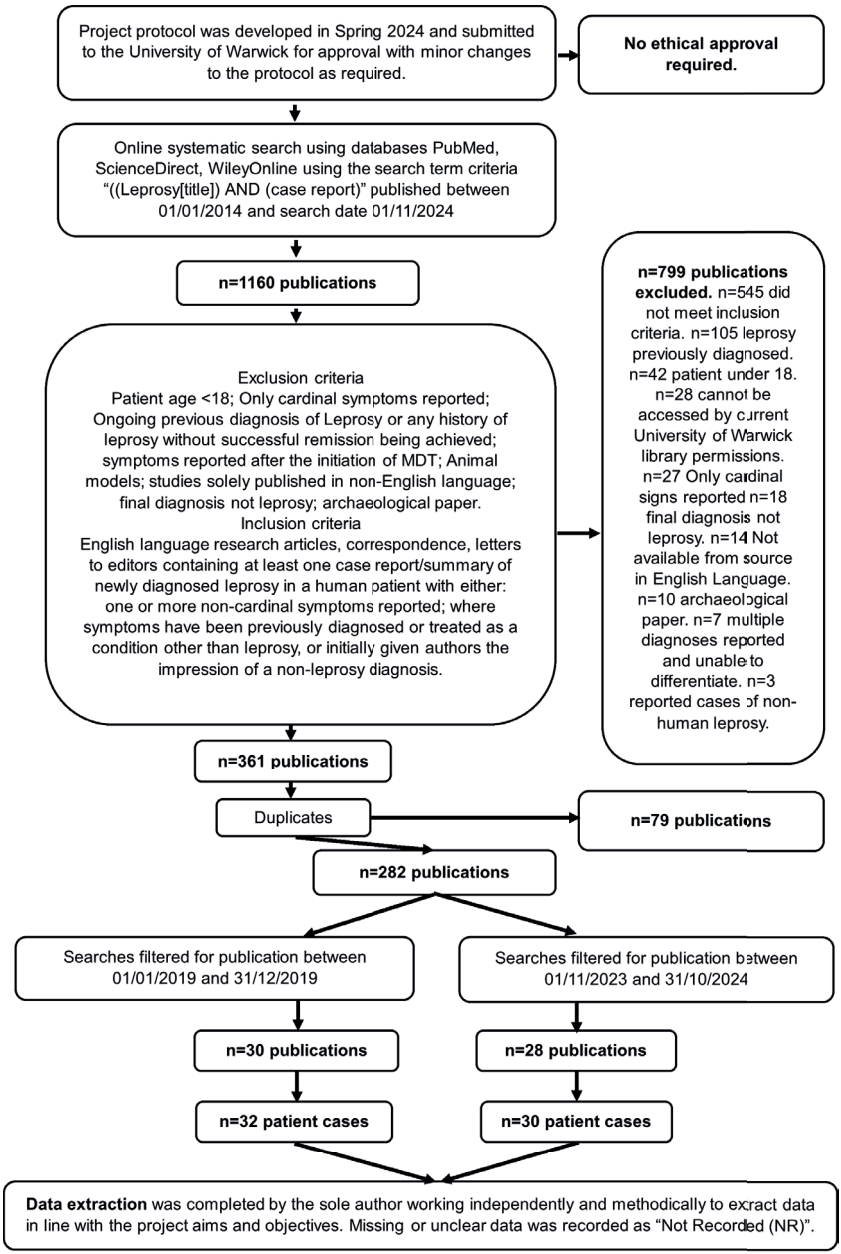

Figure 1: A flowchart summarising the methodology of this project including approval processes, search strategy, and data interrogation.

3. RESULTS

Across the two sample years, a higher proportion of patients were male (75% and 67%) with the average age at diagnosis being 37 for females and 43 for males. Sequencing rate increased by 10% between 2019 and 2024 with *M. lepromatosis* reported more frequently in 2024 while M. Leprae made up 100% of sequenced cases in 2019. The reporting of musculoskeletal symptoms was lower in 2024 (47%) than 2019 (63%). However, a broader variety of symptoms were reported in 2024 with 60% of patients reporting symptoms of disease which cannot be classified as dermatological, neurological, respiratory, or as any cardinal symptom of leprosy. The initial misdiagnosis rate for both 2019 and 2024 was over 40%, with 32 different misdiagnoses reported across both years. Challenges in microscopy were more commonly reported in 2024, where 3 cases failed to produce a positive microscopy sample (table 5). Field microscopy is extremely dependent on user and equipment.

Symptomatic relief was reported in a majority of patients to be noticed within one week of starting appropriate therapy. For the remaining minority of patients, mean time to review was 27 weeks in 2019 and 16 weeks in 2024 meaning that their symptoms were left unmanaged or drug reactions were experienced for a prolonged period. In the interest of improving patient engagement with healthcare and their medical regimes, patient reviews should be held sooner following treatment initiation, perhaps within 2 weeks where possible.

Of significance, fewer than 10% of patients in 2019 reported a known contact with a current or previous diagnosis of leprosy, this proportion reduced in 2024 to 3%, highlighting unidentified transmission routes and that potential background infection rates may be higher than data shows, with unevaluated and poorly understood reservoirs of community infection still existing unmanaged. Just half of reported cases in 2019 lived in an endemic region. This reduced in 2024 to 37% with patients living in non-endemic regions reporting emigration from endemic regions at reducing rates from 54% in 2019 to 38% in 2024. Cases with identified travel exposure were reported at a rate of just 15% in both 2019 and 2024. When risk of exposure was evaluated holistically given the information which the patient shared, over one third of patients in 2019 had no identifiable exposure to leprosy, this rate increased in 2024 to almost half. When considered together, cases from 2019 and 2024 reported the first symptom to be a cardinal sign in just 16% of cases, and there was an absence of clinical cardinal symptoms at a rate of 47% although some aspects of clinical cardinal signs were reported in 93% of these. They were identified only retrospectively, however, due to these symptoms not meeting all the typical cardinal sign features.

In 2019 an accurate diagnosis of leprosy was achieved quickly after the identification of a clinical cardinal sign in both endemic and non-endemic regions, the time over which the patient lived with symptoms of disease before diagnosis was significantly longer. The same can be said for non-endemic regions in 2024, however the time between the first symptoms of disease and the accurate diagnosis of leprosy was not significantly longer to the time between the first identification of a clinical cardinal sign and accurate diagnosis in endemic regions in 2024 demonstrating the clinical suspicion is a key factor in correctly and accurately diagnosing leprosy early.

There was no significant statistical difference detected in symptom to diagnosis time between 2019 and 2024 in both endemic and non-endemic regions, the same can be said for the difference in detected clinical cardinal sign to diagnosis time. This shows that despite increased efforts to screen for and identify cases of leprosy, there were no significant improvements in reducing the delay of diagnosis between 2019 and 2024.

There was no significant sex-based difference in length of diagnostic delay following the onset of symptoms, the data suggests that females may have a slower response to medication and experience symptoms for a longer duration following the initiation of treatment, however this study found that the difference was not statistically significant. The age of the patient did not significantly affect the time between symptom onset and diagnosis.

Patients definitively diagnosed with lepromatous leprosy endured a significantly longer duration of symptoms before the accurate diagnosis was achieved compared to patients diagnosed with tuberculoid leprosy. Similar significant differences were detected in borderline lepromatous and borderline tuberculoid patients. This significant result was not detected between lepromatous leprosy and histoid leprosy, nor was it for the time between clinical cardinal signs and diagnosis of lepromatous or tuberculoid leprosy.

With patients diagnosed with tuberculoid leprosy, there was no significant difference detected between the delay between first symptom onset and diagnosis and the first cardinal sign being detected and diagnosis, meaning that the first symptom was often a cardinal sign. Contrastingly however, patients diagnosed with lepromatous leprosy were symptomatic of disease for significantly longer periods of time before diagnosis than the duration for which they displayed cardinal clinical signs, this is shown in table 6. This is significant because patients who go on to be diagnosed with lepromatous leprosy have been atypically symptomatic for longer, increasing the time over which they have potentially been exposing those around them to infectious material. Table 1 presents the misdiagnoses associated with each diagnosed leprosy type.

Table 1: Final diagnoses reported in the case reports analysed alongside the misdiagnoses reported as preceding these.

Final diagnosis	Misdiagnosed condition(s)/incorrect clinical impression
"Borderline with t1 reaction"	Rheumatoid arthritis as erosive arthritis of wrists and fingers Sweet syndrome Rheumatoid arthritis-associated vasculitis Drug reaction Vasculitic neuropathy
"Chronic granulomatous inflammatory reaction with focal Fite stain positivity, suggestive of leprosy"	Central giant cell granuloma or ameloblastoma
Borderline lepromatous leprosy	Vitiligo Rheumatoid Arthritis Fungal infection Cutaneous Lymphoma
Diffuse multibacillary leprosy with Lucio's phenomenon	Lupus erythematosus panniculitis
Histiocytoid variant of lepromatous leprosy	Deep cutaneous mycoses
Indeterminate leprosy	Vasculitis, neuritis Inflammatory vasculitic neuropathy.
Lepromatous leprosy	Syphilis Perichondritis Tuberculosis Dermatophytosis Short-lasting unilateral neuralgiform headache with cranial autonomic symptoms
Lepromatous leprosy with ENL	Pyrexia of unknown origin Still's disease Collagen Vascular disease Tuberculosis Lower extremity cellulitis
Lepromatous leprosy with Lucio's phenomenon	Gout Cellulitis Antiphospholipid syndrome
Lepromatous leprosy with type 2 reaction	Testicular tuberculosis
Multibacillary borderline lepromatous leprosy	Fungal infection Carbamazepine-induced pancytopenia Erythema multiform Cryoglobulinaemic vasculitis Carpal tunnel syndrome
Multibacillary leprosy	Necrotising fasciitis Toxocariasis RS3PE syndrome

Neural leprosy	Cellulitis
Primary neural leprosy	Rheumatoid arthritis
Tuberculoid leprosy	Morbihan disease

Through the analysis of the data collected on cases reported in 2024 an illustrative retrospective pre-diagnosis timeline is presented (figure 2), outlining an indicative disease time-course between the patients last identified exposure, the first symptom of disease, and the first detectable cardinal sign of leprosy, relative to confirmed diagnosis and treatment initiation. This timeline can be used by clinicians identifying a case of leprosy to understand the possible disease time-course to the point of diagnosis and further extrapolate potential exposures to other individuals who may have subsequently become infected. By familiarising themselves with this novel timeline, a clinician may better appreciate that the patient they are assessing in clinic may indeed be presently within the pre-cardinal phase of disease. By sensitising clinicians to the pre-cardinal timeline of leprosy, as developed from the analysis of the data collected as part of this study, it may be possible for clinicians to consider leprosy in their differentials earlier in the disease course, thus reducing both the disease burden on the affected patient and additionally reducing the transmission risk to others earlier.

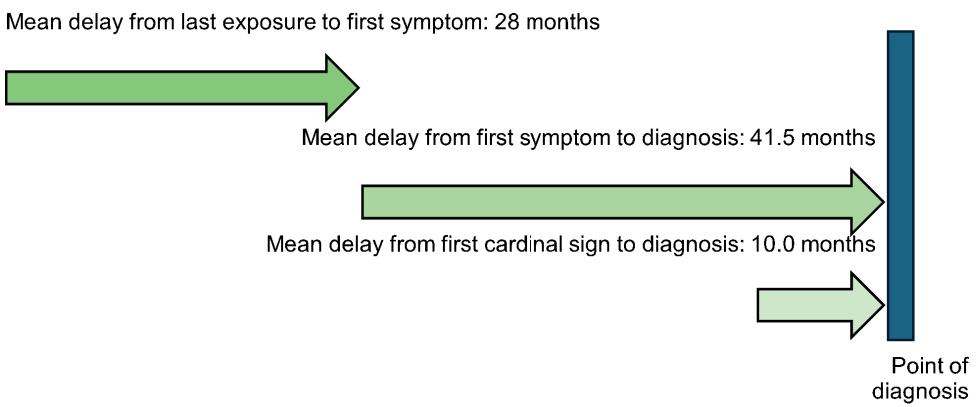

Figure 2: Illustrative retrospective pre-diagnosis timeline outlining indicative disease time-course between last reported exposure, first symptom of disease, and first cardinal sign of leprosy.

Using this timeline, a clinician evaluating a patient for unexplained or refractory symptoms within 60 months of a leprosy exposure but without cardinal symptoms may have increased clinical suspicion that the patient is presenting with early and/or atypical features of leprosy. This would then allow the clinician to request additional testing.

The earlier any case of leprosy whether typical or atypical is identified, the better the outcomes for the patient and the smaller the window of potential infectivity. Both of which are required to effectively improve our control of leprotic disease.

4. DISCUSSION

Transmission of leprosy causing bacilli is poorly understood, the primary theoretical mechanism of human-to-human bacilli movement is through exposure to the respiratory excretion (Davey & Rees, 1974) or through skin-to-skin contact (Bratschi et al., 2015) with an infectious individual. The theorised primary risk factor to transmission is extended periods of contact with infectious individuals such as household contacts (WHO, 2023). However, shedding of viable bacilli has been demonstrated in open skin lesions (Franco-Paredes & Rodriguez-Morales, 2016) as well as washings taken from competent skin and nasal mucosae of leprosy patients, even up to 3 months following the initiation of appropriate treatment (Job et al., 2008). Potential routes of human-to-human transmission require continued investigation to better understand the risks which such exposure incurs. Despite humans being considered the predominant reservoir and host for leprosy pathogens, a zoonotic distribution would explain failures to slow the progress of international eradication campaigns in endemic areas (Franco-Paredes & Rodriguez-Morales, 2016). The same authors suggest investigating the survival of such agents in extra-host environments, with the presence of viable bacilli in environmental samples being demonstrated in soil and water (Turankar et al., 2019). In addition, viability of *M. Leprae* outside the body has been previously demonstrated for up to 5 months in replicated environmental conditions (Desikan and Sreevasta, 1995). Zoonotic reservoirs exist in North and South American Armadillos (Sharma et al., 2015) and United Kingdom populations of red squirrels (Meredith et al, 2014; Simpson et al., 2015), with monkey-to-monkey transmission evidenced in 1986 (Gormus et al., 1988). Wild reservoirs of bacilli are detectable in at least 3 continents and zoonotic transmission has been previously demonstrated from wild-host to human (da Silva et al., 2018). Furthermore, Ploemacher et al. (2020) outline how vector transmission of bacilli present yet another potential exposure and transmission risk. The results of the present project affirm a need to continue to develop our understanding of both exposure risks and transmission with a significant proportion of patients presented having no discernible exposure or risk factors to explain their leprosy status.

It is surprising that despite almost two decades passing since the identification of *M. Lepromatosis* a large proportion of published articles fail to make reference to or

acknowledge the existence of two discovered causative agents of Leprosy and instead only refer to *M. Leprae* in their texts. Further to this, genetic sequencing of samples collected is completed in less than 50% of cases, genetic sequencing should be more frequently carried out on samples to confirm the exact causative agent and build a better picture of strain distribution. The literature is sparse when comparing the prevalence and disease progression of infection between each respective mycobacterium species. High rates of sequencing would likely help to develop a better understanding of clinical disease states and prognosis between each species, with *M. Lepromatosis* specifically associated with Diffuse Lepromatous Leprosy in Mexico (Collin et al., 2023), a severe manifestation of disease.

Leprosy causing mycobacteria invade the tissue of hosts with a reported affinity for peripherally located structures and tissues owing to an optimum thrive temperature slightly below that of the human core temperature of 37 degrees Celsius (Brand, 1959), this includes: skin, mucous membranes, testes, lymph nodes, synovial membrane, joint capsule, tendon, tendon sheath, connective tissue, cartilage, bone, nerve, and nerve sheath, in addition to others less well reported. Any combination of one or more tissue types may be involved in a case of leprosy, this being dependent on successful mycobacterial infiltration, one of the variables thought to be associated with genetic susceptibility (Cambri & Mira, 2018). At a cellular level macrophages and Schwann cells (Silva & Belisle, 2018) are considered the respective primary host cells for leprosy causing bacilli in cutaneous and neural variations of leprosy. Signs and symptoms of infection or disease differ based on the cell and tissue structures infiltrated by bacilli. A multitude of inflammatory cells present within leprosy lesions and may be implicated in disease states, which are determined and mediated by the immune response of the infected individual (Alter et al., 2010). These include epithelioid cells, macrophages, lymphocytes, plasma cells, neutrophils, and mast cells (Massone et al., 2015), histopathological assessment of biopsies may reveal one of several granulomatous reactions involving the aforementioned inflammatory cells. With respect to vasculature, morphological and functional abnormalities of the capillaries have been detected in leprosy patients (Treu et al., 2017) as has vascular deficit of the peripheral arteries (Kaur et al., 1976). Characteristic perineural inflammation is suggested to indicate a route of access via microvasculature in neural leprosy (Scollard et al., 2015), a theory supported by animal models demonstrating the involvement of endothelial cells of the vasa nervorum (Scollard et al., 1999). Genetic disposition is likely to explain the variation in location of leprotic infiltration, if any at all, and the severity of disability experienced by the patient over time. Protective immunity may prevent the development of disease states

(Magill & Hunter, 2013) and is multifactorial with components including low exposure loads priming immune system, protection afforded as a side-effect of BCG vaccination (Setia et al., 2006), or natural genetic immunity (van Hooij & Geluk, 2021).

Musculoskeletal symptoms are the third most frequently reported within the literature (Chauhan et al., 2010), this study shows that the proportion of patients reporting musculoskeletal symptoms is falling, whilst symptoms other than the leprotic cardinal three are on the rise. Perhaps this might be explained by increased levels of clinical suspicion in recent years resulting in more sensitive detection of atypically presenting cases followed by improved reporting of these. An alternative explanation is that the high rate of misdiagnosis and disease refractory to initial treatment resulted in the investigation of less likely differential diagnoses with advanced laboratory technology which is widening in availability and accessibility (Sengupta, 2019) leading to the identification of unexpected causative agents. Such technology will have averted potential delays to the diagnosis of the 3 patients from whom no AFB were visualised under microscopy and with over 40% of patients showing no clinical cardinal signs, a negative AFB-stain might have resulted in the diagnosis of leprosy being inappropriately excluded. Clinical suspicion for leprosy would classically be inferred by clinically detectably cardinal signs, however as over 40% of cases reported no detectable cardinal signs in this study and as such signs were demonstrated as a first presentation of disease in only 1/6 of cases, this becomes increasingly challenging alongside falling clinical awareness.

The review of patients post-initiation of appropriate therapy was 3 months sooner in 2024 than 2019 and this shows that the symptomatic improvement of disease states in the majority of cases can be achieved quickly, however extended management will still be required to mitigate the risk of relapse, antibiotic resistance, or type 2 reactions (Girdhar et al., 2000). Whilst improvement is typically measured in weeks and months, these results affirm the potential for rapid resolution of symptoms over a period of days and the importance of identifying the appropriate therapy to reduce the disease impact on the patient's quality of life. A comprehensive understanding of the appropriate therapy including prophylaxis for side effects and reversal reactions will reduce the frequency of such treatment complications from occurring.

This study demonstrates clearly that generic symptoms of disease are detectable in lepromatous leprosy patients for a significantly longer time period than cardinal signs are detectable and before an accurate diagnosis is achieved, however this cannot be said for tuberculoid disease. In this context, it is not surprising that a significant difference is present when comparing the delay between first symptom and eventual

diagnosis for both lepromatous leprosy and tuberculoid leprosy, and their respective borderline counterparts. This is unexpected and counterintuitive because tuberculoid leprosy is generally considered to be a milder and less severe form of the disease (Le et al., 2023), as such it would make sense for this form to go undetected for longer. An explanation for this phenomenon is that the clinical symptoms of lepromatous leprosy are more likely to contribute as distractors to diagnosis by mimicking other diseases, this is found particularly prominently in the literature as resulting in the initial misdiagnosis of autoimmune diseases, before the correct diagnosis of leprosy is achieved. A review of the literature as outlined in table 2 reflects this.

Table 2: A summary of the literature shows how leprosy can mimic autoimmune diseases and delay their diagnosis by presenting initially with symptoms of a rheumatic nature.

Author and year	Misdiagnosis or clinical suspicion	Sex	Age	Delay to diagnosis from first symptom of disease	Initial clinical symptoms reported, leading to misdiagnosis
Kolahi (2024) Kumar et al., (2019)					Fatigue, arthralgia, paraesthesia and ulceration, tapered digital arteries, fever, blisters, myalgia, asthenia, haemorrhagic lesions
Guevara et al., (2019)		M	42	Several weeks	
Nunzie et al., (2014)		M	38	72 months	
Kaliyadan et al., (2009)	Antiphospholipid Syndrome	F	32	Several days	
		F	76	1 week	
		M	64	24 months	
Lee et al., (2014)	Buerger's disease Systemic Sclerosis	F	82	72 months	Fever, malaise, oedema, Raynaud's
Salvi and Chopra (2013)	Clinical Rheumatoid Arthritis	F	52	4 months	Rapidly progressive polyarthritis
Horta-Baas et al., (2015)	Cutaneous lymphoma vs sarcoidosis followed by Systemic Lupus Erythema	F	50	16 months	Skin rash with pathological results consistent with Jessner's lymphocytic infiltration. Arthralgia, discoid rash, neuropathy, photosensitivity, refractory
Youssef, Mahani, Hojjati (2023)	Mixed connective tissue disease (scleroderma variant)	M	68	120 months	Erythematous plaques with persistent non-healing ulcers
Fasciano et al., (2019)	Polyarteritis nodosa	F	36	5 months	Skin nodules on right leg and foot, lower extremity paraesthesia, fatigue, low-grade fevers

Pruthi et al., (2016)	Relapsing polychondritis	M	22	1 month	Fever, pain in small joints of hand with morning stiffness, rash of elbow and knees, external ear pain
Sridana, Kurniari, and Kambayana (2007) de Andrade, et al., (2017) Salvi and Chopra (2009) Misra, et al., (2014)	Rheumatoid Arthritis (seropositive)	M M M M F	20 51 72 55 20	2 months 6 years 3 weeks 108 months 12 months	Bilateral joint tenderness and swelling of the hands, elbows, knees, and feet, articular disease.
Qiang and Sheng (2023) Kaur, M., et al., (2007) Salvi and Chopra (2009) Rath, Bhargava, Kundu (2014)	Rheumatoid Arthritis (Seronegative)	M M M F	61 70 58 35	6 months 24 months 4 months 18 months	Bilateral hand and wrist joint swelling accompanied by painless skin nodules, peripheral synovitis, polyarthritis.
Manoj and Dhakad (2020)	Rheumatoid Vasculitis	F	38	36 months	Symmetrical polyarthritis
Rath, Bhargava, Kundu (2014)	Spondylarthritis and psoriatic arthritis	M	40	30 months	Asymmetric progressive large joint pains of knees, ankles, and shoulders and lower back pain
Hsieh and Wu (2013) Wijaya, Komarasari, Esti (2024) Kusumaningrum et al., (2019) Ribeiro et al., (2007) Zawar et al., (2017)	Systemic Lupus Erythema	M F F F F	40 28 33 43 58	48 months 180 motnhs 74 months 16 months 18 months	Bilateral hand and wrist pain, swelling, and deformities, white skin spots on calves, ear paraethesis, fever, fatigue, asthenia, anorexia, myalgia, pedal oedema
Ribeiro et al., (2007)	Systemic Lupus Erythema and Polyarteritis nodosa	F	30	7 months	Symmetrical polyarthritis bilaterally in the hands, wrists, elbows, shoulders, knees, and feet.
Daameche et al., (2023) Yu et al., (2020)	Vasculitis (ANCA-associated)	F M	37 26	NR 24 months	Mono-neuritis, Polyneuropathy, Polyarthralgia, recurrent rhinosinusitis, recurrent fever, skin nodules
Pallares et al., (2019)	Vasculitis (Cryoglobulinaemic)	F	31	24 months	Palpable erythematous rash on face and arms

Camps-Garcia (2011)	Vasculitis (Necrotising)	F	32	NR	Polyarthritis of small joints with extensive ulceration on skin with low grade fevers
Wong (1987)	Vasculitis (Nodular)	F	57	24 months	Erythematous nodules with fever, chills, rigors

Even when leprosy is misdiagnosed and disease is refractory to the selected therapy, it requires clinical suspicion to consider a treatable infectious cause. This is exacerbated by the modification of symptoms or temporary relief achieved when mismanaged, acting as a false confirmation of the misdiagnosis being correct. It has been demonstrated that symptoms of leprosy may respond well to steroid therapy which modifies and dampens the body's immune responses (Hsieh and Wu 2013), thus temporarily relieving symptoms of leprosy infection without addressing the causative factor. This leaves the patient vulnerable to continued recurrence of leprotic disease states and more severe health outcomes.

5. LIMITATIONS

This project collects data from a small number of case studies representing less than 0.0002% of yearly cases detected but does so in favour of focussing on cases reported as initially missed diagnoses and misdiagnosis. Late diagnosis and high levels of disability are classically typical of leprosy and therefore such cases may not be typically considered interesting for the literature base. Due to low levels of clinical suspicion, cases are less likely to be correctly identified in non-endemic areas, this further reduces the reporting of cases which remain hidden. Reporting in case studies is variable and inconsistent, findings of "not reported" were commonplace across published literature this confounds efforts to aggregate data effectively and further specific enquiries would benefit the literature considerably.

6. CONCLUSION

The timely diagnosis of leprosy continues to be a challenge in the third decade of the 21st century leading to avoidable increases in the number of quality and disability adjusted life years lost by the leprosy patient cohort and an extensively prolonged period of uncontrolled onwards infection risk to others. A lack of clinical suspicion for leprosy, in addition to the ability of *M. leprae* and *M. lepromatosis* to mimic other more common diseases continues to hamper efforts to achieve the global eradication of leprosy. The

World Health Organisation has not forgotten leprosy; however clinicians are unlikely to have such a diagnosis in the forefront of their mind unless they are practicing within an endemic region. This article demonstrates the necessity for clinicians to be familiar with and retain the differential of leprosy within their diagnostic repertoire irrespective of classical leprosy signs, symptoms, and exposure risk factors to improve detection rates and reduce disease burden. Additional evaluation of exposure risks associated with human, animal, and environmental reservoirs is required to address the findings of this project in relation to the high rates of patients without a reported exposure risk.

In order to effectively address the ongoing transmission of leprosy and continued disease burden of this disease. We must, as a clinical cohort, be ready to consider leprosy even before clinical cardinal signs present. The identification and diagnosis of leprosy from unexplained, atypical, or refractory instances of disease, on a background of suspected exposure could be achieved up to 60 months sooner than cardinal signs present reducing the duration of risk of onwards transmission and reducing disease progression within individuals. Whilst the current education of clinicians is invaluable for identifying, treating, and rehabilitating typically presenting leprosy patients, it must be developed further to specifically educate on the extent and nature of disease prior to the patient development of classic cardinal signs. Without this educational development and broadened scope of clinical suspicion, leprosy will not be fully controlled as is required for future eradication due to prolonged mycobacterial transmission opportunity and the growth of unidentified reservoirs.

BIBLIOGRAPHY

Ahmed, S. *et al.* (2024) 'Leprosy presenting with Scleroderma and Cataract: A clinical conundrum', *Cureus* [Preprint]. doi:10.7759/cureus.64698.

Al-Omair, A. *et al.* (2024) 'Morbihan disease-like presentation of tuberculoid leprosy', *JAAD Case Reports*, 45, pp. 18–20. doi:10.1016/j.jdcr.2023.12.012.

Alter, A. *et al.* (2010) 'Leprosy as a genetic disease', *Mammalian Genome*, 22(1–2), pp. 19–31. doi:10.1007/s00335-010-9287-1.

Anaje, C.C. *et al.* (2024) 'A case report of de Novo histoid leprosy in a Nigerian male: A diagnostic dilemma', *Tropical Doctor*, 54(4), pp. 380–382. doi:10.1177/00494755241263615.

Andrade, T.C. *et al.* (2017) 'Lepromatous leprosy simulating rheumatoid arthritis - report of a neglected disease', *Anais Brasileiros de Dermatologia*, 92(3), pp. 389–391. doi:10.1590/abd1806-4841.20175423.

Aslam, S. *et al.* (2019) 'Major risk factors for leprosy in a non-endemic area of the United States: A case series', *IDCases*, 17. doi:10.1016/j.idcr.2019.e00557.

Asperges, E. *et al.* (2024) 'A case of leprosy in a nonendemic country', *International Journal of Infectious Diseases*, 143, p. 107004. doi:10.1016/j.ijid.2024.107004.

Assis Daameche, L.N. *et al.* (2023) 'Leprosy mimicking ANCA-associated vasculitis', *International Journal of Family & Community Medicine*, 7(3), pp. 83–86. doi:10.15406/ijfcm.2023.07.00317.

Baldissera, R.L. *et al.* (2019) 'Erythroderma as a manifestation of leprosy', *Anais Brasileiros de Dermatologia*, 94(1), pp. 89–92. doi:10.1590/abd1806-4841.20197887.

Benlamkadam, S. *et al.* (2024) 'Neurologic complications of leprosy: A case series', *Cureus*, 16(5), p. e59884. doi:10.7759/cureus.59884.

Benlamkadam, S. *et al.* (2024a) 'Neurologic complications of leprosy: A case series', *Cureus*, 16(5). doi:10.7759/cureus.59884. Palaniappan, V., Raveendran, P. and Karthikeyan, K. (2024) 'Borderline leprosy with unilateral blepharoptosis in reversal reaction', *Oman Journal of Ophthalmology*, 17(2), pp. 299–300. doi:10.4103/ojo.ojo_243_21.

Bhandari, A. *et al.* (2022) 'Reactions in leprosy patients triggered by covid-19 vaccination – a cross-sectional study from a tertiary care centre in India', *Journal of the European Academy of Dermatology and Venereology*, 36(12). doi:10.1111/jdv.18390.

Blanchard, Dr.A. *et al.* (2019) 'Destructive lesion of the anterior mandible: A unique presentation of leprosy', *Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology*, 128(1). doi:10.1016/j.oooo.2019.02.112.

Bossalini, J.P., Bandino, J.P. and Miletta, N.R. (2019) 'Delayed diagnosis of leprosy in a micronesian soldier – case report', *Military Medicine*, 184(9–10), pp. 561–564. doi:10.1093/milmed/usz138.

Braghiroli, C.S. *et al.* (2019) 'Lepromatous leprosy, melanoma, and basal cell carcinoma: Clinical-histopathologic association', *Anais Brasileiros de Dermatologia*, 94(5), pp. 586–589. doi:10.1016/j.abd.2019.09.008.

Brand, P.W. (1959) 'Temperature variation and leprosy deformity.', *International Journal of Leprosy* , 27(1), pp. 1–7. doi:10.5555/19592902309.

Bratschi, M.W. *et al.* (2015) 'Current knowledge on mycobacterium leprae transmission: A systematic literature review', *Leprosy Review*, 86(2), pp. 142–155. doi:10.47276/lr.86.2.142.

Camaclang, M. and Liesl, E. (2019) 'Lepromatous leprosy and human immunodeficiency virus: A rare coinfection', *Journal of the American Academy of Dermatology*, 81(4), p. AB232. doi:10.1016/j.jaad.2019.06.848.

Cambri, G. and Mira, M.T. (2018) 'Genetic susceptibility to leprosy – from classic immune-related candidate genes to hypothesis-free, whole genome approaches', *Frontiers in Immunology*, 9. doi:10.3389/fimmu.2018.01674.

Camps-García, T. *et al.* (2011) 'Clinical images: Cutaneous necrotizing vasculitis in a patient with lepromatous leprosy', *Arthritis & Rheumatism*, 63(11), pp. 3639–3639. doi:10.1002/art.30602.

Chauhan, S., Wakhlu, A. and Agarwal, V. (2010) 'Arthritis in leprosy', *Rheumatology*, 49(12), pp. 2237–2242. doi:10.1093/rheumatology/keq264.

Chen, L. *et al.* (2023) 'Analysis of misdiagnosed or delayed-diagnosed leprosy bacillus infection from 1990 to 2020 with a prophet time series prediction in Hubei Province, China', *Medicine*, 102(32). doi:10.1097/md.0000000000034714.

Chen, H. *et al.* (2024) 'Fever of unknown origin, blood and cerebrospinal fluid involvement: A leprosy case report', *Frontiers in Immunology*, 15. doi:10.3389/fimmu.2024.1450490.

Chin, N. *et al.* (2024) 'A case of multibacillary borderline lepromatous leprosy in the United States treated with alternative therapy', *Cureus* [Preprint]. doi:10.7759/cureus.66275.

Collin, S.M. *et al.* (2023) 'Systematic review of Hansen disease attributed to*mycobacterium lepromatosis*', *Emerging Infectious Diseases*, 29(7), pp. 1376–1385. doi:10.3201/eid2907.230024.

Craig, *et al.* (2019) 'Case report: A case of type 1 leprosy reaction and dapsone hypersensitivity syndrome complicating the clinical course of Multibacillary Leprosy', *The American Journal of Tropical Medicine and Hygiene*, 100(5), pp. 1145–1148. doi:10.4269/ajtmh.18-0953.

D. Donoghue, H. *et al.* (2019) 'The distribution and origins of ancient leprosy', *Hansen's Disease - The Forgotten and Neglected Disease* [Preprint]. doi:10.5772/intechopen.75260.

da Silva, M.B. *et al.* (2018) 'Evidence of zoonotic leprosy in Pará, Brazilian Amazon, and risks associated with human contact or consumption of armadillos', *PLOS Neglected Tropical Diseases*, 12(6). doi:10.1371/journal.pntd.0006532.

da Silva, M.B. *et al.* (2021) 'Latent leprosy infection identified by dual RLEP and anti-PGL-I positivity: Implications for new control strategies', *PLOS ONE*, 16(5). doi:10.1371/journal.pone.0251631.

Danielssen, D.C., Boeck, W. and Losting, J.L. (1847) *Om Spedalskhed*. Christiania: Chr. Grøndahl.

Davey, T.F. and Rees, R.J. (1974) 'The nasal discharge in leprosy: Clinical and bacteriological aspects', *Leprosy Review*, 45(2), pp. 121–134. doi:10.5935/0305-7518.19740014.

Desikan, K.V. and Sreevatsa (1995) 'Extended studies on the viability of*mycobacterium leprae*outside the human body', *Leprosy Review*, 66(4), pp. 287–295. doi:10.5935/0305-7518.19950032.

Diaz Pallares, C. *et al.* (2019) 'Leprosy: Challenges in diagnosis', *Official Journal of the Association of Medical Microbiology and Infectious Disease Canada*, 4(3), pp. 187–189. doi:10.3138/jammi.2019.05.24.01.

Driedger, M., Teo, I. and Roth, V. (2023) 'Leprosy with type 1 reaction in a patient from Ontario, Canada without recent travel misdiagnosed as vasculitic neuropathy: A case report', *BMC Infectious Diseases*, 23(1). doi:10.1186/s12879-023-08811-x.

Elwan, N.M. and Neinaa, Y.M. (2019) 'Borderline lepromatous leprosy: Uncommon clinical presentation', *The American Journal of Dermatopathology*, 41(3), pp. 211–213. doi:10.1097/dad.0000000000001262.

Fasciano, D. *et al.* (2019) 'Lepromatous leprosy: An elusive mimicker mistaken for polyarteritis nodosa and disseminated tuberculosis', *SKIN The Journal of Cutaneous Medicine*, 3(4), pp. 266–270. doi:10.25251/skin.3.4.6. Diaz Pallares, C. *et al.* (2019) 'Leprosy: Challenges in diagnosis', *Official Journal of the Association of Medical Microbiology and Infectious Disease Canada*, 4(3), pp. 187–189. doi:10.3138/jammi.2019.05.24.01.

Ferreira, M.E. *et al.* (2019) 'Diagnostic delay in a patient with reactional lepromatous leprosy treated as testicular tuberculosis', *Anais Brasileiros de Dermatologia*, 94(2), pp. 236–238. doi:10.1590/abd1806-4841.20198327.

Fleischmann, H.B., Sureshkumar, N. and Stratman, E.J. (2024) 'Lepromatous leprosy infection from mycobacterium lepromatosis without known risk factors or exposures in the Upper Midwest United States', *JAAD Case Reports*, 45, pp. 21–23. doi:10.1016/j.jdcr.2023.12.015.

Franco-Paredes, C. and Rodriguez-Morales, A.J. (2016) 'Unsolved matters in leprosy: A Descriptive Review and call for further research', *Annals of Clinical Microbiology and Antimicrobials*, 15(1). doi:10.1186/s12941-016-0149-x.

Freitas, R.C. *et al.* (2019) 'Primary neural leprosy mimicking rheumatological disorders', *Revista da Associação Médica Brasileira*, 65(6), pp. 767–770. doi:10.1590/1806-9282.65.6.767.

Gao, W. *et al.* (2019) ' diffuse multibacillary leprosy patient with lucio's phenomenon and positive anticardiolipin antibody misdiagnosed as lupus erythematosus panniculitis in the People's Republic of china ', *Infection and Drug Resistance*, Volume 12, pp. 741–744. doi:10.2147/idr.s202386.

Garate, D. *et al.* (2024) '54631 lepromatous leprosy masquerading as necrotizing fasciitis with septic shock', *Journal of the American Academy of Dermatology*, 91(3). doi:10.1016/j.jaad.2024.07.986.

Girdhar, B.K., Girdhar, A. and Kumar, A. (2000) 'Relapses in multibacillary leprosy patients: Effect of length of therapy', *Leprosy Review*, 71(2), pp. 144–153. doi:10.5935/0305-7518.20000017.

Global leprosy (hansen disease) update, 2023: Elimination of leprosy disease is possible – time to act! (2024) *World Health Organization*. Available at: https://www.who.int/publications/i/item/who-wer9937-501-521 (Accessed: 08 November 2024).

Godal, T. and Negassi, K. (1973) 'Subclinical infection in leprosy', *BMJ*, 3(5880), pp. 557–559. doi:10.1136/bmj.3.5880.557.

Gormus, B.J. *et al.* (1988) 'A second sooty mangabey monkey with naturally acquired leprosy: first reported possible monkey-to-monkey transmission', *International Journal of Leprosy and Other Mycobacterial Disease*, 56(1), pp. 61–65. Available at: https://pubmed.ncbi.nlm.nih.gov/3373087/ (Accessed: 2024).

Guerra, M.G. *et al.* (2019) 'Leprosy presenting as remitting seronegative symmetrical synovitis with pitting oedema syndrome – A case report', *BMC Infectious Diseases*, 19(1). doi:10.1186/s12879-019-4098-9.

Guevara, B.E.K. *et al.* (2019) 'Lucio phenomenon mimicking antiphospholipid syndrome: The occurrence of antiphospholipid antibodies in a leprosy patient', *Journal of Cutaneous Pathology*, 46(5), pp. 347–352. doi:10.1111/cup.13425.

Guidelines for the diagnosis, treatment and prevention of leprosy (2018) *World Health Organization*. Available at: https://www.who.int/publications/i/item/9789290226383 (Accessed: 11 April 2024).

Gupta, N. *et al.* (2019) 'Bilateral greater auricular nerve thickening in leprosy', *QJM: An International Journal of Medicine*, 113(8), pp. 579–579. doi:10.1093/qjmed/hcz287.

Han, X.Y. *et al.* (2008) 'A new *mycobacterium* species causing diffuse lepromatous leprosy', *American Journal of Clinical Pathology*, 130(6), pp. 856–864. doi:10.1309/ajcpp72fjzzrrvmm.

Hedar, A.M. *et al.* (2021) 'Autoimmune rheumatic diseases and vascular function: The concept of autoimmune atherosclerosis', *Journal of Clinical Medicine*, 10(19), p. 4427. doi:10.3390/jcm10194427.

Hingtgen, G. *et al.* (2024) 'Erythema nodosum leprosum as the initial presentation of lepromatous leprosy', *JAAD Case Reports*, 52, pp. 137–141. doi:10.1016/j.jdcr.2024.07.034.

Horta-Baas, G. *et al.* (2015) 'Multibacillary leprosy mimicking systemic lupus erythematosus: Case report and literature review', *Lupus*, 24(10), pp. 1095–1102. doi:10.1177/0961203315574557.

Hsieh, T.-T. and Wu, Y.-H. (2014) 'Leprosy mimicking lupus erythematosus', *Dermatologica Sinica*, 32(1), pp. 47–50. doi:10.1016/j.dsi.2013.01.004.

Jariyakulwong, N., Julanon, N. and Saengboonmee, C. (2022) 'Lepromatous leprosy with a suspected 30-year incubation period: A case report of a practically eradicated area', *Journal of Taibah University Medical Sciences*, 17(4), pp. 602–605. doi:10.1016/j.jtumed.2021.12.005.

Job, C.K. *et al.* (2008) 'Transmission of leprosy: A study of skin and nasal secretions of household contacts of leprosy patients using PCR', *The American Journal of Tropical Medicine and Hygiene*, 78(3), pp. 518–521. doi:10.4269/ajtmh.2008.78.518.

K.C., S.R. *et al.* (2019) 'Leprosy – eliminated and Forgotten: A case report', *Journal of Medical Case Reports*, 13(1). doi:10.1186/s13256-019-2198-1.

Kahawita, I.P., Walker, S.L. and Lockwood, D.N.J. (2008) 'Leprosy type 1 reactions and erythema nodosum leprosum', *Anais Brasileiros de Dermatologia*, 83(1), pp. 75–82. doi:10.1590/s0365-05962008000100010.

Kaliyadan, F. *et al.* (2009) 'Anti-phospholipid syndrome preceding a diagnosis of lepromatous leprosy', *Dermatology Online Journal*, 15(6). doi:10.5070/d32g75646r.

Kansal, N.K. *et al.* (2019) 'Umbilicated lesions in a *de novo* case of histoid leprosy', *JDDG: Journal der Deutschen Dermatologischen Gesellschaft*, 17(3), pp. 333–335. doi:10.1111/ddg.13777.

Kaur, M.R. *et al.* (2007) 'Delayed diagnosis of leprosy due to presentation with a rheumatoid-like polyarthropathy', *Clinical and Experimental Dermatology*, 32(6), pp. 784–785. doi:10.1111/j.1365-2230.2007.02525.x.

Kaur, S. *et al.* (1976) 'Peripheral vascular deficit in leprosy', *International Journal of Leprosy and Other Mycobacterial Disease*, 44(3), pp. 332–339.

Kolahi, S. *et al.* (2024) 'Challenging in leprosy relapse with antiphospholipid syndrome diagnosis: A case report', *Clinical Case Reports*, 12(4). doi:10.1002/ccr3.8705.

Kolahi, S. *et al.* (2024) 'Challenging in leprosy relapse with antiphospholipid syndrome diagnosis: A case report', *Clinical Case Reports*, 12(4). doi:10.1002/ccr3.8705.

Krause-Kyora, B. *et al.* (2018) 'Ancient DNA study reveals hla susceptibility locus for leprosy in medieval Europeans', *Nature Communications*, 9(1). doi:10.1038/s41467-018-03857-x.

Kumari, S. *et al.* (2023) 'Lepra reactions: Mimickers and mirror to unmask complex cases of leprosy', *Indian Dermatology Online Journal*, 15(3), pp. 500–503. doi:10.4103/idoj.idoj_294_23.

Kusumaningrum, N. *et al.* (2019) 'Lepromatous leprosy mimicking systemic lupus erithematosus: A case report', *Medical Journal of Indonesia*, 28(1), pp. 77–81. doi:10.13181/mji.v28i1.1793.

Labuda, S.M. *et al.* (2017) 'Hansen's disease and rheumatoid arthritis crossover of clinical symptoms: A case series of 18 patients in the United States', *The American Journal of Tropical Medicine and Hygiene*, 97(6), pp. 1726–1730. doi:10.4269/ajtmh.17-0197.

Le, P.H. *et al.* (2023) 'Pathogenesis, clinical considerations, and treatments: A narrative review on leprosy', *Cureus* [Preprint]. doi:10.7759/cureus.49954.

Lee, J.Y. *et al.* (2014) 'Case of lepromatous leprosy misdiagnosed as systemic sclerosis', *The Journal of Dermatology*, 41(4), pp. 343–345. doi:10.1111/1346-8138.12406.

Leprosy (2017) *World Health Organization*. Available at: https://iris.who.int/bitstream/handle/10665/340774/9789290228509-eng.pdf?sequence=1 (Accessed: 02 December 2024).

Leprosy (2023) *World Health Organization*. Available at: https://www.who.int/news-room/fact-sheets/detail/leprosy#:~:text=Transmission,disease%20when%20they%20begin%20treatment. (Accessed: 02 December 2024).

Li, X. *et al.* (2024) 'Leprosy: Treatment, prevention, immune response and gene function', *Frontiers in Immunology*, 15. doi:10.3389/fimmu.2024.1298749.

Londoño-Echeverri, M.A. *et al.* (2024) 'Syphilis and leprosy coinfection: A diagnostic conundrum', *JAAD Case Reports*, 43, pp. 98–101. doi:10.1016/j.jdcr.2023.11.014.

Magill, A.J. and Hunter, G.W. (2013) *Hunter's Tropical Medicine and Emerging Infectious Diseases*. New York: Saunders.

Malhi, K. *et al.* (2024) 'Lepromatous leprosy masquerading as lichenoid infiltrated rash – a diagnostic predicament', *Transactions of The Royal Society of Tropical Medicine and Hygiene*, 118(6), pp. e3–e5. doi:10.1093/trstmh/trad095.

Mannu, A. *et al.* (2024) 'Histoid leprosy mimicking nevus comedonicus', *International Journal of Dermatology* [Preprint]. doi:10.1111/ijd.17393.

Manoj, M. and Dhakad, U. (2020) 'Leprosy mimicking rheumatoid vasculitis with scleromalacia perforans', *BMJ Case Reports*, 13(7). doi:10.1136/bcr-2020-236796.

Mark, S. (2017) 'Early human migrations (ca. 13,000 years ago) or postcontact Europeans for the earliest spread of*mycobacterium lepraeandmycobacterium lepromatosis*to the Americas', *Interdisciplinary Perspectives on Infectious Diseases*, 2017, pp. 1–8. doi:10.1155/2017/6491606.

Massone, C., Belachew, W.A. and Schettini, A. (2015) 'Histopathology of the lepromatous skin biopsy', *Clinics in Dermatology*, 33(1), pp. 38–45. doi:10.1016/j.clindermatol.2014.10.003.

Maymone, M.B.C. *et al.* (2020) 'Leprosy: Treatment and management of complications', *Journal of the American Academy of Dermatology*, 83(1), pp. 17–30. doi:10.1016/j.jaad.2019.10.138.

Meredith, A. *et al.* (2014) 'Leprosy in red squirrels in Scotland', *Veterinary Record*, 175(11), pp. 285–286. doi:10.1136/vr.g5680.

Mi, Z., Liu, H. and Zhang, F. (2024) 'Advances in the pathogenic, genetic and immunological studies of leprosy', *hLife*, 2(1), pp. 6–17. doi:10.1016/j.hlife.2023.10.003.

Minyoung, L. *et al.* (2019) 'Borderline lepromatous leprosy', *Journal of the American Academy of Dermatology*, 81(4), p. AB176. doi:10.1016/j.jaad.2019.06.656.

Misra, D.P. *et al.* (2014) 'Lepra reaction with Lucio phenomenon mimicking cutaneous vasculitis', *Case Reports in Immunology*, 2014, pp. 1–4. doi:10.1155/2014/641989.

Misra, U. *et al.* (2019) 'Unusual association of leprosy with Lucio phenomenon with secondary antiphospholipid antibody syndrome and ischemic stroke', *Neurology India*, 67(7), pp. 150–151. doi:10.4103/0028-3886.250724.

Mohd Yusuf, S. *et al.* (2019) 'Isolated bilateral pinna swelling: A rare initial presentation of leprosy', *Open Access Macedonian Journal of Medical Sciences*, 7(11), pp. 1815–1817. doi:10.3889/oamjms.2019.481.

Monot, M. *et al.* (2009) 'Comparative genomic and phylogeographic analysis of mycobacterium leprae', *Nature Genetics*, 41(12), pp. 1282–1289. doi:10.1038/ng.477.

Musso, D. *et al.* (2019) 'Leprosy in French Polynesia', *New Microbes and New Infections*, 29, p. 100514. doi:10.1016/j.nmni.2018.10.010.

Nambiar, P.H. *et al.* (2019) 'Leprosy after interleukin 6 inhibitor therapy in a patient with rheumatoid arthritis', *The Lancet Infectious Diseases*, 19(7), p. 787. doi:10.1016/s1473-3099(19)30056-8.

Nery, J.A. *et al.* (2013) 'Understanding the type 1 reactional state for early diagnosis and treatment: A way to avoid disability in leprosy', *Anais Brasileiros de Dermatologia*, 88(5), pp. 787–792. doi:10.1590/abd1806-4841.20132004.

Nunzie, E. *et al.* (2014) 'Lucio leprosy with Lucio's phenomenon, digital gangrene and anticardiolipin antibodies', *Leprosy Review*, 85(3), pp. 194–200. doi:10.47276/lr.85.3.194.

Obi, A. *et al.* (2024) 'Pseudokebnorization of leprosy: A unique phenomenon from MPOX virus coinfection', *JAAD Case Reports*, 47, pp. 35–37. doi:10.1016/j.jdcr.2023.12.021.

Oliveira Neto, R.R. *et al.* (2024) 'Neural leprosy investigation using electroneuromyography and the ML flow rapid test: A case report', *Revista da Sociedade Brasileira de Medicina Tropical*, 57. doi:10.1590/0037-8682-0586-2023.

Olivier, M.A., Modi, D. and Gunduz, O. (2019) 'De Novo histoid leprosy: An expatriate case recently diagnosed in Johannesburg', *Revista da Sociedade Brasileira de Medicina Tropical*, 53. doi:10.1590/0037-8682-0468-2018.

Paliwal, V.K. *et al.* (2019) 'Pearls & OY-sters: Supraorbital neuralgia in lepromatus leprosy masquerading as Suna', *Neurology*, 93(20), pp. 902–904. doi:10.1212/wnl.0000000000008487.

Parikh, S. (2019) 'All in the family: A rare report of concomitant pulmonary tuberculosis and leprosy', *Journal of the American Academy of Dermatology*, 81(4), p. AB168. doi:10.1016/j.jaad.2019.06.627.

Pelser, S. *et al.* (2024) 'A case of leprosy in an immunocompromised traveller', *Journal of Travel Medicine*, 31(4). doi:10.1093/jtm/taae060.

Pfrengle, S. *et al.* (2021) 'Mycobacterium leprae diversity and population dynamics in medieval Europe from novel ancient genomes', *BMC Biology*, 19(1). doi:10.1186/s12915-021-01120-2.

Ploemacher, T. *et al.* (2020) 'Reservoirs and transmission routes of leprosy; a systematic review', *PLOS Neglected Tropical Diseases*, 14(4). doi:10.1371/journal.pntd.0008276.

Poondru, S., Shi, V. and Rajpara, A. (2023) 'Leonine facies of Lepromatous Leprosy', *JAMA Dermatology*, 159(12), p. 1385. doi:10.1001/jamadermatol.2023.3062.

Pruthi, P. *et al.* (2016) 'Leprosy with atypical skin lesions masquerading as relapsing polychondritis', *Case Reports in Infectious Diseases*, 2016, pp. 1–3. doi:10.1155/2016/7802423.

Qiang, F. and Sheng, J. (2023) 'Leprosy misdiagnosed as rheumatoid arthritis', *Internal Medicine Journal*, 53(3), pp. 445–446. doi:10.1111/imj.16037.

Rath, D., Bhargava, S. and Kundu, B.K. (2014) 'Leprosy mimicking common rheumatologic entities: A trial for the clinician in the era of Biologics', *Case Reports in Rheumatology*, 2014, pp. 1–5. doi:10.1155/2014/429698.

Ribeiro, S.L. *et al.* (2007) 'Vasculite na Hanseníase mimetizando Doenças Reumáticas', *Revista Brasileira de Reumatologia*, 47(2), pp. 140–144. doi:10.1590/s0482-50042007000200013.

Rinaldi, A. (2007) 'Tiny Travel Companions', *EMBO reports*, 8(2), pp. 121–125. doi:10.1038/sj.embor.7400908.

Robbins, K.K. *et al.* (2024) 'A case of lepromatous leprosy in Arizona, United States', *JAAD Case Reports*, 43, pp. 9–11. doi:10.1016/j.jdcr.2023.10.021.

Rometsch, C. *et al.* (2024) 'Prevalence of functional disorders across Europe: A systematic review and meta-analysis', *European Journal of Epidemiology* [Preprint]. doi:10.1007/s10654-024-01109-5.

Rusyati, L.M. *et al.* (2024) 'Rare variant of leprosy reaction (Lucio Phenomenon): A case series', *The International Journal of Mycobacteriology*, 13(1), pp. 105–111. doi:10.4103/ijmy.ijmy_184_23.

Rusyati, L.M. *et al.* (2024) 'Rare variant of leprosy reaction (Lucio Phenomenon): A case series', *The International Journal of Mycobacteriology*, 13(1), pp. 105–111. doi:10.4103/ijmy.ijmy_184_23.

Salvi, S. and Chopra, A. (2013) 'Leprosy in a rheumatology setting: A challenging mimic to expose', *Clinical Rheumatology*, 32(10), pp. 1557–1563. doi:10.1007/s10067-013-2276-5.

Schmitz, S. *et al.* (2019) 'When amplified mycobacterium tuberculosis direct (MTD) testing confuses leprosy diagnosis: A case report', *JAAD Case Reports*, 5(2), pp. 131–133. doi:10.1016/j.jdcr.2018.11.012.

Scollard, D.M., McCormick, G. and Allen, J.L. (1999) 'Localization of mycobacterium leprae to endothelial cells of epineurial and perineurial blood vessels and lymphatics', *The American Journal of Pathology*, 154(5), pp. 1611–1620. doi:10.1016/s0002-9440(10)65414-4.

Scollard, D.M., Truman, R.W. and Ebenezer, G.J. (2015) 'Mechanisms of nerve injury in leprosy', *Clinics in Dermatology*, 33(1), pp. 46–54. doi:10.1016/j.clindermatol.2014.07.008.

Sengupta, U. (2019) 'Recent laboratory advances in diagnostics and monitoring response to treatment in leprosy', *Indian Dermatology Online Journal*, 10(2), pp. 106–114. doi:10.4103/idoj.idoj_260_18.

Setia, M.S. *et al.* (2006) 'The role of BCG in prevention of leprosy: A meta-analysis', *The Lancet Infectious Diseases*, 6(3), pp. 162–170. doi:10.1016/s1473-3099(06)70412-1.

Sharma, R. *et al.* (2015) 'Zoonotic leprosy in the Southeastern United States', *Emerging Infectious Diseases*, 21(12). doi:10.3201/eid2112.150501.

Sheetal, S. and Arvind, C. (2009) 'Lest we forget Hansen's disease (leprosy): An unusual presentation with an acute onset of inflammatory polyarthritis and the rheumatology experience', *International Journal of Rheumatic Diseases*, 12(1), pp. 64–69. doi:10.1111/j.1756-185x.2009.01382.x.

Shi, C. *et al.* (2018) 'A rare case of type 1 leprosy reactions following tetanus infection in a borderline tuberculoid leprosy patient and a literature review', *Infectious Diseases of Poverty*, 7(1). doi:10.1186/s40249-018-0441-4.

Shine, R. *et al.* (2024) 'A rare cause of pancytopenia from lepromatous leprosy diagnosed in bone marrow aspiration: A bolt from the blue', *Cureus* [Preprint]. doi:10.7759/cureus.69223.

Silva, C.A. and Belisle, J.T. (2018) 'Host lipid mediators in leprosy: The hypothesized contributions to pathogenesis', *Frontiers in Immunology*, 9. doi:10.3389/fimmu.2018.00134.

Simpson, V. *et al.* (2015) 'Leprosy in red squirrels on the Isle of Wight and Brownsea Island', *Veterinary Record*, 177(8), pp. 206–207. doi:10.1136/vr.h4491.

Singh, P. *et al.* (2015) 'Insight into the evolution and origin of leprosy bacilli from the genome sequence of *mycobacterium lepromatosis*', *Proceedings of the National Academy of Sciences*, 112(14), pp. 4459–4464. doi:10.1073/pnas.1421504112.

Sinha, S. *et al.* (2024) 'Unmasking the hidden burden: A delayed diagnosis of leprosy patients with grade 2 disability and its effects on the healthcare system in Bangladesh', *Cureus* [Preprint]. doi:10.7759/cureus.58708.

Smoot, M. *et al.* (2019), 'Intrapartum Leprosy', *Baylor University Medical Center Proceedings*, 32(3), pp. 431–432. doi:10.1080/08998280.2019.1616520.

Soares-Neto, R.F. *et al.* (2024) 'Anetoderma as an initial presentation of leprosy in a patient with prolonged steroid use', *Australasian Journal of Dermatology*, 65(7), pp. e215–e218. doi:10.1111/ajd.14348.

Somasundaram, A. *et al.* (2024) 'Facial ulceration in a patient with lepromatous leprosy', *International Journal of Dermatology*, 63(11), pp. 1607–1609. doi:10.1111/ijd.17233.

Sridana, M.E., Kurniari, P.K. and Kambayana, G. (2021) 'Leprosy mimicking as rheumatoid arthritis: A case report', *Open Access Macedonian Journal of Medical Sciences*, 9(C), pp. 277–279. doi:10.3889/oamjms.2021.7629.

Sumangala, S. *et al.* (2019) 'Leprosy neuropathy masquerading as cellulitis', *Postgraduate Medical Journal*, 95(1122), pp. 225–226. doi:10.1136/postgradmedj-2019-136392.

Suvirya, S. *et al.* (2019) 'A case of diffuse lepromatous leprosy with Lucio Phenomenon', *QJM: An International Journal of Medicine*, pp. 138–139. doi:10.1093/qjmed/hcz146.

Taggart, M. *et al.* (2022) 'Multibacillary leprosy with an incubation period exceeding 50 years', *BMJ Case Reports*, 15(7). doi:10.1136/bcr-2022-250835.

Tan, Y.E. *et al.* (2019) 'Report of a leprosy case in Singapore: An age-old disease not to be forgotten in developed countries with low-prevalence settings', *Access Microbiology*, 1(3). doi:10.1099/acmi.0.000014.

Towards Zero Leprosy. Global Leprosy (Hansen's disease) Strategy 2021–2030. (2021) New Delhi: World Health Organization, Regional Office for South-East Asia; 2017. Licence: CC BY-NCSA 3.0 IGO. 978-92-9022-850-9

Treu, C. *et al.* (2017) 'Structural and functional changes in the microcirculation of lepromatous leprosy patients - observation using orthogonal polarization spectral imaging and laser Doppler flowmetry iontophoresis', *PLOS ONE*, 12(4). doi:10.1371/journal.pone.0175743.

Turankar, R.P. *et al.* (2019) 'Survival of mycobacterium leprae and association with Acanthamoeba from environmental samples in the inhabitant areas of active leprosy cases: A cross sectional study from endemic pockets of Purulia, West Bengal', *Infection, Genetics and Evolution*, 72, pp. 199–204. doi:10.1016/j.meegid.2019.01.014.

Uaska Sartori, P.V. *et al.* (2020) 'Human genetic susceptibility of leprosy recurrence', *Scientific Reports*, 10(1). doi:10.1038/s41598-020-58079-3.

van Hooij, A. and Geluk, A. (2021) 'In search of biomarkers for leprosy by unraveling the host immune response to *mycobacterium leprae*', *Immunological Reviews*, 301(1), pp. 175–192. doi:10.1111/imr.12966.

Walker, S.L. (2020) 'Leprosy reactions', *International textbook of leprosy* [Preprint]. doi:10.1489/itl.2.2.

Wijaya, E., Komarasari, E. and Esti, P.K. (2024) 'Case report of a 28 years old woman with lepromatous leprosy mimicking systemic lupus erythematosus', *Bali Dermatology Venereology and Aesthetic Journal*, pp. 15–18. doi:10.51559/balidervenaesthj.v7i1.87.

WONG, W.S. (1987) 'Leprosy presenting as nodular vasculitis', *Rheumatology*, 26(5), pp. 398–398. doi:10.1093/rheumatology/26.5.398.

Xie, C.B. *et al.* (2023) 'Erythema nodosum leprosum after allergen immunotherapy as initial presentation of lepromatous leprosy treated with novel multidrug regimen', *JAAD Case Reports*, 41, pp. 77–80. doi:10.1016/j.jdcr.2023.09.012.

Youssef, H., Mahani, T. and Hojjati, M. (2023) 'Leprosy, the great imitator of rheumatic diseases: A case study', *Cureus* [Preprint]. doi:10.7759/cureus.39527.

Yu, S.-N. *et al.* (2020) 'Recurrent fever and cutaneous nodules: Leprosy masquerading as anti-neutrophil cytoplasmic antibodies associated vasculitis', *Chinese Medical Journal*, 133(16), pp. 2004–2006. doi:10.1097/cm9.0000000000000937.

Zawar, V. *et al.* (2017) 'Tuberculoid leprosy masquerading as systemic lupus erythematosus: An interesting observation', *Acta Dermatovenerologica Alpina Pannonica et Adriatica*, 26(3), pp. 81–83. doi:10.15570/actaapa.2017.25.

SOBRE OS ORGANIZADORES

Guillermo Julián González-Pérez

Sociólogo, Demógrafo y Doctor en Ciencias de la Salud. Orientación socio-médica. Profesor-Investigador Titular "C" y responsable del Cuerpo Académico Consolidado “Salud, Población y Desarrollo Humano” en el Centro Universitario de Ciencias de la Salud de la Universidad de Guadalajara, México. Miembro desde 1993 del Sistema Nacional de Investigadores de México auspiciado por CONAHCYT (actualmente Nivel III) y miembro de la Academia Mexicana de Ciencias desde 2002. Ha publicado más de 100 artículos científicos en revistas indizadas del campo de las Ciencias Sociales aplicadas a la salud y la Salud Pública, diversos libros como autor, editor o coordinador y dirigido más de 50 tesis de posgrado.

María Guadalupe Vega-López

Licenciada en Trabajo Social; Maestra en Salud Pública; Maestra en Sociología y Doctora en Ciencias de la Salud, Orientación Socio-médica. Profesora-Investigadora Titular "C" y directora del Centro de Estudios en Salud, Población y Desarrollo Humano, en el Centro Universitario de Ciencias de la Salud de la Universidad de Guadalajara, México. Miembro desde 1999 del Sistema Nacional de Investigadores de México (actualmente Nivel II); integrante del Cuerpo Académico Consolidado “Salud, Población y Desarrollo Humano”. Ha publicado más de 60 artículos científicos en revistas indizadas del área de las Ciencias Sociales aplicadas a la salud y la Salud Pública, así como diversos libros como autora y coordinadora, de carácter internacional. Es revisora en varias revistas científicas de carácter internacional.

ÍNDICE REMISSIVO

T

V

W

EDITORA ARTEMIS
2026