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Publisher: Multidisciplinary Digital Publishing Institute (MDPI)

E-ISSN: 2414-6366

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Tropical Medicine and Infectious Disease

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SUBJECT AREA AND CATEGORY

Immunology and Microbiology
 Immunology and Microbiology (miscellaneous)
 Medicine
 Infectious Diseases
 Public Health, Environmental and Occupational Health

PUBLISHER

MDPI AG

H-INDEX

24

PUBLICATION TYPE

Journals

ISSN

24146366

COVERAGE

2016-2021

INFORMATION

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SCOPE

Tropical Medicine and Infectious Disease publishes on all tropical diseases of global significance, as well as neglected tropical diseases as defined from time-to-time by the World Health Organization. The scope of the journal includes, but is not limited to: Clinical tropical medicine; Tropical public health; Tropical infectious diseases; Parasitology and entomology; Bacteriology, mycology and virology; Epidemiological and social science studies; Chemotherapy and pharmacology; Immunology; Disease prevention, control and elimination; Emerging and re-emerging infectious diseases; Emerging public health threats; Global health and One Health.

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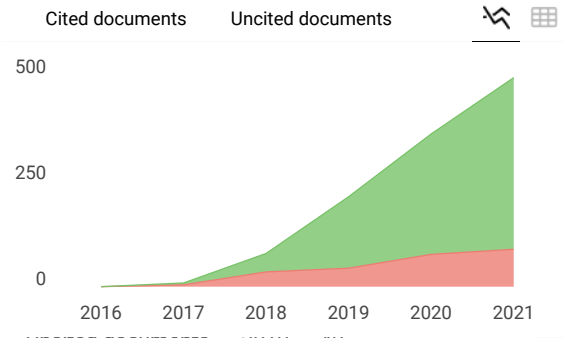
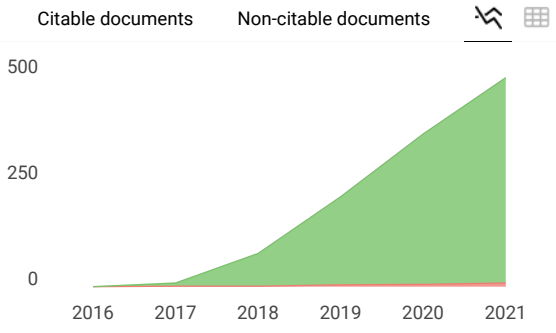
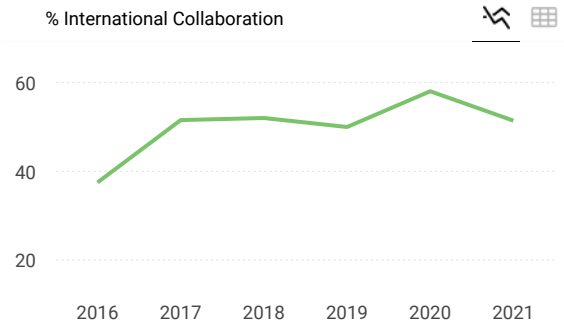
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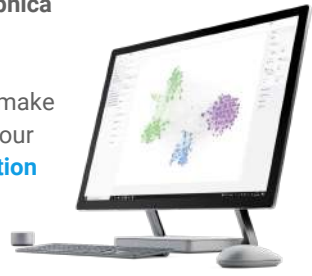
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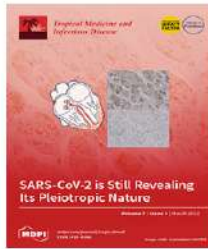
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Trop. Med. Infect. Dis., Volume 7, Issue 3 (March 2022) – 17 articles



Cover Story (view full-size image): In addition to the already known variety of dysfunctions of many tissues, new-onset cardiac arrhythmias have emanated, being common during acute SARS-CoV-2 infection, but also in patients with post-COVID-19 syndrome. The occurrence of arrhythmias poses an additional factor worsening the outcome, especially in critically ill patients. Although arrhythmias can arise secondary to hypoxemia/hypoxia and hyperinflammatory response in COVID-19 patients, recent findings show that SARS-CoV-2 can directly infect cardiac conducting cardiomyocytes obtained from the atrioventricular (AV) node, leaving behind a typical immunohistochemical signature. This finding indicates that viral-mediated impairment of the cardiac conduction system could underlie COVID-19-provoked cardiac arrhythmias. [View this paper](#)

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The Effectiveness of the Use of Regdanvimab (CT-P59) in Addition to Remdesivir in Patients with Severe COVID-19: A Single Center Retrospective Study

by Ganghee Chae, Aram Choi, Soyeoun Lim, Sooneun Park, Seungjun Lee, Youngick Ahn, Jinhyoung Kim, Seungwon Ra, Yangjin Jegal, Jongjoon Ahn, Eunji Park, Jaebum Jun, Woonjung Kwon and Taehoon Lee

Trop. Med. Infect. Dis. 2022, 7(3), 51; <https://doi.org/10.3390/tropicalmed7030051> - 18 Mar 2022
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Abstract Introduction: Coronavirus disease 2019 (COVID-19) still has a high mortality rate when it is severe. Regdanvimab (CT-P59), a neutralizing monoclonal antibody that has been proven effective against mild to moderate COVID-19, may be effective against severe COVID-19. This study was conducted to determine [...] [Read more](#).

(This article belongs to the Special Issue COVID-19: Current Status and Future Prospects)

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The History of Intravenous and Oral Rehydration and Maintenance Therapy of Cholera and Non-Cholera Dehydrational Diarrheas: A Deconstruction of Translational Medicine: From Bench to Bedside?

by David R. Nalin

Trop. Med. Infect. Dis. 2022, 7(3), 50; <https://doi.org/10.3390/tropicalmed7030050> - 12 Mar 2022
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Abstract The "bench to bedside" (BTB) paradigm of translational medicine (TM) assumes that medical progress emanates from basic science discoveries transforming clinical therapeutic models. However, a recent report found that most published medical research is false due, among other factors, to small samples, inherent [...] [Read more](#).

(This article belongs to the Special Issue Cholera Control in 2021: Bioecology, Immunology, Current and Future Vaccines and Treatment Options)

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Digital Storytelling and Community Engagement to Find Missing TB Cases in Rural Nuh, India

by Subhi Quraishi, Hilmi Quraishi, Hemlata Yadav, Ayushi Singh, Ilmana Fasih, Nathaly Aguilera Vasquez, Lavanya Huria, Tripti Pande, Olive Mumba, Vishnu Vardhan Kamineni and Amera Khan

Trop. Med. Infect. Dis. 2022, 7(3), 49; <https://doi.org/10.3390/tropicalmed7030049> - 11 Mar 2022
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Abstract Nuh, Haryana, is one of India's least developed districts. To improve TB case notifications, ZMQ carried out an active case-finding (ACF) intervention conducted by community health workers (MIRAs) using a digital TB storytelling platform to create TB awareness in the community. The combined [...] [Read more](#).

(This article belongs to the Special Issue New Tools and Approaches to End TB)

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The Biological and Clinical Aspects of a Latent Tuberculosis Infection

by Nelli F. Khabibullina, Daria M. Kutuzova, Irina A. Burmistrova and Irina V. Lyadova

Trop. Med. Infect. Dis. 2022, 7(3), 48; <https://doi.org/10.3390/tropicalmed7030048> - 08 Mar 2022

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Abstract Tuberculosis (TB), caused by bacilli from the *Mycobacterium tuberculosis* complex, remains a serious global public health problem, representing one of the main causes of death from infectious diseases. About one quarter of the world's population is infected with *Mtb* and has a latent [...] [Read more](#).

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Malignant Syphilis in a Female Patient: A Case Report and Mini-Review

by Julija Dimnik, Maja Benko, Violeta Hosta, Andreja Murnik Rauh, Andreja Pagon, Vesna Cvitković Špik, Saba Battelino and Domen Vozel

Trop. Med. Infect. Dis. 2022, 7(3), 47; <https://doi.org/10.3390/tropicalmed7030047> - 08 Mar 2022

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Abstract Malignant syphilis (MS) is a rare form of secondary syphilis with grotesque skin lesions, systemic manifestation and life-threatening complications. This article presents a case of MS in an immunocompetent 41-year-old female, who initially manifested with a generalized nonpruritic erythematous rash and systemic symptoms. [...] [Read more.](#)

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Analysis of *Puumala orthohantavirus* Genome Variants Identified in the Territories of Volga Federal District

by Emmanuel Kabwe, Walaa Al Sheikh, Anton F. Shamsutdinov, Ruzilya K. Ismagilova, Ekaterina V. Martynova, Olesia V. Ohlopkova, Yuri A. Yurchenko, Tatiana A. Savitskaya, Guzel S. Isaeva, Svetlana F. Khaiboullina, Albert A. Rizvanov, Sergey P. Morzunov and Yuriy N. Davidyuk

Trop. Med. Infect. Dis. 2022, 7(3), 46; <https://doi.org/10.3390/tropicalmed7030046> - 06 Mar 2022

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Abstract Hemorrhagic fever with renal syndrome (HFRS) is a zoonotic disease commonly diagnosed in the Volga Federal District (VFD). HFRS is caused by *Puumala orthohantavirus* (PUUV), and this virus is usually detected in bank voles as its natural host (*Myodes glareolus*). [...] [Read more.](#)

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The Geographical Distribution and Influencing Factors of COVID-19 in China

by Weiwei Li, Ping Zhang, Kaixu Zhao and Sidong Zhao

Trop. Med. Infect. Dis. 2022, 7(3), 45; <https://doi.org/10.3390/tropicalmed7030045> - 06 Mar 2022

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Abstract The study of the spatial differentiation of COVID-19 in cities and its driving mechanism is helpful to reveal the spatial distribution pattern, transmission mechanism and diffusion model, and evolution mechanism of the epidemic and can lay the foundation for constructing the spatial dynamics [...] [Read more.](#)

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Analysis of Excess All-Cause Mortality and COVID-19 Mortality in Peru: Observational Study

by Max Carlos Ramirez-Soto and Gutia Ortega-Cáceres

Trop. Med. Infect. Dis. 2022, 7(3), 44; <https://doi.org/10.3390/tropicalmed7030044> - 05 Mar 2022

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Abstract During the COVID-19 pandemic, an excess of all-cause mortality has been recorded in several countries, including Peru. Most excess deaths were likely attributable to COVID-19. In this study, we compared the excess all-cause mortality and COVID-19 mortality in 25 Peruvian regions to determine [...] [Read more.](#)

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Open Access Editor's Choice Case Report



Detection of SARS-CoV-2 Antigens in the AV-Node of a Cardiac Conduction System—A Case Report

by Hrvoje Jakovac, Antun Ferenčić, Christophe Stemberger, Bojana Mohar Vitezić and Dražen Cuculić
Trop. Med. Infect. Dis. 2022, 7(3), 43; <https://doi.org/10.3390/tropicalmed7030043> - 04 Mar 2022

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Abstract Mounting evidence indicates that new arrhythmic events frequently occur during and after coronavirus disease (COVID-19), posing additional mortality risk in older-aged and critically ill patients. However, the underlying mechanisms and cardio pathological substrates of COVID-related arrhythmias have not been clarified yet. Here, we [...] [Read more.](#)

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Antimicrobial Resistance and Predisposing Factors Associated with Catheter-Associated UTI Caused by Uropathogens Exhibiting Multidrug-Resistant Patterns: A 3-Year Retrospective Study at a Tertiary Hospital in Mogadishu, Somalia

by Abdikarim Hussein Mohamed, Nasteho Mohamed Sheikh Omar, Marian Muse Osman, Hussein Ali Mohamud, Aşır Eraslan and Metin Gur

Trop. Med. Infect. Dis. 2022, 7(3), 42; <https://doi.org/10.3390/tropicalmed7030042> - 04 Mar 2022

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Abstract Background: Widespread and rapidly emerging multidrug-resistant uropathogens, particularly carbapenem-resistant pathogens, are a public health concern that impairs the determination of empirical therapy. This study aims to evaluate the antimicrobial susceptibility profile and factors associated with catheter-associated urinary tract infection (CA-UTI). Method: This retrospective [...] [Read more.](#)

Open Access Systematic Review



Intrathecal/Intraventricular Colistin for Antibiotic-Resistant Bacterial CNS Infections in Pediatric Population: A Systematic Review

by Ibrahim Alnaami and Zubaidah Alahmari

Trop. Med. Infect. Dis. 2022, 7(3), 41; <https://doi.org/10.3390/tropicalmed7030041> - 03 Mar 2022

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Abstract Central nervous system (CNS) infections constitute a life-threatening condition, especially in children. Treatment limitations exist for drug-resistant CNS bacterial infections. Inadequate CNS penetration and intravenous (IV) antibiotic treatment failure represent a major clinical challenge. However, patients with antibiotic-resistant bacterial CNS infections may benefit [...] [Read more.](#)

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Delayed Diagnosis of Whipple's Disease Complicated by Jarisch–Herxheimer Reaction to Ceftriaxone Treatment: A Case Report and Literature Review

by Marcus C. C. Clarke and Ric N. Price

Trop. Med. Infect. Dis. 2022, 7(3), 40; <https://doi.org/10.3390/tropicalmed7030040> - 03 Mar 2022

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Abstract Whipple's disease is a rare chronic infection caused by the actinomycete *Tropheryma whippelii*. Patients commonly present with gastrointestinal symptoms. We present a case of classic Whipple's disease complicated by a probable Jarisch–Herxheimer reaction following the initiation of ceftriaxone treatment. **Full article**

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Diagnostic Value of Neutrophil-to-Lymphocyte Ratio, Lymphocyte-to-Monocyte Ratio, and Platelet-to-Lymphocyte Ratio in the Diagnosis of Erythema Nodosum Leprosum: A Retrospective Study

by Natalia Tanojo, Damayanti, Budi Utomo, Evy Ervianti, Dwi Murtiastutik, Cita Rosita Sigit Prakoeswa and Muhammad Yulianto Listiawan

Trop. Med. Infect. Dis. 2022, 7(3), 39; <https://doi.org/10.3390/tropicalmed7030039> - 02 Mar 2022

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Abstract Erythema nodosum leprosum (ENL) is an acute immune complex-mediated condition of the dermis, subcutaneous tissue, and other tissues seen in patients with multibacillary (MB) leprosy, causing severe impairment to patients' quality of life. To date, there is no standard diagnostic criteria for ENL. [...] [Read more](#).

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Genetic Analysis of Influenza A/H1N1pdm Strains Isolated in Bangladesh in Early 2020

by Abu Hasan, Tadahiro Sasaki, Juthamas Phadungsombat, Ritsuko Koketsu, Rummana Rahim, Nikhath Ara, Suma Mita Biswas, Riku Yonezawa, Emi E. Nakayama, Mizanur Rahman and Tatsuo Shioda

Trop. Med. Infect. Dis. 2022, 7(3), 38; <https://doi.org/10.3390/tropicalmed7030038> - 28 Feb 2022

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Abstract Influenza is one of the most common respiratory virus infections. We analyzed hemagglutinin (HA) and neuraminidase (NA) gene segments of viruses isolated from influenza patients who visited Evercare Hospital Dhaka, Bangladesh, in early 2020 immediately before the coronavirus disease 2019 (COVID-19) pandemic. All [...] [Read more](#).

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The Use of Proton Pump Inhibitors and COVID-19: A Systematic Review and Meta-Analysis

by Kaneez Fatima, Talal Almas, Shan Lakhani, Arshia Jahangir, Abdullah Ahmed, Ayra Siddiqui, Aiman Rahim, Saleha Ahmed Qureshi, Zukhruf Arshad, Shilpa Golani and Adeena Musheer

Trop. Med. Infect. Dis. 2022, 7(3), 37; <https://doi.org/10.3390/tropicalmed7030037> - 28 Feb 2022

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Abstract COVID-19 has proved to be a serious, and consequential disease that has affected millions of people globally. Previously, the adverse effects of proton pump inhibitors (PPI) have been observed with increasing the risk of pneumonia and COVID-19. This meta-analysis aims to address the [...] [Read more](#).

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Holistic Approach to Tuberculosis Detection, Treatment and Prevention: Emerging Evidence and Strategies from the Field

by Abu Naser Zafar Ullah, Sourya Shrestha, Amyr A. Malik and Tapash Roy

Trop. Med. Infect. Dis. 2022, 7(3), 36; <https://doi.org/10.3390/tropicalmed7030036> - 25 Feb 2022

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Abstract The global fight against tuberculosis (TB) has gained momentum since the adoption of the 'End TB Strategy' in 2014 [...] [Full article](#)

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Depriving Out-of-School Children of Deworming Tablets for Soil-Transmitted Helminth Infection in Bangladesh: The Irony of a School-Based Deworming Programme

by  Avijit Saha,  Srizan Chowdhury,  Edwin Theophilus Goswami,  Konica Gop,  Ariful Alam,  Asadur Rahman and  Malabika Sarker

Trop. Med. Infect. Dis. 2022, 7(3), 35; <https://doi.org/10.3390/tropicalmed7030035> - 24 Feb 2022

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Abstract Since 2008, Bangladesh has had a school-based deworming programme to combat soil-transmitted helminth (STH) infection among school-aged children (SACs). Existing programmes have trouble reaching SACs, especially those out-of-school (OSCs). This study evaluated deworming coverage among school going children (SGCs) and OSCs in two [...] **Read more.**

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Interests: vaccines; zoonotic diseases; biocontainment; vaccinology; facultative intracellular bacteria; animal models**Special Issues, Collections and Topics in MDPI journals**Special Issue in ***Tropical Medicine and Infectious Disease: Development of Vaccines for Zoonotic Diseases*** (/journal/tropicalmed/special_issues/vaccines_zoonotic).**Prof. Dr. Ayola Akim Adegnika****Website** (https://www.researchgate.net/profile/Ayola_Adegnika)

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Interests: vector molecular biology; saliva of blood feeding insects; mosquitoes; transcriptomics; malaria; non-coding RNAs; gene expression**Prof. Dr. Omar Bagasra****Website** (<https://www.clafliin.edu/academics-research/faculty-research/meet-our-faculty/omar-bagasra>)**SciProfiles** (<https://sciprofiles.com/profile/41004>)

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2. Burnet Institute, Melbourne, Victoria, Australia

Interests: malaria; infectious disease; genomics; epidemiology



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Interests: infectious diseases; neglected tropical diseases; antibiotic resistance; tropical medicine



Prof. Dr. Zeno Bisoffi

SciProfiles (<https://sciprofiles.com/profile/250152>).

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Interests: strongyloidiasis; clinical research on malaria and other tropical and parasitic diseases; surveillance of imported tropical and infectious diseases; assessment of diagnostic tools in tropical medicine and parasitology; clinical epidemiology and clinical decision-making applied to tropical medicine



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1. Centre for Tropical Medicine and Global Health, Nuffield Department of Clinical Medicine, University of Oxford, Oxford, UK

2. Mahidol Oxford Tropical Medicine Research Unit (MORU), Bangkok, Thailand

Interests: Scrub typhus; rickettsia; zoonoses; diagnostics; biosafety

Special Issues, Collections and Topics in MDPI journals

Special Issue in *Tropical Medicine and Infectious Disease: Tropical Laboratory Safety Including Biosafety*.

(/journal/tropicalmed/special_issues/Biosafety).

Special Issue in *Tropical Medicine and Infectious Disease: Selected Papers from The 2nd Asia Pacific Rickettsia Conference*

(/journal/tropicalmed/special_issues/APRC2).

Special Issue in *Pathogens: Latest Updates on Scrub Typhus (Orientia spp.)* (/journal/pathogens/special_issues/4L4WP7V45M).



Prof. Dr. Lucille Blumberg

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Deputy Director, Epidemiology, and Medical Consultant, Centre for Emerging and Zoonotic Diseases, Head of the Public Health Surveillance and Response Division, National Institute for Communicable Diseases, Johannesburg 2192, South Africa

Interests: viral haemorrhagic fevers (VHF); rabies; malaria; travel related infections

Special Issues, Collections and Topics in MDPI journals

Special Issue in *Tropical Medicine and Infectious Disease: COVID-19: Current Challenges and Future Perspectives*

(/journal/tropicalmed/special_issues/COVID-19_challenges_perspectives).

Special Issue in *Tropical Medicine and Infectious Disease: COVID-19: Current Status and Future Prospects*

(/journal/tropicalmed/special_issues/COVID_19_current_status_future_prospects).



Prof. Dr. Paul J. Brindley

Website (<https://smhs.gwu.edu/brindley-lab/>) **SciProfiles** (<https://sciprofiles.com/profile/411335>).

Department of Microbiology, Immunology and Tropical Medicine and of the Research Center for Neglected Diseases of Poverty, George Washington University, School of Medicine and Health Sciences, Washington, DC 20037, USA

Interests: neglected tropical diseases (NTDs); schistosomiasis; food borne trematodiasis; functional genomics; genome editing; helminth infection associated cancers

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Interests: neglected tropical diseases; zoonoses; parasitic diseases; echinococcosis; cysticercosis; epidemiology; disease burden; One Health



Prof. Dr. Christian Burri

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Department of Medicine, Swiss Tropical & Public Health Institute, Socinstrasse 57, 4051 Basel, Switzerland

Interests: sleeping sickness (human African trypanosomiasis); drug and vaccine development against neglected tropical diseases; clinical trials in low resource settings; implementation research; public health

Special Issues, Collections and Topics in MDPI journals

Special Issue in *Tropical Medicine and Infectious Disease: Human African Trypanosomiasis (Sleeping Sickness): The Road to Elimination Revisited—Achievements and Remaining Challenges* (/journal/tropicalmed/special_issues/HAT)



Dr. Guido Calleri

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Travel Medicine Unit, Department of Internal Medicine, Amedeo di Savoia Hospital, Torino, Italy

Interests: parasitology; malaria; clinical tropical medicine; vector borne diseases; travel medicine



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Department of Disease Control, Faculty of Infectious and Tropical Disease, London School of Hygiene & Tropical Medicine, London WC1E 7HT, UK

Interests: spatial epidemiology; geostatistics; geographic information system (GIS); remote sensing; neglected tropical diseases; vector-borne diseases



Prof. Dr. Hélène Carabin

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Canada Research Chair in Epidemiology and One Health; Department of pathology and microbiology, Faculty of Veterinary Medicine & Department of Social and Preventive Medicine, École de Santé Publique de l'Université de Montréal, 3200 rue Sicotte, Local 2202-35, Saint-Hyacinthe, QC J2S 2M2, Canada

Interests: infectious disease epidemiology; zoonoses; neglected tropical diseases; global health; Bayesian statistics; cysticercosis; One Health

Special Issues, Collections and Topics in MDPI journals

Special Issue in *Tropical Medicine and Infectious Disease: Risks and Benefits of Human, Animal and Environmental Interactions: Application of the One Health Approach* (/journal/tropicalmed/special_issues/Application_One_Health)



Prof. Dr. Rudi Cassini

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Department of Animal Medicine, Production and Health, University of Padova, 35020, Legnaro, Italy

Interests: veterinary parasitology; tick-borne diseases; leishmaniasis; cystic echinococcosis; one-health



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Prof. Dr. Francesco Castelli

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Department of Infectious and Tropical Diseases, University of Brescia and Brescia Spedali Civili General Hospital, UNESCO Chair "Training and Empowering human resources for health development in resource-limited countries", Brescia, Italy

Interests: tropical medicine; migration medicine; imported and travel-related diseases; HIV infection; viral hepatitis; training health personnel in resource-limited areas



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2. European Union Reference Laboratory for Parasites; Department of Infectious Diseases, Istituto Superiore di Sanità, Viale Regina Elena, 299, 00161 Rome, Italy

Interests: alveolar and cystic echinococcosis; medical and veterinary foodborne parasitology; clinical and molecular epidemiology; public health; anthelmintic drugs



Prof. Dr. Phaik Yeong Cheah

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2. Centre for Tropical Medicine & Global Health, Nuffield Department of Medicine, University of Oxford, Oxford, UK

Interests: bioethics; community engagement; public engagement; antimicrobial resistance; AMR

Special Issues, Collections and Topics in MDPI journals

Special Issue in ***Antibiotics: Social Dimensions of Antibiotic Resistance in Asia - a One Health Perspective***

([/journal/antibiotics/special_issues/Asia_antibiotics](https://journal/antibiotics/special_issues/Asia_antibiotics)).



Prof. Dr. Junhu Chen

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1. National Institute of Parasitic Diseases, Chinese Center for Diseases Control and Prevention (Chinese Center for Tropical Diseases Research), Shanghai, China
2. School of Global Health, Chinese Center for Tropical Diseases Research, Shanghai Jiao Tong University School of Medicine, Shanghai, China

Interests: vector-borne parasitic diseases (malaria, schistosomiasis); infection and immunity; population genetics; diagnosis and vaccine discovery

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Interests: hepatitis B; hepatitis C; AIDS and viral hepatitis



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Interests: zoonoses; emerging zoonoses; veterinary public health; epidemiology



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Interests: neglected tropical diseases; helminth infections; allergy and asthma; epidemiology



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Interests: tuberculosis; infectious disease epidemiology; artificial intelligence; case detection; diagnostics; monitoring and evaluation

Special Issues, Collections and Topics in MDPI journals

Special Issue in ***Tropical Medicine and Infectious Disease: New Tools and Approaches to End TB*** (/journal/tropicalmed/special_issues/approaches_to_end_tuberculosis).



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3. Director, International Health Management Consultants S.A., Geneva, Switzerland

Interests: travel health; travel health education; malaria; arboviral disease



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Interests: leishmaniasis; neglected tropical diseases; malaria; clinical pharmacology; drug development

Special Issues, Collections and Topics in MDPI journals

Special Issue in ***Tropical Medicine and Infectious Disease: Feature Papers in Neglected and Emerging Tropical Disease*** (/journal/tropicalmed/special_issues/NETD_FP).



Prof. Dr. André Luis Souza Dos Santos

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2. Rede Micologia RJ – Fundação de Amparo à Pesquisa do Estado do Rio de Janeiro (FAPERJ), Rio de Janeiro, Brazil

Interests: chemotherapy, antifungal resistance; biochemistry; cell biology; enzymes; biofilm; virulence

Special Issues, Collections and Topics in MDPI journals

Special Issue in ***Tropical Medicine and Infectious Disease: Feature Papers in Tropical Medicine and Infectious Disease*** (/journal/tropicalmed/special_issues/tropical_feature_papers).

Special Issue in ***Tropical Medicine and Infectious Disease: Advances in Chagas Disease Control*** (/journal/tropicalmed/special_issues/Chagas_Disease_Control).

Special Issue in ***Journal of Fungi: New Strategies to Combat Human Fungal Infections*** (/journal/jof/special_issues/VB098F1XYD).

Topics: **Novel Therapeutic Strategies against *Leishmania* and *Trypanosoma*** (</topics/Leishmania>).



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Special Issues, Collections and Topics in MDPI journals

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Interests: mycetoma

Special Issues, Collections and Topics in MDPI journals

Special Issue in ***Tropical Medicine and Infectious Disease: Community Engagement and Neglected Tropical Diseases (NTDs)*** ([/journal/tropicalmed/special_issues/Community_NTDs](http://journal.tropicalmed/special_issues/Community_NTDs)).



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Department of Molecular Parasitology and Tropical Diseases, School of Medicine, College of Medicine, Taipei Medical University, 250 Wu-Xing Street, Taipei, Taiwan

Interests: toxocarasis; toxoplasmosis; dirofilariasis; parasite immunology & molecular biology; molecular pathogenesis of parasitic diseases



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Head of Department of Public Health, Travel Medicine & Infectious Diseases, Epidemiology, Biostatistics and Prevention Institute, University of Zurich, Hirschengraben 84, 8001 Zurich, Switzerland

Interests: HIV; co-infections; tuberculosis; prevention; travelling; viral hepatitis; emerging infectious diseases; public health

Special Issues, Collections and Topics in MDPI journals

Special Issue in ***Tropical Medicine and Infectious Disease: HIV and Co-Infections: Old and New Challenges*** ([/journal/tropicalmed/special_issues/HIV_coinfections](http://journal.tropicalmed/special_issues/HIV_coinfections)).



Prof. Dr. Mark C. Field

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2. Biology Centre, Czech Academy of Sciences, Institute of Parasitology, Faculty of Science, University of South Bohemia, České Budějovice, Czech Republic

Interests: parasitology; cell biology; proteomics; molecular evolution; trafficking; gene expression



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Infectious Disease Division, Department of Medicine, National University Health System, Singapore

Interests: melioidosis; OPAT; outbreak response; surveillance; infection prevention and control



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2. Instituto Nacional de Salud, Hospital Infantil de México, Federico Gomez, México City 06720, México

Interests: tropical medicine; Chagas disease; cryptococcosis



Special Issues, Collections and Topics in MDPI journals

Special Issue in [Tropical Medicine and Infectious Disease: The Global Burden of Disease of Chagas Disease \(American Trypanosomiasis\)](#) ([/journal/tropicalmed/special_issues/c_d](#))

Special Issue in [Vaccines: Vaccines in the Age of the Infodemic: Vaccine Knowledge and How to Improve Health Literacy](#) ([/journal/vaccines/special_issues/vaccines_in_the_age_of_the_infodemic_vaccine_knowledge_and_how_to_improve_health_literacy](#))



Dr. Hans-Peter Fuehrer

Website (https://vetdoc.vu-wien.ac.at/vetdoc/suche.person_uebersicht?sprache_in=en&ansicht_in=&menue_id_in=101&id_in=3676)

SciProfiles (<https://sciprofiles.com/profile/1045055>)

Institute of Parasitology, Department of Pathobiology, University of Veterinary Medicine, Vienna, Austria

Interests: mosquitoes and mosquito-borne pathogens; vectors and vector-borne pathogens; *Calodium hepaticum*; *Plasmodium malariae*; *Plasmodium ovale spp*

Special Issues, Collections and Topics in MDPI journals

Special Issue in [Pathogens: Zoonotic Parasitoses](#) ([/journal/pathogens/special_issues/Zoonotic_Parasitoses](#))

Special Issue in [Pathogens: Advances in Parasitic Diseases](#) ([/journal/pathogens/special_issues/Advances_ParasiticDiseases](#))

Special Issue in [Parasitologia: Global Change and Parasites](#) ([/journal/parasitologia/special_issues/Z5MSAN3K9P](#))

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Interests: tropical diseases; parasitic diseases; infectious disease epidemiology; PCR; molecular biology; antibodies; ELISA; genetics; DNA; infection

Special Issues, Collections and Topics in MDPI journals

Special Issue in [Microorganisms: Molecular Epidemiology and Diagnosis of Parasitic Zoonosis](#)

([/journal/microorganisms/special_issues/parasitic_zoonosis](#))

Special Issue in [Animals: Parasitic Diseases in Canine and Feline and Their Vectors](#)

([/journal/animals/special_issues/Parasitic_Canine_Feline](#))



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2. Member of the Research Group 920411—Epidemiology and Control of Communicable Diseases in Veterinary, Universidad Complutense de Madrid, Madrid, Spain

Interests: spatial analysis; geographic information system (GIS); medical entomology; sand flies

Special Issues, Collections and Topics in MDPI journals

Special Issue in [Tropical Medicine and Infectious Disease: Arthropods of Medical and Veterinary Importance: Scientific and Social Approaches](#) ([/journal/tropicalmed/special_issues/Scientific_and_Social_Approaches](#))



Prof. Dr. Sandra Gemma

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Interests: medicinal chemistry; small molecules; drug discovery; structure-activity relationships; anti-infective agents; parasitic diseases; chemotherapeutics; synthesis of biologically active compounds

Special Issues, Collections and Topics in MDPI journals

Special Issue in [Molecules: Structure-Based Design of Biologically Active Compounds](#)

([/journal/molecules/special_issues/structure_based_design](#))

Special Issue in [Molecules: Recent Contributions of Female Scientists to the Advancement of Medicinal Chemistry](#)

([/journal/molecules/special_issues/Med_Chem_Fem](#))

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Special Issue in ***Molecules: Cancer and Tuberculosis Drug Discovery: A Theme Issue in Honor of Prof. William A. Denny***
([/journal/molecules/special_issues/William_Denny](https://journal/molecules/special_issues/William_Denny)).

Special Issue in ***Tropical Medicine and Infectious Disease: Women's Special Issue Series: Tropical Medicine and Infectious Disease***
([/journal/tropicalmed/special_issues/women_series](https://journal/tropicalmed/special_issues/women_series))

Special Issue in ***Tropical Medicine and Infectious Disease: SARS-CoV-2 Omicron Variant: Current Perspectives and New Developments***
([/journal/tropicalmed/special_issues/3RZUM238VG](https://journal/tropicalmed/special_issues/3RZUM238VG)).



Prof. Dr. Musie Ghebremichael

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Harvard Medical School & Ragon Institute of Massachusetts Institute of Technology, Massachusetts General Hospital and Harvard, Cambridge, MA, USA

Interests: biostatistics; immunology; infectious diseases; tuberculosis; malaria; HIV; herpes; statistical modeling



Prof. Dr. Nick Golding

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1. Telethon Kids Institute, Perth Children's Hospital, 15 Hospital Ave, Nedlands, WA 6009, Australia

2. Faculty of Health Sciences, Curtin University, Kent St, Bentley, WA 6102, Australia

Interests: infectious disease models; vector ecology; malaria models; COVID-19 models; Bayesian statistics; research software



Prof. Dr. Patricia Graves

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College of Public Health, Medical and Veterinary Sciences, Division of Tropical Health and Medicine, James Cook University, Cairns, QLD 4870, Australia

Interests: neglected tropical diseases; lymphatic filariasis; mosquito control; malaria elimination; Pacific islands; Papua New Guinea; Myanmar; surveillance

Special Issues, Collections and Topics in MDPI journals

Special Issue in ***Tropical Medicine and Infectious Disease: Neglected and Emerging Tropical Diseases in South and Southeast Asia and Northern Australia*** ([/journal/tropicalmed/special_issues/neglected_emerging_tropical_diseases](https://journal/tropicalmed/special_issues/neglected_emerging_tropical_diseases)).

Prof. Dr. Darren Gray

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Department of Global Health, Research School of Population Health, ANU College of Health and Medicine, 62 Mills Rd, The Australian National University, Canberra, Australia

Interests: global health; tropical health; international health; infectious disease epidemiology; Schistosomiasis; soil-transmitted helminths; clinical trials; medical parasitology

Special Issues, Collections and Topics in MDPI journals

Special Issue in ***Tropical Medicine and Infectious Disease: Prospects for Schistosomiasis Elimination***
([/journal/tropicalmed/special_issues/schistosomiasis](https://journal/tropicalmed/special_issues/schistosomiasis)).

Special Issue in ***Tropical Medicine and Infectious Disease: Trematode Infections: The Asian Perspective***
([/journal/tropicalmed/special_issues/trematode_infections](https://journal/tropicalmed/special_issues/trematode_infections)).



Prof. Dr. Wayne Grayson

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1. Ampath Laboratories, Cedar Histopathology Laboratory, Fourways, Sandton, South Africa

2. School of Pathology, University of the Witwatersrand, Johannesburg, South Africa

Interests: infectious diseases of the skin; HIV/AIDS-related cutaneous pathology; skin cancer; Kaposi sarcoma

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USDA-ARS National Animal Disease Center, Ames, IA, USA

Interests: disease ecology; eco-epidemiology; environmental health; leptospirosis; melioidosis; neglected tropical diseases; phylogenetics and evolution; zoonoses; One Health; antimicrobial resistance

Special Issues, Collections and Topics in MDPI journals

Special Issue in *Tropical Medicine and Infectious Disease: Leptospirosis in Humans, Animals and the Environment—A “One Health” Perspective* (/journal/tropicalmed/special_issues/leptospirosis_one_health)



Dr. Diana Hansen

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Infectious Disease and Immune Defence Division, The Walter and Eliza Hall Institute, 1G Royal Parade, Parkville, VIC 3052, Australia

Interests: malaria; dengue; immunity; pathogenesis; immune response to infection; biomarkers; antibodies; B cells; global health



Dr. Chun Hao

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2. Sun Yat-sen Global Health Institute, Institute of State Governance, Sun Yat-sen University, Guangzhou 510080, China

Interests: HIV/AIDS; infectious diseases; social network; global health; implementation science



Prof. Dr. Anthony D. Harries

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2. Honorary Professor, Faculty of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HU, UK

Interests: tuberculosis; HIV/AIDS; tropical medicine; operational research



Prof. Dr. Shimon Harrus

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Interests: vector-borne pathogens; Bartonella; Ehrlichia



Prof. Dr. Roderick J. Hay

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St Johns Institute of Dermatology, King's College London, London, UK

Interests: infections of the skin; tropical dermatology; medical mycology

Special Issues, Collections and Topics in MDPI journals

Special Issue in *Tropical Medicine and Infectious Disease: Skin-Related Neglected Tropical Diseases (Skin-NTDs)—A New Challenge* (/journal/tropicalmed/special_issues/Skin_NTDs)

Special Issue in *Tropical Medicine and Infectious Disease: Community Engagement and Neglected Tropical Diseases (NTDs)* (/journal/tropicalmed/special_issues/Community_NTDs)

Special Issue in *Journal of Fungi: Biology, Immunology, Epidemiology, and Therapy of Fungal Infections: A Themed Issue Dedicated to Professor David A. Stevens* (/journal/fungi/special_issues/honor_fungal_infections)



Prof. Dr. Jorg Heukelbach

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Department of Community Health, School of Medicine, Federal University of Cear, Fortaleza 60430-140, CE, Brazil

Interests: public health; tropical neglected diseases; epidemiology



Special Issues, Collections and Topics in MDPI journals

Special Issue in ***Tropical Medicine and Infectious Disease: Control of Communicable Diseases in Human and in Animal Populations: 70th Anniversary Year of the Birth of Professor Rick Speare (2 August 1947 – 5 June 2016)***

(/journal/tropicalmed/special_issues/rick_speare)

Special Issue in ***Tropical Medicine and Infectious Disease: Chagas Disease*** (/journal/tropicalmed/special_issues/chagas_disease)



Prof. Dr. Paul Horrocks

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Interests: malaria; Plasmodium falciparum; cell biology; drug action; pharmacodynamics; leishmaniasis; assay development; natural products; medical education; postgraduate research



Dr. Paul Horwood

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Interests: emerging infectious diseases; zoonoses; molecular epidemiology; diagnostics

Special Issues, Collections and Topics in MDPI journals

Special Issue in ***Pathogens: One Health and Transboundary Diseases***

(/journal/pathogens/special_issues/One_Health_Transboundary_Diseases)



Dr. Hamidah Hussain

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Interests: TB active case finding; TB prevention; cost-effectiveness; implementation research

Special Issues, Collections and Topics in MDPI journals

Special Issue in ***Tropical Medicine and Infectious Disease: Innovation and Evidence for Achieving TB Elimination in the Asia–Pacific Region*** (/journal/tropicalmed/special_issues/TB_elimination)

Special Issue in ***Tropical Medicine and Infectious Disease: Women’s Special Issue Series: Tropical Medicine and Infectious Disease*** (/journal/tropicalmed/special_issues/women_series)



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1. Medical Director, Berlin Centre for Travel & Tropical Medicine, Berlin, Germany

2. Scientific Director, Centre for Travel Medicine, Dusseldorf, Germany

Interests: travel medicine; vaccine preventable diseases; vaccination studies; dengue; malaria drug resistance; imported infectious diseases



Prof. Dr. Shigeyuki Kano

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Interests: malaria; tropical medicine



Prof. Dr. Ayman Khattab



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Department of Bacteriology and Immunology, Faculty of Medicine, P.O. Box 21 (Haartmaninkatu 3), FIN-00014, University of Helsinki, Helsinki, Finland

Interests: malaria; vector control; vector-borne diseases; antimalarial drug discovery; innate immunity; complement; vaccines

Special Issues, Collections and Topics in MDPI journals

Special Issue in *Tropical Medicine and Infectious Disease: Spatial Epidemiology of Vector-Borne Diseases*

([/journal/tropicalmed/special_issues/vector_borne_diseases_tropicalmed](#))

Special Issue in *Life: Spatial Epidemiology of Vector-Borne Diseases* ([/journal/life/special_issues/vector_borne_diseases_life](#))



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Institute of International Animal Health, Friedrich-Loeffler-Institut, Federal Research Institute for Animal Health, 17493 Greifswald, Island - Riems, Germany

Interests: treponematoses; spirochaetes; neglected tropical diseases; transboundary diseases; One Health; Eco Health; disease reservoirs; disease ecology; host-pathogen evolution; epidemiology of infectious diseases



Prof. Dr. Lizette Koekemoer

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1. Wits Research Institute for Malaria, School of Pathology, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg 2001, South Africa

2. Centre for Emerging Zoonotic and Parasitic Diseases, National Institute for Communicable Diseases of the National Health Laboratory Service, Johannesburg 2131, South Africa

Interests: entomology; malaria vector control; vector biology and mechanisms of insecticide resistance



Prof. Dr. Anil Koul

Website (<https://www.lshtm.ac.uk/aboutus/people/koul.anil#affiliations>)

London School of Hygiene & Tropical Medicine, Keppel Street, London, UK

Interests: bacteria; drug discovery and development; drug resistance; bacteriology; microbiology; tuberculosis



Dr. Roman Kuchta

Website (<https://www.paru.cas.cz/pracovnici/profil/114/>)

Institute of Parasitology, Biology Centre, Czech Academy of Sciences, Branišovská 31, 370 05 České Budějovice, Czech Republic

Interests: parasitic flatworms; tapeworms; diphyllobothriosis; sparganosis



Prof. Dr. Nirbhay Kumar

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SciProfiles (<https://sciprofiles.com/profile/656887>)

Department of Global Health, Milken Institute, School of Public Health and Community Medicine, George Washington University, Washington, DC 20052, USA

Interests: malaria transmission; malaria drugs and diagnostics; diphtheria and co-infection; intestinal nematodes and co-infection; malaria transmission; malaria drugs and diagnostics

Special Issues, Collections and Topics in MDPI journals

Special Issue in *Vaccines: The 10th Anniversary of Vaccines—Vaccines against Emerging and Tropical Infectious Diseases*

([/journal/vaccines/special_issues/10th_VETID_vaccines](#))

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Prof. Dr. Eliningaya J. Kweka



Catholic University of Health and Allied Sciences (CUHAS), Bugando, Tanzania

Interests: malaria; parasitology; mosquitoes; tsetse; bed bugs; lice; tabanids; houseflies; filariasis



Prof. Dr. Colleen Lau

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School of Public Health, Faculty of Medicine, University of Queensland, Brisbane, QLD 4006, Australia

Interests: infectious disease epidemiology; emerging infectious diseases; neglected tropical diseases; travel medicine

Special Issues, Collections and Topics in MDPI journals

Special Issue in ***Tropical Medicine and Infectious Disease: Medical Geography of Tropical Infections: Disease Patterns in a Changing Environment*** (/journal/tropicalmed/special_issues/Medical_Geography).

Special Issue in ***Tropical Medicine and Infectious Disease: Harnessing the Power of Data and Technology to Improve Infectious Disease Control*** (/journal/tropicalmed/special_issues/Improve_Infectious_Disease_Control).



Prof. Dr. Shizhu Li

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1. National Institute of Parasitic Diseases, Chinese Center for Diseases Control and Prevention (Chinese Center for Tropical Diseases Research), Shanghai, China

2. School of Global Health, Chinese Center for Tropical Diseases Research, Shanghai Jiao Tong University School of Medicine, Shanghai, China

Interests: schistosomiasis; vector-borne diseases; transmission risk evaluation; epidemiology of parasitology; parasitic diseases control

Special Issues, Collections and Topics in MDPI journals

Special Issue in ***Tropical Medicine and Infectious Disease: Control of Schistosome Intermediate Hosts*** (/journal/tropicalmed/special_issues/6772K925EH).



Prof. Dr. Alun L. Lloyd

Website (<https://math.sciences.ncsu.edu/people/allloyd/>)

Drexel Professor of Mathematics, Department of Mathematics, North Carolina State University Raleigh, NC 27695, USA

Interests: mathematical modeling; dengue; mosquito population dynamics; genetic control strategies



Prof. Dr. Xuejun Ma

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National Health Commission (NHC) Key Laboratory of Medical Virology and Viral Diseases, National Institute for Viral Disease Control and Prevention, Chinese Center for Disease Control and Prevention, Beijing 102206, China

Interests: pathogen discovery; molecular diagnostics; detection; virus

Special Issues, Collections and Topics in MDPI journals

Special Issue in ***Tropical Medicine and Infectious Disease: SARS-CoV-2 Omicron Variant: Current Perspectives and New Developments*** (/journal/tropicalmed/special_issues/3RZUM238VG).



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Menzies School of Health Research, Darwin, Australia

Interests: infectious diseases; parasitology; malaria; molecular epidemiology; diagnostics; surveillance

Special Issues, Collections and Topics in MDPI journals

Special Issue in ***Tropical Medicine and Infectious Disease: Drug Resistance in the Malaria Parasite: Biology and Epidemiology*** ([/journal/tropicalmed/special_issues/malaria_parasite](https://journal/tropicalmed/special_issues/malaria_parasite))



Dr. Ivo C. Martins

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1. Instituto de Medicina Molecular (iMM), Faculty of Medicine, University of Lisbon, Lisbon, Portugal
2. DART Diagnostics. Tec Labs - Centro de Inovação. Campus da FCUL, Lisbon, Portugal

Interests: amyloid fibrils; dengue virus; Zika virus; biophysics; protein-ligand interactions



Prof. Dr. Santiago Mas-Coma

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Departamento de Parasitología, Facultad de Farmacia, Universidad de Valencia, Av. Vicent Andres Estelles s/n, 46100 Burjassot, Valencia, Spain

Interests: epidemiology; molecular biology; ecology; pathology; diagnosis; fascioliasis; zoonosis; trematodology; helminthology; parasitology; tropical medicine

Special Issues, Collections and Topics in MDPI journals

Special Issue in ***Tropical Medicine and Infectious Disease: Advances in Vector-Borne Diseases: Celebrating the First Impact Factor of TMID and in Memory of Sir Patrick Manson (1844-1922)*** ([/journal/tropicalmed/special_issues/if_celebrating](https://journal/tropicalmed/special_issues/if_celebrating))



Prof. Dr. Richard J. Maude

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2. Associate Professor, Centre for Tropical Medicine and Global Health, University of Oxford, Oxford OX3 7FZ, UK
3. Visiting Scientist, Harvard TH Chan School of Public Health, Harvard University, Boston, MA 02115, USA

Interests: epidemiology; malaria; dengue; infectious; environment; GIS; spatial



Prof. Dr. Mayfong Mayxay

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2. Lao-Oxford-Mahosot Hospital-Wellcome Trust Research Unit (LOMWRU), Microbiology Laboratory, Vientiane 594, Laos
3. Nuffield Department of Medicine, Centre for Tropical Medicine and Global Health, Churchill Hospital, Oxford OX3 7LG, UK

Interests: antimalarial drug resistance (AMR); causes of fever; sepsis; dengue; rickettsial infections; melioidosis; leptospirosis; Japanese encephalitis virus infection and infantile beriberi



Prof. Dr. John McBride

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Cairns Clinical School, College of Medicine and Dentistry, James Cook University, Cairns City, QLD 4870, Australia

Interests: dengue; Rickettsia; leptospirosis; HIV; Papua New Guinea

Special Issues, Collections and Topics in MDPI journals

Special Issue in ***Tropical Medicine and Infectious Disease: Epidemiology of Dengue: Past, Present and Future***

([/journal/tropicalmed/special_issues/dengue](https://journal/tropicalmed/special_issues/dengue))

Special Issue in ***Tropical Medicine and Infectious Disease: Epidemiology of Dengue: Past, Present and Future (Volume II)***

([/journal/tropicalmed/special_issues/epidemiology_dengue](https://journal/tropicalmed/special_issues/epidemiology_dengue))

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Dr. Janey Messina

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School of Geography and the Environment, University of Oxford, South Parks Road, Oxford OX1 3QY, UK

Interests: health geography; spatial epidemiology of infectious diseases; the application of Geographical Information Systems (GIS) and quantitative analysis to public health and social science research questions; population-environment interactions, particularly in developing countries

Special Issues, Collections and Topics in MDPI journals

Special Issue in ***Tropical Medicine and Infectious Disease: Spatial Epidemiology of Neglected Tropical Diseases (NTDs)***
([/journal/tropicalmed/special_issues/spatial_epidemiology](http://journal.tropicalmed/special_issues/spatial_epidemiology)).



Prof. Dr. Edwin Michael

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Department of Biological Sciences, University of Notre Dame, Notre Dame, IN 46556, USA

Interests: epidemiology; population biology; neglected tropical diseases; vector ecology; mathematical modelling; computational science; complex adaptive systems; social epidemiology; integrated disease management

Special Issues, Collections and Topics in MDPI journals

Special Issue in ***Tropical Medicine and Infectious Disease: Population Ecology, Epidemiology, and Control of Neglected Tropical Diseases*** ([/journal/tropicalmed/special_issues/neglected_tropical_diseases](http://journal.tropicalmed/special_issues/neglected_tropical_diseases)).

Special Issue in ***Tropical Medicine and Infectious Disease: Elimination of Lymphatic Filariasis: Endgame Prospects, Challenges and Complexities*** ([/journal/tropicalmed/special_issues/lymphatic_filariasis](http://journal.tropicalmed/special_issues/lymphatic_filariasis)).



Dr. Goudarz Molaei

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1. Center for Vector Biology & Zoonotic Diseases, Northeast Regional Center for Excellence in Vector-borne Diseases, The Connecticut Agricultural Experiment Station, New Haven, CT 06504, USA

2. Department of Epidemiology of Microbial Diseases, School of Public Health, Yale University, New Haven, 06511 CT, USA

Interests: medical entomology; vector biology; zoonotic diseases; ecoepidemiology of vector-borne diseases; mosquito vectors of human disease-causing pathogens; tick vectors of human disease-causing pathogens; vector-host-pathogen interactions; vector population genetics; molecular medical entomology and physiology; vector-borne tropical diseases



Dr. Serge Morand

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1. Faculty of Veterinary Technology, Kasetsart University, Bangkok, Thailand

2. Centre National de la Recherche Scientifique, Centre de Coopération, Internationale en Recherche Agronomique pour le Développement, Montpellier University, Paris, France

Interests: rodents and other wildlife-borne diseases

Special Issues, Collections and Topics in MDPI journals

Special Issue in ***Tropical Medicine and Infectious Disease: Selected Papers from The 2nd Asia Pacific Rickettsia Conference***
([/journal/tropicalmed/special_issues/APRC2](http://journal.tropicalmed/special_issues/APRC2)).

Special Issue in ***Viruses: Viral Zoonoses: Interactions and Factors Driving Virus Transmission***
([/journal/viruses/special_issues/Viral_Zoonoses_Interactions_Factors_Driving_Virus_Transmission](http://journal/viruses/special_issues/Viral_Zoonoses_Interactions_Factors_Driving_Virus_Transmission)).

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Center for Immunology and Microbial Diseases, Albany Medical College, Albany, NY 12208, USA

Interests: vaccine development; vaccinology; immunology of infectious diseases; intestinal infectious and pathophysiology; cholera; hepatitis; malaria

Special Issues, Collections and Topics in MDPI journals

Special Issue in *Tropical Medicine and Infectious Disease: Cholera Control in 2021: Bioecology, Immunology, Current and Future Vaccines and Treatment Options* (/journal/tropicalmed/special_issues/cholera_tropicalmed)

Special Issue in *Life: Cholera Control in 2021: Bioecology, Immunology, Current and Future Vaccines and Treatment Options* (/journal/life/special_issues/cholera_life)



Dr. Susana Vaz Nery

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Public Health Interventions Research Group, Kirby Institute Level 6, University of New South Wales, Wallace Wurth Building, Sydney, Australia

Interests: neglected tropical diseases; malaria and NTDs control and elimination in developing countries; intervention studies to inform health policy changes for more effective and sustainable disease control strategies; WASH and chemotherapy for NTD control; soil-transmitted helminths

Special Issues, Collections and Topics in MDPI journals

Special Issue in *International Journal of Environmental Research and Public Health: Water, Sanitation and Hygiene Related Disease* (/journal/ijerph/special_issues/WSH)



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1. Swiss Tropical and Public Health Institute, Basel, Switzerland

2. Faculty of Medicine, University of Basel, Basel, Switzerland

3. Division of Tropical Health and Medicine, James Cook University, Townsville, QLD, Australia

Interests: clinical tropical medicine; clinical parasitology; neglected tropical diseases; emerging infectious diseases; travel medicine



Prof. Dr. Paul Newton

Website (<https://www.ndm.ox.ac.uk/principal-investigators/researcher/paul-newton>)

Professor of Tropical Medicine & Hon. Consultant Physician, Centre for Tropical Medicine & Global Health & MORU Tropical Health Network, University of Oxford, Oxford, UK

Interests: infectious disease; typhus; Asia; Laos; neglected tropical disease; central nervous system infections; health policy; medicine quality; falsified medicines; substandard medicines



Dr. Morten Agertou Nielsen

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Department of Immunology & Microbiology, University of Copenhagen, Blegdamsvej 3B, DK 2200 Copenhagen N, Denmark

Interests: malaria immunology with focus on antibodies; translational research; vaccine development; cancer immunology; parasite cell biology



Prof. Dr. Eric James Nilles

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1. Harvard Humanitarian Initiative, Cambridge, MA 02138, USA

2. Harvard Medical School, Boston, MA 02115, USA

3. Brigham and Women's Hospital, Boston, MA 02115, USA

Interests: emerging infectious diseases; tropical infectious diseases; epidemiology; seroepidemiology; epidemics; disease outbreaks; surveillance



Prof. Dr. Daniel H. Paris

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1. Swiss Tropical and Public Health Institute, P.O. Box, CH-4002 Basel, Switzerland

2. University of Basel, P.O. Box, CH-4003 Basel, Switzerland

Interests: rickettsia; scrub typhus; murine typhus; diagnostics; pathophysiology; vaccine; host response and immune response

Special Issues, Collections and Topics in MDPI journals

Special Issue in *Tropical Medicine and Infectious Disease: The Past and Present Threat of Rickettsial Diseases (Volume II)*

(/journal/tropicalmed/special_issues/rickettsial_diseases_ii)



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Institute of Tropical Medicine, Antwerp, Belgium

Interests: medical anthropology; ecohealth; planetary health; malaria; tropical infectious diseases; science and technology studies; vector control; transdisciplinary research; interdisciplinarity; social sciences



Dr. Watcharapong Piyaphanee

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Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

Interests: tropical medicine; travel medicine; malaria



Prof. Dr. Michael Ramharter

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Department of Tropical Medicine, Bernhard Nocht Institute for Tropical Medicine & I Department of Medicine, University Medical Center Hamburg-Eppendorf, Bernhard Nocht Str. 74, 20359 Hamburg, Germany

Interests: clinical research (drug and vaccine development) in the field of tropical diseases; malaria; Lassa fever; loiasis; echinococcosis



Prof. Dr. Andrew Ramsay

Website ([https://risweb.st-andrews.ac.uk/portal/en/persons/andrew-ramsay\(d3bc883e-e1b5-4609-bdc8-3ad2d6d21644\).html](https://risweb.st-andrews.ac.uk/portal/en/persons/andrew-ramsay(d3bc883e-e1b5-4609-bdc8-3ad2d6d21644).html))

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1. Division of Infection and Global Health, St Andrews University Medical School, St Andrews KY16 9TF, UK

2. National Institute of Parasitic Diseases, Chinese Center for Disease Control and Prevention, Shanghai 200025, China

Interests: tuberculosis; infectious disease diagnostics; parasitic diseases; infectious disease outbreak response; leprosy

Special Issues, Collections and Topics in MDPI journals

Special Issue in *Tropical Medicine and Infectious Disease: Leprosy Elimination: Strategies, Partnerships, Progress, Challenges and Research* (/journal/tropicalmed/special_issues/LESPPCR)

Special Issue in *Tropical Medicine and Infectious Disease: Elimination of Lymphatic Filariasis: Strategies, Partnerships, Progress, Challenges and Research* (/journal/tropicalmed/special_issues/Elimination_LF)

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Website (<https://www.sydney.edu.au/medicine-health/about/our-people/academic-staff/harunor-rashid.html>)

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1. National Centre for Immunisation Research and Surveillance (NCIRS) Kids Research, The Children's Hospital at Westmead, Westmead, NSW 2145, Australia

2. Discipline of Child and Adolescent Health, The University of Sydney, Camperdown, NSW 2006, Australia

Interests: travel vaccine; vaccine-preventable infectious diseases; vaccination evaluation; vaccine prioritisation

Special Issues, Collections and Topics in MDPI journals

Special Issue in ***Tropical Medicine and Infectious Disease: Travel and Tropical Medicine***

(/journal/tropicalmed/special_issues/travel_tropical_medicine)

Special Issue in ***Vaccines: Infectious Diseases: The Role of Vaccines and Complementary Measures***

(/journal/vaccines/special_issues/Infectious_complementary)

Special Issue in ***Tropical Medicine and Infectious Disease: Travel Health*** (/journal/tropicalmed/special_issues/travel_health)



Prof. Dr. Serge Resnikoff

Website (https://www.researchgate.net/profile/Serge_Resnikoff)

Brien Holden Vision Institute, Sydney, Australia

Interests: epidemiology; eye diseases; neglected tropical diseases – especially trachoma, health systems



Prof. Dr. Allen L. Richards

Website (<https://researchchain.net/profile/Allen-L-Richards-523081>) **SciProfiles** (<https://sciprofiles.com/profile/353750>)

Department of Preventive Medicine and Biostatistics, Uniformed Services University of the Health Sciences, Bethesda, MD, USA

Interests: Rickettsial diseases; scrub typhus; vector-borne diseases; zoonoses

Special Issues, Collections and Topics in MDPI journals

Special Issue in ***Pathogens: Latest Updates on Scrub Typhus (Orientia spp.)*** (/journal/pathogens/special_issues/4L4WP7V45M)



Dr. Koert Ritmeijer

Website (<https://www.iddo.org/vl/vl-scientific-advisory-committee/dr-koert-ritmeijer>)

Public Health Department, Médecins Sans Frontières, 1018 DD Amsterdam, The Netherlands

Interests: leishmaniasis; human African trypanosomiasis; snakebites; noma

Special Issues, Collections and Topics in MDPI journals

Topics: ***Novel Therapeutic Strategies against Leishmania and Trypanosoma*** (/topics/Leishmania)



Dr. Mark Robinson

Website (<https://www.qub.ac.uk/schools/SchoolofBiologicalSciences/Connect/AcademicStaff/DrMarkRobinson/>)

Institute for Global Food Security, School of Biological Sciences, Queens University Belfast, Belfast BT9 5DL, UK

Interests: molecular biology of trematode parasites and their host interactions

Special Issues, Collections and Topics in MDPI journals

Special Issue in ***Pathogens: Proteomics of Host-Helminth Interactions*** (/journal/pathogens/special_issues/Proteomics_Helminth)



Prof. Dr. Allen G. P. Ross

Website (https://www.icddr.org/index.php?option=com_content&view=article&id=4223&Itemid=2202&staffID=235)

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1. International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR, B), Dhaka 1212, Bangladesh

2. Menzies Health Institute Queensland, Griffith University, Gold Coast 4222, Australia

Interests: global health; tropical infectious diseases; enteric diseases; urban slum health; disease control; pandemic planning; vaccination

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Prof. Dr. Mary Ross

[SciProfiles \(https://sciprofiles.com/profile/355160\)](https://sciprofiles.com/profile/355160)

School of Public Health, University of the Witwatersrand, Johannesburg, South Africa

Interests: occupational medicine; tropical medicine; public health medicine; travel medicine



Dr. Brice Rotureau

[Website \(https://research.pasteur.fr/en/team/group-brice-rotureau/\)](https://research.pasteur.fr/en/team/group-brice-rotureau/) [SciProfiles \(https://sciprofiles.com/profile/2155608\)](https://sciprofiles.com/profile/2155608)

Trypanosome Transmission Group, Trypanosome Cell Biology Unit, INSERM U1201 & Department of Parasites and Insect Vectors, Institut Pasteur, 25, rue du Docteur Roux, 75015 Paris, France

Interests: parasitology; medical entomology; epidemiology; trypanosomatids; leishmaniases; trypanosomiasis

Special Issues, Collections and Topics in MDPI journals

Special Issue in [Tropical Medicine and Infectious Disease: Advances in Vector-Borne Diseases: Celebrating the First Impact Factor of TMID and in Memory of Sir Patrick Manson \(1844-1922\)](https://www.mdpi.com/journal/tropicalmed/special_issues/if_celebrating) ([/journal/tropicalmed/special_issues/if_celebrating](https://www.mdpi.com/journal/tropicalmed/special_issues/if_celebrating)).



Dr. Charles E. Rupprecht

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1. Adjunct Professor, The Wistar Institute, Philadelphia, PA, USA

2. CEO, LYSSA LLC, Lawrenceville, GA 30044, USA

Interests: lyssaviruses; zoonoses; One Health; epidemiology; conservation biology

Special Issues, Collections and Topics in MDPI journals

Special Issue in [Tropical Medicine and Infectious Disease: Rabies Symptoms, Diagnosis, Prophylaxis and Treatment](https://www.mdpi.com/journal/tropicalmed/special_issues/rabies) ([/journal/tropicalmed/special_issues/rabies](https://www.mdpi.com/journal/tropicalmed/special_issues/rabies)).

Special Issue in [Tropical Medicine and Infectious Disease: Lyssaviruses and Rabies: Prevention, Control and Elimination](https://www.mdpi.com/journal/tropicalmed/special_issues/lyssaviruses) ([/journal/tropicalmed/special_issues/lyssaviruses](https://www.mdpi.com/journal/tropicalmed/special_issues/lyssaviruses)).

Special Issue in [Viruses: Innovative Techniques and Approaches in the Control and Prevention of Rabies Virus](https://www.mdpi.com/journal/viruses/special_issues/Rabies-Virus-Control) ([/journal/viruses/special_issues/Rabies-Virus-Control](https://www.mdpi.com/journal/viruses/special_issues/Rabies-Virus-Control)).



Prof. Dr. Ana Sanchez

[Website \(https://brocku.ca/applied-health-sciences/health-sciences/faculty-research/faculty-directory/ana-sanchez-phd/\)](https://brocku.ca/applied-health-sciences/health-sciences/faculty-research/faculty-directory/ana-sanchez-phd/)

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1. Department of Health Sciences, Brock University, St. Catharines, ON L2V 5A2, Canada

2. Department of Parasitology, School of Microbiology and Institute of Microbiology Research, National Autonomous University of Honduras, Tegucigalpa, Honduras

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Article

Diagnostic Value of Neutrophil-to-Lymphocyte Ratio, Lymphocyte-to-Monocyte Ratio, and Platelet-to-Lymphocyte Ratio in the Diagnosis of Erythema Nodosum Leprosum: A Retrospective Study

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Citation: Tanojo, N.; Damayanti, Utomo, B.; Ervianti, E.; Murtiastutik, D.; Prakoeswa, C.R.S.; Listiawan, M.Y. Diagnostic Value of Neutrophil-to-Lymphocyte Ratio, Lymphocyte-to-Monocyte Ratio, and Platelet-to-Lymphocyte Ratio in the Diagnosis of Erythema Nodosum Leprosum: A Retrospective Study. *Trop. Med. Infect. Dis.* **2022**, *7*, 39. <https://doi.org/10.3390/tropicalmed7030039>

Academic Editors: Roderick J. Hay, Ahmed Hassan Fahal and John Frean

Received: 19 January 2022
Accepted: 25 February 2022
Published: 2 March 2022

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Abstract: Erythema nodosum leprosum (ENL) is an acute immune complex-mediated condition of the dermis, subcutaneous tissue, and other tissues seen in patients with multibacillary (MB) leprosy, causing severe impairment to patients' quality of life. To date, there is no standard diagnostic criteria for ENL. We aimed to study the diagnostic value and accuracy of Neutrophil-to-Lymphocyte ratio (NLR), Lymphocyte-to-Monocyte ratio (LMR), and Platelet-to-Lymphocyte ratio (PLR) in diagnosing ENL. This is an analytic retrospective study with a cross-sectional design that describes the distribution and clinical characteristics of all newly diagnosed MB patients of Dr. Soetomo General Hospital Surabaya in the years 2018–2020. NLR, LMR, and PLR were calculated for all patients, and a receiver operating characteristic curve (ROC) was generated to identify the cut-off points. Among a total of 182 patients with MB leprosy, 22 cases (12.09%) were reported with ENL. WBC, neutrophils, monocytes, and thrombocytes showed a positive correlation with the incidence of ENL, but not lymphocytes. The NLR cut-off point for the diagnosis of ENL was 4.99 (sensitivity 86.4%, specificity 82.5%, accuracy 82.97), while that of PLR was 237.46 (sensitivity 63.6%, specificity 73.1%, accuracy 71.98%). LMR had poor sensitivity and specificity levels of 50% and 28.7%, with cut-off point of 2.28 and accuracy of 31.32%. These results suggest that NLR and PLR could be potential biomarkers for the diagnosis of ENL.

Keywords: neutrophil-to-lymphocyte ratio; lymphocyte-to-monocyte ratio; platelet-to-lymphocyte ratio; erythema nodosum leprosum; leprosy; tropical disease; infectious disease; neglected disease

1. Introduction

Leprosy is one of 20 neglected tropical diseases caused by *Mycobacterium leprae*, with more than 200,000 new cases reported every year from more than 120 countries [1,2]. The clinical manifestations of leprosy vary depending on the host immune response. In 1981, the WHO introduced a simple disease classification based on the number of skin lesions and the finding of acid-fast bacilli (AFB) to aid the prescription of multidrug regimens. Paucibacillary (PB) leprosy is associated with five or less skin lesions and negative AFB findings, while multibacillary (MB) patients present with more than five skin lesions and positive AFB findings [2]. The majority of leprosy cases in Indonesia, which has the third highest number of global leprosy cases, are MB leprosy (84%) [3,4].

Erythema nodosum leprosum (ENL) is an acute inflammatory complication of leprosy that exclusively occurs in MB leprosy [5,6]. It presents as a sudden onset of generalized

painful erythematous nodules with or without symptoms of systemic inflammation that may occur before, during, or after multi-drug therapy (MDT) [6–8]. The clinical criteria proposed by B. Naafs et al. for leprosy diagnosis are considered sufficient in daily clinical practice, although histopathological findings such as findings such as increased vascularity with dilated capillaries in the dermis with neutrophil infiltration may aid in disease confirmation [9]. ENL has frequent recurrence, with the possibility to persist for years [10]. Leprosy patients with ENL are prone to nerve damage and potential physical disabilities which severely impact their quality of life, the social and economic burden, and patients' mortality [7,8,10,11]. The diagnosis of ENL often relies on the medical expertise of doctors and their ability to recognize the disease's clinical manifestations [10]. The histopathology of ENL resembles that of MB leprosy without ENL, except for the possible presence of neutrophil infiltration, microabscesses, or vasculitis [9]. The increase of acute-phase proteins, such as C-reactive protein, gamma globulin, α 1-antitrypsin, and α 1-acid glycoprotein, may help the diagnosis, although related tests are often expensive and not available [10].

ENL is described as a neutrophilic immune-complex-mediated condition with a complex interaction of multiple immune system elements, including monocytes, lymphocytes, and platelets [5,12]. Neutrophil infiltration is the histological hallmark of ENL [12]. A recent study indicated that the number of peripheral neutrophils, especially of low-density neutrophils (LDNs), is increased especially in severe ENL [6]. Monocytes are rarely studied in ENL, although the expression of tumor necrosis factor (TNF)- α is higher in patients with MB leprosy with ENL than in those without ENL [12]. Platelet or thrombocyte helps to trap pathogens during cellular immunity by forming microthrombi [9]. The involvement of lymphocytes in ENL is often limited to increased T-helper lymphocytes and decreased T-cytotoxic lymphocytes, with an increase of the T-helper-to-T-cytotoxic lymphocyte ratio in comparison to the control group. B-lymphocytes are not associated with the formation of ENL [12].

Recently, the Neutrophil-to-Lymphocyte ratio (NLR), Lymphocyte-to-Monocyte ratio (LMR), and Platelet-to-Lymphocyte ratio (PLR) have been used in different conditions to reflect the host inflammatory response, hence enabling medical providers to confirm disease diagnosis, predict the prognosis, and monitor treatment outcome. A study by Gomes et al. [10] indicated that NLR was 78% accurate in diagnosing leprosy reactions.

This study aimed to study the diagnostic value of NLR, LMR, and PLR as biomarkers in diagnosing ENL in endemic leprosy.

2. Materials and Methods

This was a cross-sectional retrospective study of data obtained from medical records of patients who presented, between January 2018 and December 2020, at the Leprosy Division of dr. Soetomo General Academic Hospital, Surabaya, Indonesia. Eligible patients were males and females aged 18 years and above, with a confirmed diagnosis of MB leprosy from skin lesions and AFB analysis, who were subjected to a complete blood test on the same day of diagnosis. Patients with HIV, secondary syphilis, hypertension, and diabetes mellitus were excluded. Patients with a history of steroid and other immunomodulators use in the last two weeks were excluded, due to the possibility of host immunity alteration. Ethical clearance was obtained from the Ethical Committee of Dr. Soetomo General Academic Hospital, Surabaya, with reference number 0459/LOE/301.4.2/V/2021.

Physicians experienced in the diagnosis and treatment of leprosy determined the diagnosis of leprosy based on WHO criteria, which include the finding of hypopigmented or erythematous skin lesion(s) with impairment or loss of sensation, peripheral nerves thickening or sensory impairment, or positive acid-fast bacilli smear. Patients were further classified into MB leprosy when presented with six or more lesions with or without positive bacterial index. Patients who did not fulfil the criteria were classified as PB leprosy and excluded from this study. ENL was clinically determined by the findings of a sudden eruption of tender papules, nodules, or plaques and three of the following symptoms: mild fever, tender enlarged nerves, arthritis, lymphadenitis, increased loss of sensation or muscle

power, epididymo-orchitis, edema of the extremities or face, positive Ryrie or Ellis test, and iridocyclitis or episcleritis. The same physicians obtained demographic data including comorbidities, gender, age, and the onset of ENL through anamnesis and performed tests necessary to determine physical disabilities, which were graded using the WHO 2-point scale. Bodyweight and height were measured for body mass index (BMI) calculation to determine the nutritional status based on the cutoff for Asian and Asian Americans. The bacterial and morphological indexes were determined from skin smears obtained from three different sites. The number of white blood cells and differentials, including neutrophils, monocytes, and lymphocytes, as well as thrombocyte counts, were recorded and used to calculate NLR, LMR, and PLR by dividing the absolute count of neutrophils by that of lymphocytes, the absolute count of lymphocytes by that of monocytes, and the absolute count of thrombocytes by that of lymphocytes, respectively.

A descriptive analysis was performed for all study variables and reported as median (minimum–maximum) for non-parametric data and mean (\pm standard deviation) for parametric data. Two-times-two Pearson's chi-square analyses were done on gender, BI, and MI data, while the non-parametric Kruskal–Wallis test was used to determine the relationship between other variables and ENL. The correlation between blood counts and incidence of ENL was analyzed by using Spearman's rho correlation test. A receiver operator characteristic (ROC) curve was constructed to evaluate the sensitivity and specificity of NLR, LMR, and PLR.

3. Results

A total of 280 new patients visited the Leprosy Division in January 2018–December 2020, including 6 subclinical leprosy, 6 neural leprosy, 13 PB leprosy, and 255 MB leprosy cases. Approximately 98 subjects were excluded from the study due to age, diagnosis of non-MB, or absence of laboratory results. Out of the 182 cases included in this study, only 22 cases (12.09%) were diagnosed with ENL. The 22 ENL patients were free from any comorbidity, while the non-ENL patients were reported to have HIV (1.65%), diabetes mellitus (1.09%), Cushing syndrome (0.55%), and secondary syphilis (0.55%).

Table 1 showed that most ENL patients were men (72.72%) aged 18–40 years (68.18%) who had never received multi-drug therapy (45.45%) or with a history of complete MDT treatment (31.82%). Grade 2 disability (G2D) was found in 9.09% of newly diagnosed ENL patients. Nutritional status was determined through BMI measurement and indicated that most ENL cases had normal BMI (59.09%). Most ENL cases had a BI of less than 3 (77.27%) and an MI of less than 5 (90.9%). The onset of ENL treatment was the only variable that was significantly different between the ENL and the non-ENL groups ($p = 0.001$).

Table 2 indicates that the median WBC of ENL subjects (14,820 (4,160–30,330); $p = 0.001$) was almost twice higher than that of subjects without ENL (7,405 (4,380–21,980)). Neutrophil count in the ENL group (12,355 (3,520–26,840); $p = 0.001$) was almost three times higher than that in the non-ENL group (4,840 (2,010–19,540)). Monocyte count was just slightly higher in ENL cases (775 (210–1,910); $p = 0.051$), while lymphocyte count was lower (1,526.82 (\pm 655.57), $p = 0.159$), but none of these two values showed a statistically significant differences between the two groups. The medians of NLR, LMR, and PLR in ENL cases were 8.19 (2.9–21.46), 2.28 (0.75–4.94), and 283.97 (126.48–1,267.65), respectively. NLR and PLR revealed a positive correlation with the incidence of ENL with coefficients of 0.45 and 0.26, respectively, while LMR showed a negative correlation, with a coefficient of -0.205 .

Table 1. Clinical characteristics of ENL in new MB leprosy patients.

Characteristics		ENL			p-Value
		n (%)	Absent	Present	
Gender	Males	131 (71.97)	115 (71.87)	16 (72.72)	0.986 ^a
	Females	51 (28.02)	45 (28.12)	6 (27.27)	
Age	18–40	104 (57.14)	89 (55.62)	15 (68.18)	0.245 ^b
	41–59	63 (34.61)	56 (35)	7 (31.81)	
	≥60	15 (8.24)	15 (9.375)	0 (0)	
Treatment Onset	New	146 (80.21)	136 (85)	10 (45.45)	0.001 ^{b,c}
	On MDT	5 (2.74)	3 (1.87)	2 (9.09)	
	RFT/RFC	9 (4.94)	2 (1.25)	7 (31.81)	
	Dropout	22 (12.08)	19 (11.87)	3 (13.63)	
Disability	0	125 (68.68)	112 (70)	13 (59.09)	0.236 ^b
	1	37 (20.32)	30 (18.75)	7 (31.81)	
	2	20 (10.98)	18 (11.25)	2 (9.09)	
Nutritional Status	Underweight	32 (17.58)	28 (17.5)	4 (18.18)	0.545 ^b
	Normal	89 (48.90)	76 (47.5)	13 (59.09)	
	Overweight	49 (26.92)	44 (27.5)	5 (22.72)	
	Obese	12 (6.59)	12 (7.5)	0 (0)	
Bacterial Index	<3	146 (80.21)	129 (80.62)	17 (77.27)	0.083 ^a
	≥3	36 (19.78)	31 (19.37)	5 (22.72)	
Morphological Index	<5	160 (87.91)	140 (87.5)	20 (90.90)	0.919 ^a
	≥5	22 (12.08)	20 (12.5)	2 (9.09)	

ENL: Erythema nodosum leprosum; ^a Pearson's chi square; ^b Kruskal–Wallis test; ^c Significant p value < 0.05.

Table 2. Blood count of new MB leprosy cases.

Blood Count	ENL		Correlation Coefficient	p-Value	
	Present	Absent			
WBC ^a	7,720 (4,160–30,330)	14,820 (4,160–30,330)	7,405 (4,380–21,980)	0.438 ^c	0.001
Neutrophil ^a	5,110 (2,010–26,840)	12,355 (3,520–26,840)	4,840 (2,010–19,540)	0.461 ^c	0.001
Lymphocyte ^b	1,711.97 (±629.04)	1,526.82 (±655.57)	1,737.43 (±623.13)	−0.105 ^d	0.159
Monocyte ^a	590 (200–1,910)	775 (210–1,910)	570 (200–1,450)	0.145 ^c	0.051
Thrombocyte ^a	308,000 (116,000–909,000)	375,000 (229,000–909,000)	302,000 (116,000–721,000)	0.263 ^c	0.001
NLR ^a	3.19 (0.86–21.46)	8.19 (2.9–21.46)	2.93 (0.86–12.85)	0.450 ^c	0.001
LMR ^a	3 (0.69–8.67)	2.28 (0.75–4.94)	3.13 (0.69–8.67)	−0.205 ^c	0.005
PLR ^a	186.59 (72.96–1,267.65)	283.97 (126.48–1,267.65)	173.41 (72.96–893.33)	0.262 ^c	0.001

ENL: erythema nodosum leprosum, WBC: white blood cells, NLR: neutrophil/lymphocyte ratio, LMR: lymphocyte/monocyte ratio, PLR: platelet/lymphocyte ratio; ^a Non-parametric distribution; median (minimum–maximum); ^b Parametric distribution; mean (±standard deviation); ^c Spearman's rho; ^d Pearson correlation test.

The AUCs of NLR, LMR, and PLR were 0.899, 0.318, and 0.732 for the diagnosis of ENL, respectively. The NLR cutoff point for the diagnosis of ENL was 4.99 (sensitivity 86.4%, specificity 82.5%, accuracy 82.97%) (Figure 1), while for LMR, it was 2.28 (sensitivity 50%, specificity 28.7%, accuracy 31.32%) (Figure 2), and for PLR, 237.46 (sensitivity 63.6%, specificity 73.1%, accuracy 71.98%) (Figure 3).

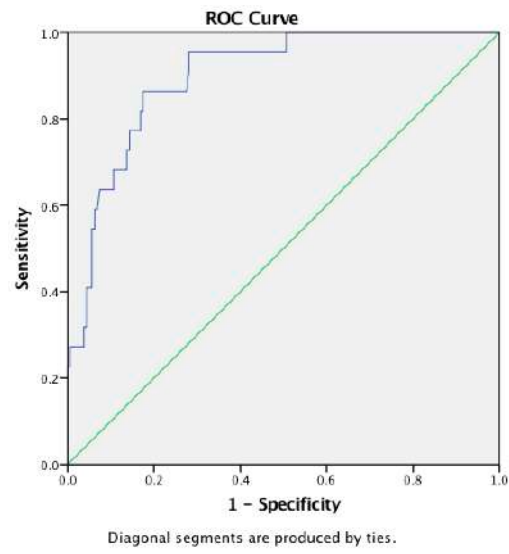


Figure 1. ROC curve of NLR.

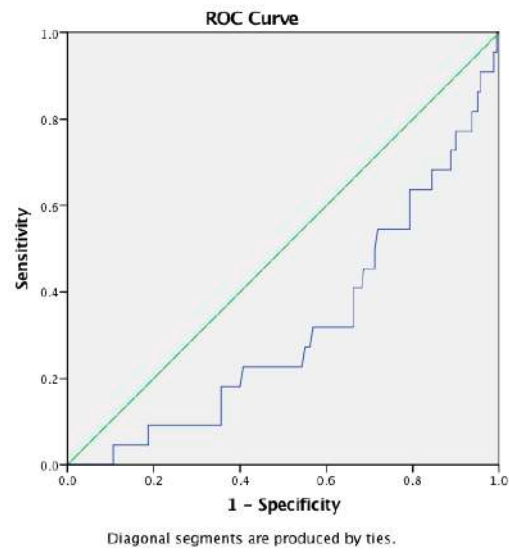


Figure 2. ROC curve of LMR.

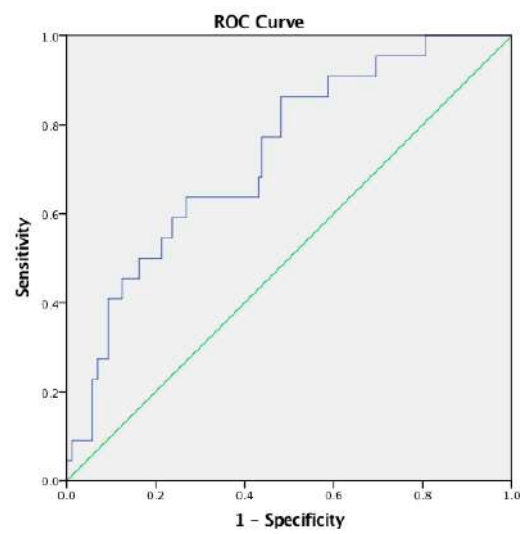


Figure 3. ROC curve of PLR.

4. Discussion

This study describes the distribution and clinical characteristics of ENL, showing a relatively low incidence corresponding to 12.09% of all new MB patients. A previous study by Fransisca C., et al. [13] in the same hospital in 2015–2017 reported a higher ENL incidence of 33% in all MB cases. This difference may be related to the fact that in this study, we eliminated a group of patients, who could have been suffering from ENL but did not perform the necessary laboratory analysis to complete the study. Comorbidities, such as HIV, secondary syphilis, hypertension, and diabetes mellitus may complicate the disease manifestations and hinder treatment [14]. None of the ENL-positive subjects in this study had comorbidities or a history of medications that might affect the results.

The demographic data showed that ENL predominantly occurred in normal BMI male aged 18–40 years with or without a history of MDT treatment. The slit-skin smear analysis indicated that the majority of ENL subjects had a BI of less than 3 (77.27%) and an MI of less than 5 (90.9%). None of these predominant characteristics displayed a significant difference with respect to the non-ENL group, except for the treatment onset. MDT is an effective treatment against *M. leprae* that has successfully suppressed the incidence of leprosy since its introduction in 1981 [15]. Ironically, MDT used for leprosy treatment, which leads to bacterial fragmentation, is hypothesized to elicit the formation of antigen–antibody complexes in ENL [12]. The cause–effect relationship between MDT treatment and ENL explains the higher incidence of ENL found in patients on MDT therapy or after being released from MDT, in comparison to newly treated patients [12,13]. The incidence of ENL during MDT can be at least twice higher than that at the time of initial diagnosis [11].

Macrophages, which are tissue monocytes, are the main resident cells activated by *M. leprae* infection [6,16]. Earlier studies indicated that ENL patients experienced a greater release of TNF- α from monocytes upon contact with *M. leprae* [12,17]. However, the number of circulating monocytes did not differ between groups with and without leprosy reactions [12,18]. Monocytes are unlikely to actively participate in the pathogenesis of ENL even though the immune complex reaction in ENL involves intricate interactions between antigens released from foamy macrophages and antibodies generated by lymphocytes [9,18].

Neutrophils, the most abundant type of WBC, provide protection through phagocytosis, the release of antimicrobial peptides, and the generation of neutrophils extracellular traps [12]. Histological studies showed an intense perivascular infiltrate of neutrophils throughout the dermis and subcutis, especially within 72 h of ENL onset [11,12]. The circulating neutrophils appeared to contain *M. leprae* bacilli, albeit in the absence of systemic inflammation [16]. Neutrophilic degranulation was observed in ENL, with a subsequent high production of low-density neutrophils [6]. The released granules acted as mediators of innate and adaptive immunity that inflicted collateral tissue damage in ENL [16].

Lymphocytes are involved in both cellular and humoral immune responses. T-lymphocytes actively eliminate bacterial, viral, and parasitic infections through an adaptive immune response. The antigen specificity of T-cells is based on the major histocompatibility complex molecules presented by antigen-presenting cells, such as skin dendritic cells, macrophages, and B-cells [12]. B-lymphocytes produce the antibodies that form immune complexes leading to the Arthus phenomenon in the pathogenesis of ENL [10]. However, the active involvement of lymphocytes in different aspects of immune reactions makes lymphocyte count unreliable in differentiating ENL from non-ENL [10].

Platelets function in the blood coagulation system and fibrinolysis and play a major role in immunothrombosis by promoting microvessel thrombosis that allows capturing pathogens thus limiting pathogen dissemination [19]. Elevated platelet count was observed in ENL patients, especially in the early phase of the disease [19,20]. One of the important mediators of thrombocytosis, interleukin-6, is also elevated during the initial phase of ENL [21].

The involvement of WBCs, including neutrophils, monocytes, and lymphocytes, as well as platelets throughout the pathogenesis of ENL may lead to an increase in cell counts during laboratory analysis. However, in this study, only WBC, neutrophils, and

platelets showed a significant difference in their number in patients during ENL episodes in comparison to MB patients without ENL formation. NLR was determined by dividing the absolute neutrophil count by the absolute lymphocyte count. The use of this ratio may help to better evaluate the immune status of the host than the use of the neutrophil or lymphocyte count alone [10]. Nevertheless, NLR is not a specific biomarker, and its value may be affected by hormonal changes, hypovolemic change, the use of oral steroids, hematological diseases, and HIV [22]. Our study described a non-parametric distribution of NLR, with a median of 8.19 (2.9–21.46) in ENL patients with no comorbidity and no history of steroid use, and a median of 2.93 (0.86–12.85) in non-ENL patients. Further analysis showed that the NLR value had a positive relationship with the incidence of ENL (ρ 0.450; $p < 0.05$). The diagnostic value of NLR was found to have a cut-off value of 4.99, with 86.4% sensitivity, 82.5% specificity, and 82.97% accuracy. A previous study by Gomes et al. [10] used a lower cut-off point of 2.95 to diagnose ENL, with a sensitivity of 81% and a specificity of 74%.

The LMR was calculated by dividing the absolute lymphocyte count by the absolute monocyte count. LMR has been used in a variety of tumor and malignancy-related conditions and has been shown up to help establish a prognosis [23]. This study found a median of 3 (0.69–8.67) for LMR, with a negative correlation with the incidence of ENL. The ROC curve of LMR indicated a cut-off point of 2.28, with only 50% sensitivity and 28.7% specificity. Despite the correlation, LMR had very poor sensitivity and specificity in the diagnosis of ENL.

The PLR was calculated by dividing the platelet count by the absolute lymphocyte count. PLR has been used as an inflammatory and prognostic marker associated with various types of cancer [24]. This study found a median PLR in ENL patients of 186.59 (72.96–1,267.65). An increase of PLR had a positive relationship with the incidence of ENL ($p < 0.05$), with a median of 283.97 (126.48–1,267.65). The ROC curve helped to find that a cut-off point of 237.46 displayed 63.6% sensitivity, 73.1% specificity, and 71.98% accuracy in diagnosing ENL.

The diagnosis of ENL often relies on the medical expertise of the examining physicians and their ability to recognize the disease clinical manifestations, while non-expert medical providers have to rely on histopathology findings and the assessment of the levels of acute phase proteins; however, these tests may not be widely available in rural areas of endemic countries, such as Indonesia [9]. This study indicates that NLR and PLR had 82.95% and 71.98% accuracy in diagnosing the occurrence of ENL in MB patients. These biomarkers can be evaluated by performing a simple differential count that is readily feasible and relatively inexpensive. The results of this paper may help medical providers especially in endemic areas of leprosy in the diagnosis of ENL.

This study has some limitations. The diagnosis of ENL in this study was made on the basis of clinical observations only, as a reference test for the diagnosis of ENL does not exist. Histopathological results may help to better confirm the diagnosis of ENL and to solidify the key findings of this study. ENL is more likely to occur during MDT, yet this research was only limited to patients' initial visits. Therefore, misdiagnosis or under-diagnosis of ENL might have occurred. This is the first study proposing NLR, LMR, and PLR as diagnostic biomarkers of ENL. The relatively high specificity and sensitivity of NLR and PLR, which are simple and low-cost tools, may support clinicians in the diagnosis of ENL. These findings may help improve disease control, thus preventing possible complications and disabilities. Additional studies are needed to confirm the results of this study.

Author Contributions: N.T., D., M.Y.L. and C.R.S.P. conceived and planned the study. N.T. wrote the manuscript with input from all authors. N.T. and B.U. performed the analytic calculations. D., E.E., D.M., C.R.S.P. and M.Y.L. revised the manuscript. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki, and approved by the Ethics Committee of Dr. Soetomo General Academic Hospital, Surabaya (no. 0459/LOE/301.4.2/V/2021, date of approval: 5 May 2021).

Informed Consent Statement: Not applicable.

Acknowledgments: We thank the anonymous reviewers for many useful suggestions. We also acknowledge members of the Dermatology and Venereology department in the Dr. Soetomo General Academic Hospital for providing the retrospective data.

Conflicts of Interest: We have no conflict of interest to declare. All authors have seen and approved the submitted manuscript. We warrant that the article has not received prior publication and is not under consideration for publication elsewhere. On behalf of all Co-Authors, the corresponding Author shall bear full responsibility for the submission.

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