



Veille scientifique

Maladies tropicales négligées

Semaine 14
03 au 09 avril 2023

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Dengue, chikungunya et maladie à virus Zika

Correction: Absence of Zika virus among pregnant women in Vietnam in 2008.

Chiu YC, Baud D, Fahmi A, Zumkehr B, Vouga M, Pomar L, Musso D, Thuong BC, Alves MP, Stojanov M.

06-04-2023

Trop Dis Travel Med Vaccines.

<https://pubmed.ncbi.nlm.nih.gov/37024979/>

Effects of temperature, rainfall, and El Niño Southern Oscillations on dengue-like-illness incidence in Solomon Islands.

Andhikaputra G, Lin YH, Wang YC.

06-04-2023

BMC Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/37024812/>

Background: This study investigated associations between climate variables (average temperature and cumulative rainfall), and El Niño Southern Oscillation (ENSO) and dengue-like-illness (DLI) incidence in two provinces (Western and Guadalcanal Provinces) in Solomon Islands (SI). **Methods:** Weekly DLI and meteorological data were obtained from the Ministry of Health and Medical Services SI and the Ministry of Environment, Climate Change, Disaster Management and Meteorology from 2015 to 2018, respectively. We used negative binomial generalized estimating equations to assess the effects of climate variables up to a lag of 2 months and ENSO on DLI incidence in SI. **Results:** We captured an upsurge in DLI trend between August 2016 and April 2017. We found the effects of average temperature on DLI in Guadalcanal Province at lag of one month (IRR: 2.186, 95% CI: 1.094-4.368). Rainfall had minor but consistent effect in all provinces. La Niña associated with increased DLI risks in Guadalcanal Province (IRR: 4.537, 95% CI: 2.042-10.083), whereas El Niño associated with risk reduction ranging from 72.8% to 76.7% in both provinces. **Conclusions:** Owing to the effects of climate variability and ENSO on DLI, defining suitable and sustainable measures to control dengue transmission and enhancing community resilience against climate change in low- and middle-developed countries are important.

Elevated Interleukin-37 Associated with Dengue Viral Load in Patients with Dengue Fever.

Zhang JA, Wang JJ, Zhang WT, Zhang L, Zheng BY, Liu GB, Liang J, Lu YB, Wu XJ, Yao SY, Chen GY, Xie YQ, Wu JY, Shi JH, Pi J, Li SP, Xu JF.

06-04-2023

Curr Microbiol.

<https://pubmed.ncbi.nlm.nih.gov/37024713/>

Dengue remains a public health issue worldwide. Similar to chronic infectious diseases, stimulation of cytokine production is not enough to drive immune effector cells for effective virus clearance. One possible mechanism is

the virus induces a large number of negative stimulatory cytokines inhibiting immune response. Interleukin 37 (IL-37) plays a crucial regulatory role in infection and immunity, inhibits innate and adaptive immunity as an anti-inflammatory cytokine by inhibiting proinflammatory mediators and pathways. To date, there are few studies reporting correlations between dengue fever (DF) and IL-37. In this study we found that the serum IL-37b and IL-37b-producing monocytes in patients were significantly increased in DF patients. A majority of the IL-37b produced by DF patients was produced by monocytes, not lymphocytes. Increased levels of IL-6, IL-10, and IFN- α were also found in DF patients. However, we failed to detect IL-1 β , IL-17A and TNF- α in plasma, because of off-target. In our study, there was no relation between IL-6, IL-10, and IFN- α expressions and IL-37b in serum ($P > 0.05$). The IL-37b-producing monocytes were negatively correlated with the level of IFN- α in serum and platelet count, and positively correlated with lymphocytes percentage ($P < 0.05$, respectively). Additionally, serum DENV nonstructural protein 1 levels were positively correlated with monocytes percentages ($P < 0.05$). Our data represents findings for IL-37b expression and its potential mechanisms in DF patients' immune response.

Chikungunya fever.

Bartholomeeusen K, Daniel M, LaBeaud DA, Gasque P, Peeling RW, Stephenson KE, Ng LFP, Ariën KK.

06-04-2023

Nat Rev Dis Primers.

<https://pubmed.ncbi.nlm.nih.gov/37024497/>

Chikungunya fever.

[No authors listed]

06-04-2023

Nat Rev Dis Primers.

<https://pubmed.ncbi.nlm.nih.gov/37024494/>

Automated Long-Term Monitoring of the Heat-Seeking Behavior of Mosquitoes.

Sakuma C, Maekawa E, Kanuka H.

06-04-2023

Cold Spring Harb Protoc.

<https://pubmed.ncbi.nlm.nih.gov/37024242/>

Key Features and Considerations for Using Automated Long-Term Monitoring of Heat-Seeking Behavior of Mosquitoes.

Sakuma C, Maekawa E, Kanuka H.

06-04-2023

Cold Spring Harb Protoc.

<https://pubmed.ncbi.nlm.nih.gov/37024241/>

Mosquitoes are vectors of various deadly infectious diseases, including malaria and dengue fever. Because these pathogens are transmitted by mosquito blood-feeding behavior, it is important to understand how mosquitoes are attracted to their hosts and how they feed on blood. The simplest method is to observe their behavior with the naked eye or video recording. Furthermore, various devices have been invented to assay mosquito

behavior, such as olfactometers. Although each method has distinctive advantages, all have disadvantages, such as limitations in the number of individuals that can be assayed at one time and in observable durations, objective quantification methods, and others. To solve these problems, we have developed an automated device to quantify the carbon dioxide-activated heat-seeking behavior of *Anopheles stephensi* and *Aedes aegypti* with continuous monitoring for up to 1 week. This device, which is detailed in an accompanying protocol, can be applied to search for substances and molecules that affect heat-seeking behavior. It may also be applicable to other hematophagous insects.

Quantifying Mosquito Attraction Behavior Using Olfactometry.

Castillo JS, Bellantuono AJ, DeGennaro M.

06-04-2023

Cold Spring Harb Protoc.

<https://pubmed.ncbi.nlm.nih.gov/37024240/>

When blood feeding from human hosts, female mosquitoes can transmit life-threatening pathogens to humans, including dengue virus, chikungunya virus, and Zika virus. Olfaction is the primary sense mosquitoes use to locate and differentiate hosts and studying it can lead to new strategies to reduce the risk of disease. To effectively study host-seeking behavior in mosquitoes, a repeatable, quantitative assay that isolates olfaction from other cues is critical for interpreting mosquito behavior. Here, we contribute an overview of methods and best practices for the study of mosquito attraction (or lack thereof) by using olfactometry to quantify behavior. In the accompanying protocols, we present an olfactory-based behavioral assay using a uniport olfactometer that measures mosquito attraction rate to specific stimuli. We include construction details, setup of the uniport olfactometer, details of the behavioral assay, and data analysis guidelines, as well as how to prepare the mosquitoes before their introduction into the olfactometer. This uniport olfactometer behavioral assay is currently one of the most reliable methods to study mosquito attraction to a single olfactory stimulus.

Circulation of West Nile virus in mosquitoes approximate to the migratory bird stopover in West Coast Malaysia.

Natasha JA, Yasmin AR, Sharma RSK, Nur-Fazila SH, Nur-Mahiza MI, Arshad SS, Mohammed HO, Kumar K, Loong SK, Ahmad Khusaini MKS.

06-04-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/37023172/>

Zika virus infection of retinal cells and the developing mouse eye induces host responses that contrasts to the brain and dengue virus infection.

Cowell E, Kris LP, Bracho-Granado G, Jaber H, Smith JR, Carr JM.

06-04-2023

J Neurovirol.

<https://pubmed.ncbi.nlm.nih.gov/37022660/>

Immunological impact of cytokines on the chikungunya virus pathophysiology: A literature narrative review.

Nunes JAL, Sousa JR, Smith VC, Quaresma JS, Vasconcelos PFDC, Chiang JO.

05-04-2023

Rev Med Virol.

<https://pubmed.ncbi.nlm.nih.gov/37021332/>

The chikungunya virus (CHIKV) is a member of the genus Alphavirus, family Togaviridae. CHIKV causes an acute systemic febrile condition, accompanied by severe polyarthralgia, intense muscle pain, and maculopapular exanthema, which may still occur in many patients. In rare cases, unusual symptoms may occur, eventually worsening the condition and resulting in a fatal outcome. It is a single-stranded, non-segmented RNA virus with a genome of approximately 11,805 nucleotides that organises a genetic and molecular chain that encodes non-structural proteins (nsP1, nsP2, nsP3, nsP4) and structural proteins (E3, E2, 6K, and E1). The fundamental role of immune response in the evolution of the disease is known. Understanding the role of immune response in the pathogenesis of CHIKV infection is challenging. In this context, innate and adaptive immune responses establish a connective interface that induces the production of various mediators that modulate the strategy of inhibiting viral replication. However, the immune escape articulated by the virus indicates that the action of pro- and anti-inflammatory cytokines contributes to the worsening of the disease and potentiates tissue damage with joint involvement. In this review, we discuss the role of the primary pro- and anti-inflammatory cytokines in the immunopathological processes of chikungunya fever.

Quantifying Mosquito Attraction Using a Uniport Olfactometer.

Castillo JS, Bellantuono AJ, DeGennaro M.

05-04-2023

Cold Spring Harb Protoc.

<https://pubmed.ncbi.nlm.nih.gov/37019611/>

Female mosquitoes respond to the world around them by using chemosensory organs, such as their antennae, to detect volatile compounds emitted from a vertebrate host. These chemosensory systems facilitate the interpretation of external stimuli from the periphery by connecting to the central nervous system and eliciting behaviors necessary for survival, such as obtaining a blood meal. This innate behavior leads to the transmission of pathogens, including dengue virus, chikungunya virus, and Zika virus. Olfaction is a primary sense mosquitoes use to differentiate between vertebrate hosts, and studying it can lead to novel strategies to reduce the risk of disease. In this protocol, we present an olfactory-driven behavioral assay using a uniport olfactometer that measures mosquito attraction rate to a specific stimulus. We include details of the behavioral assay and data analysis as well as how to prepare the mosquitoes before their introduction into the olfactometer. This uniport olfactometer

behavioral assay is currently one of the most reliable methods to study mosquito attraction to a single stimulus.

[Evaluation of technological development in health from the occurrence of the zika and chikungunya epidemics in Brazil].

Fernandes MDCR, Monte WSD, Bezerra FSB.

31-03-2023

Cad Saude Publica.

<https://pubmed.ncbi.nlm.nih.gov/37018775/>

Commonly Reported Mosquito-Borne Viruses in the United States: A Primer for Pharmacists.

Drwiega EN, Danziger LH, Burgos RM, Michienzi SM.

05-04-2023

J Pharm Pract.

<https://pubmed.ncbi.nlm.nih.gov/37018738/>

Mosquito-borne diseases are a public health concern. Pharmacists are often a patient's first stop for health information and may be asked questions regarding transmission, symptoms, and treatment of mosquito borne viruses (MBVs). The objective of this paper is to review transmission, geographic location, symptoms, diagnosis and treatment of MBVs. We discuss the following viruses with cases in the US in recent years: Dengue, West Nile, Chikungunya, LaCrosse Encephalitis, Eastern Equine Encephalitis Virus, and Zika. Prevention, including vaccines, and the impact of climate change are also discussed.

The E2 glycoprotein holds key residues for Mayaro virus adaptation to the urban *Aedes aegypti* mosquito.

Cereghino C, Roesch F, Carrau L, Hardy A, Ribeiro-Filho HV, Henrion-Lacritick A, Koh C, Marano JM, Bates TA, Rai P, Chuong C, Akter S, Vallet T, Blanc H, Elliott TJ, Brown AM, Michalak P, LeRoith T, Bloom JD, Marques RE, Saleh MC, Vignuzzi M, Weger-Lucarelli J.

05-04-1996

PLoS Pathog.

<https://pubmed.ncbi.nlm.nih.gov/37018377/>

A cryopreservation method to recover laboratory- and field-derived bacterial communities from mosquito larval habitats.

Zhao SY, Hughes GL, Coon KL.

05-04-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/37018374/>

Mosquitoes develop in a wide range of aquatic habitats containing highly diverse and variable bacterial communities that shape both larval and adult traits, including the capacity of adult females of some mosquito species to transmit disease-causing organisms to humans. However, while most mosquito studies control for host genotype and environmental conditions, the impact of

microbiota variation on phenotypic outcomes of mosquitoes is often unaccounted for. The inability to conduct reproducible intra- and inter-laboratory studies of mosquito-microbiota interactions has also greatly limited our ability to identify microbial targets for mosquito-borne disease control. Here, we developed an approach to isolate and cryopreserve bacterial communities derived from lab and field-based larval rearing environments of the yellow fever mosquito *Aedes aegypti*-a primary vector of dengue, Zika, and chikungunya viruses. We then validated the use of our approach to generate experimental microcosms colonized by standardized lab- and field-derived bacterial communities. Our results overall reveal minimal effects of cryopreservation on the recovery of both lab- and field-derived bacteria when directly compared with isolation from non-cryopreserved fresh material. Our results also reveal improved reproducibility of bacterial communities in replicate microcosms generated using cryopreserved stocks over fresh material. Communities in replicate microcosms further captured the majority of total bacterial diversity present in both lab- and field-based larval environments, although the relative richness of recovered taxa as compared to non-recovered taxa was substantially lower in microcosms containing field-derived bacteria. Altogether, these results provide a critical next step toward the standardization of mosquito studies to include larval rearing environments colonized by defined microbial communities. They also lay the foundation for long-term studies of mosquito-microbe interactions and the identification and manipulation of taxa with potential to reduce mosquito vectorial capacity.

WHO: Concerning Spread of Dengue, Chikungunya in Latin America.

Harris E.

05-04-2023

JAMA.

<https://pubmed.ncbi.nlm.nih.gov/37017997/>

Research progress toward the influence of mosquito salivary proteins on the transmission of mosquito-borne viruses.

Wang ZY, Nie KX, Niu JC, Cheng G.

05-04-1996

Insect Sci.

<https://pubmed.ncbi.nlm.nih.gov/37017683/>

Mosquito-borne viruses (MBVs) are a large class of viruses transmitted mainly through mosquito bites, including dengue virus, Zika virus, Japanese encephalitis virus, West Nile virus, and chikungunya virus, which pose a major threat to the health of people around the world. With global warming and extended human activities, the incidence of many MBVs has increased significantly. Mosquito saliva contains a variety of bioactive protein components. These not only enable blood feeding but also play a crucial role in regulating local infection at the bite site and the remote dissemination of MBVs as well as in remodeling the innate and adaptive immune responses of host vertebrates. Here, we review the physiological functions of mosquito salivary proteins (MSPs) in detail,

the influence and the underlying mechanism of MSPs on the transmission of MBVs, and the current progress and issues that urgently need to be addressed in the research and development of MSP-based MBV transmission blocking vaccines.

Chromobacterium Biopesticide Exposure Does Not Select for Resistance in Aedes Mosquitoes.

Engdahl CS, Caragata EP, Tavadia M, Dimopoulos G.

05-04-2023

mBio.

<https://pubmed.ncbi.nlm.nih.gov/37017525/>

Genetic polymorphisms rs1800871 and rs1800872 of IL-10 gene are associated with dengue infection, especially with serotype 1 and DwoWS in Mexican population.

Eloisa Monroy-Muñoz I, Esteban Muñoz-Medina J, Manuel Frago J, Esperanza Santacruz-Tinoco C, Sevilla-Montoya R, Hidalgo-Bravo A, Montes-Herrera D, Bravo-Flores E, Angeles-Martínez J.

Apr-2023

Cytokine.

<https://pubmed.ncbi.nlm.nih.gov/37015157/>

Introduction: Dengue infection is generated by a complex interaction between DENV (Dengue Virus) and the host's immune response. Interleukin-10 is an immunoregulatory cytokine during DENV infection. The objective of this study was to investigate whether genetic variants in IL-10 could be useful as a predictive and susceptibility marker in the prognosis of DENV infection, particularly with serotype 1, and in participants with dengue without warning signs.

Material and methods: A study of cases (n = 365) and controls (n = 364) was carried out. Genotyping was performed by real-time PCR using TaqMan probes. Sample size power was calculated using Quanto software. **RESULTS:** This is the first report showing the independent association of the T allele of rs1800871 (P = 0.023) and the A allele of rs1800872 (P = 0.010) with the risk of dengue infection. Statistical analysis established the genotypic association of IL-10 SNPs with DENV infection under different inheritance models. Our results also showed the association of the CC, TC, and CA haplotypes (P = 0.0064, P = 0.0032, and P = 0.0010 respectively) with infection. Furthermore, both polymorphic sites were associated with the risk of DwoWS and serotype 1 (Den-1) under different inheritance models. Finally, under the dominant model, we identified a positive correlation between IL-10 levels vs. IFN- γ and IL-8. **Conclusion:** Our results show the first independent association of the T and A alleles of the polymorphic sites rs1800871 and rs1800872, with dengue infection, particularly with Den-1, and in participants with DwoWs.

Mathematical modeling of plus-strand RNA virus replication to identify broad-spectrum antiviral treatment strategies.

Zitzmann C, Dächert C, Schmid B, van der Schaar H, van Hemert M, Perelson AS, van Kuppeveld FJM, Bartenschlager R, Binder M, Kaderali L.

04-04-2023

PLoS Comput Biol.

<https://pubmed.ncbi.nlm.nih.gov/37014904/>

Plus-strand RNA viruses are the largest group of viruses. Many are human pathogens that inflict a socio-economic burden. Interestingly, plus-strand RNA viruses share remarkable similarities in their replication. A hallmark of plus-strand RNA viruses is the remodeling of intracellular membranes to establish replication organelles (so-called "replication factories"), which provide a protected environment for the replicase complex, consisting of the viral genome and proteins necessary for viral RNA synthesis. In the current study, we investigate pan-viral similarities and virus-specific differences in the life cycle of this highly relevant group of viruses. We first measured the kinetics of viral RNA, viral protein, and infectious virus particle production of hepatitis C virus (HCV), dengue virus (DENV), and coxsackievirus B3 (CVB3) in the immuno-compromised Huh7 cell line and thus without perturbations by an intrinsic immune response. Based on these measurements, we developed a detailed mathematical model of the replication of HCV, DENV, and CVB3 and showed that only small virus-specific changes in the model were necessary to describe the in vitro dynamics of the different viruses. Our model correctly predicted virus-specific mechanisms such as host cell translation shut off and different kinetics of replication organelles. Further, our model suggests that the ability to suppress or shut down host cell mRNA translation may be a key factor for in vitro replication efficiency, which may determine acute self-limited or chronic infection. We further analyzed potential broad-spectrum antiviral treatment options in silico and found that targeting viral RNA translation, such as polyprotein cleavage and viral RNA synthesis, may be the most promising drug targets for all plus-strand RNA viruses. Moreover, we found that targeting only the formation of replicase complexes did not stop the in vitro viral replication early in infection, while inhibiting intracellular trafficking processes may even lead to amplified viral growth.

Current thoughts on cellular functions of numb-associated kinases.

Huang C, Ji C, Wang J.

04-04-2023

Mol Biol Rep.

<https://pubmed.ncbi.nlm.nih.gov/37014568/>

Evolution and immunopathology of chikungunya virus informs therapeutic development.

Henderson Sousa F, Ghaisani Komarudin A, Findlay-Greene F, Bowolaksono A, Sasmono RT, Stevens C, Barlow PG.

01-04-2023

Dis Model Mech.

<https://pubmed.ncbi.nlm.nih.gov/37014125/>

Chikungunya virus (CHIKV), a mosquito-borne alphavirus, is an emerging global threat identified in more than 60 countries across continents. The risk of CHIKV transmission is rising due to increased global interactions, year-round presence of mosquito vectors, and the ability of CHIKV to produce high host viral loads and undergo mutation. Although CHIKV disease is rarely fatal, it can progress to a chronic stage, during which patients experience severe debilitating arthritis that can last from several weeks to months or years. At present, there are no licensed vaccines or antiviral drugs for CHIKV disease, and treatment is primarily symptomatic. This Review provides an overview of CHIKV pathogenesis and explores the available therapeutic options and the most recent advances in novel therapeutic strategies against CHIKV infections.

Health workers' capability, opportunity, motivation, and behavior to prevent and control COVID-19 in a high-risk district in Thailand.

Sangpoom S, Adesina F, Saetang J, Thammachot N, Jeenuang K, Suwanbamrung C.
2023

Rocz Panstw Zakl Hig.

<https://pubmed.ncbi.nlm.nih.gov/37013837/>

Background: Village health volunteers have been an important group who plays the role in prevention and control of COVID-19 pandemic situations at primary care units, Thailand. **Objective:** The objective of this cross-sectional analytic study was to assess the level and analyze the association between personal information, capability, opportunities, motivations, and behaviors to prevent and control COVID-19 among Village healthy volunteers in a high risk district, Southern Thailand. **Material and methods:** G*power program was used to calculate the sample size of 145 VHVs recruited for this study. Data collection was done using a well-structured questionnaire with 5-point Likert scale for capability, opportunities, motivations, and behaviors component, and multi-stage sampling of 18 sub-district health promoting hospitals was carried out. Data analysis was done using descriptive, Chi-square and Fisher Exact test. **Results:** Majority (89.7%) of the VHVs were female, and 62.8% were 28-59 years old. More than half, 55.9% (81) have been VHVs for 11-36 years. Generally, higher capacity was found among 59.3% (86) of the VHVs, low opportunity level among 81.4% (118), high motivation among 53.8% (78) and a good behavior towards the prevention and control of COVID-19 among 72.4% (105). The VHVs' age and duration of practicing were significantly ($P < 0.01$ and $P < 0.05$ respectively) associated with COVID-19 prevention behavior ($\chi^2 = 6.894$ and 5.255 respectively). Likewise, there are significant association between capacity ($p \leq 0.001$ and $\chi^2 = 31.014$), opportunity ($p \leq 0.05$ and $\chi^2 = 9.473$), motivation ($p \leq 0.001$ and $\chi^2 = 0.0001$) and VHVs' behaviour to prevent and control COVID-19. **Conclusion:** VHVs' opportunity is very low in the study area and it negatively affects good behavior for the prevention and control of COVID-19. All stakeholders in the district can use the association among the capability, opportunity, motivation and behavioral model to develop practice

guideline and set policy for preventing COVID-19 in the community.

Solid waste management and Aedes aegypti infestation interconnections: A regression tree application.

Klafke F, Barros VG, Henning E.

04-04-2023

Waste Manag Res.

<https://pubmed.ncbi.nlm.nih.gov/37013436/>

Structure modelling of odorant receptor from Aedes aegypti and identification of potential repellent molecules.

Tiwari V, Sowdhamini R.

06-03-2023

Comput Struct Biotechnol J.

<https://pubmed.ncbi.nlm.nih.gov/37013002/>

Odorant receptors (ORs) are important class of proteins involved in olfactory behaviour of insects. These are GPCR-like heptahelical transmembrane proteins with inverted topology compared to GPCR and require a co-receptor (ORco) for their function. OR function can be modulated through small molecules and negative modulation can be beneficial in case of disease vectors like *Aedes aegypti*. OR4 of *A. aegypti* is implicated in host recognition through human odour. *Aedes aegypti* is a vector for viruses that spread diseases like dengue, Zika and Chikungunya. In this study, we have attempted to model the full-length structure of OR4 and the ORco of *A. aegypti* due to lack of experimental structure. Further, we have screened a library of natural compounds (>0.3 million) along with known repellent molecules against ORco and OR4. Many natural compounds, including those from plants like *Ocimum tenuiflorum* (Holy Basil) and *Piper nigrum* (Black pepper), were found to have better binding affinity towards ORco compared to known repellents like DEET providing an alternative to existing repellent molecules. For specific inhibitor of OR4, several natural compounds (including those from plant like Mulberry) were identified. Further, we have utilized multiple docking approaches and conservation analysis to understand the interaction between OR4 and ORco. It was observed that the residues from the seventh transmembrane helix of OR4 and pore forming helix of ORco could play an important role along with known intracellular loop 3 residues in mediating the heteromer formation of OR and ORco.

Potential use of the cholesterol transfer inhibitor U18666A as an antiviral drug for research on various viral infections.

Assefi M, Bijan Rostami R, Ebrahimi M, Altafi M, Tehrany PM, Zaidan HK, Talib Al-Naqeeb BZ, Hadi M, Yasamineh S, Gholizadeh O.

01-04-2023

Microb Pathog.

<https://pubmed.ncbi.nlm.nih.gov/37011734/>

Cholesterol plays critical functions in arranging the biophysical attributes of proteins and lipids in the plasma membrane. For various viruses, an association with

cholesterol for virus entrance and/or morphogenesis has been demonstrated. Therefore, the lipid metabolic pathways and the combination of membranes could be targeted to selectively suppress the virus replication steps as a basis for antiviral treatment. U18666A is a cationic amphiphilic drug (CAD) that affects intracellular transport and cholesterol production. A robust tool for investigating lysosomal cholesterol transfer and Ebola virus infection is an androstenolone derived termed U18666A that suppresses three enzymes in the cholesterol biosynthesis mechanism. In addition, U18666A inhibited low-density lipoprotein (LDL)-induced downregulation of LDL receptor and triggered lysosomal aggregation of cholesterol. According to reports, U18666A inhibits the reproduction of baculoviruses, filoviruses, hepatitis, coronaviruses, pseudorabies, HIV, influenza, and flaviviruses, as well as chikungunya and flaviviruses. U18666A-treated viral infections may act as a novel in vitro model system to elucidate the cholesterol mechanism of several viral infections. In this article, we discuss the mechanism and function of U18666A as a potent tool for studying cholesterol mechanisms in various viral infections.

Structure-first identification of RNA elements that regulate dengue virus genome architecture and replication.

Boerneke MA, Gokhale NS, Horner SM, Weeks KM.

11-04-2023

Proc Natl Acad Sci U S A.

<https://pubmed.ncbi.nlm.nih.gov/37011200/>

Evolutionary dynamics of dengue virus in India.

Jagtap S, Pattabiraman C, Sankaradoss A, Krishna S, Roy R.

03-04-2023

PLoS Pathog.

<https://pubmed.ncbi.nlm.nih.gov/37011104/>

More than a hundred thousand dengue cases are diagnosed in India annually, and about half of the country's population carries dengue virus-specific antibodies. Dengue propagates and adapts to the selection pressures imposed by a multitude of factors that can lead to the emergence of new variants. Yet, there has been no systematic analysis of the evolution of the dengue virus in the country. Here, we present a comprehensive analysis of all DENV gene sequences collected between 1956 and 2018 from India. We examine the spatio-temporal dynamics of India-specific genotypes, their evolutionary relationship with global and local dengue virus strains, interserotype dynamics and their divergence from the vaccine strains. Our analysis highlights the co-circulation of all DENV serotypes in India with cyclical outbreaks every 3-4 years. Since 2000, genotype III of DENV-1, cosmopolitan genotype of DENV-2, genotype III of DENV-3 and genotype I of DENV-4 have been dominating across the country. Substitution rates are comparable across the serotypes, suggesting a lack of serotype-specific evolutionary divergence. Yet, the envelope (E) protein displays strong signatures of evolution under immune selection. Apart from drifting away from its ancestors and

other contemporary serotypes in general, we find evidence for recurring interserotype drift towards each other, suggesting selection via cross-reactive antibody-dependent enhancement. We identify the emergence of the highly divergent DENV-4-Id lineage in South India, which has acquired half of all E gene mutations in the antigenic sites. Moreover, the DENV-4-Id is drifting towards DENV-1 and DENV-3 clades, suggesting the role of cross-reactive antibodies in its evolution. Due to the regional restriction of the Indian genotypes and immunity-driven virus evolution in the country, ~50% of all E gene differences with the current vaccines are focused on the antigenic sites. Our study shows how the dengue virus evolution in India is being shaped in complex ways.

Challenges of acute febrile illness diagnosis in a national infectious diseases center in Rio de Janeiro: 16-year experience of syndromic surveillance.

Bressan CDS, Teixeira MLB, Gouvêa MIFDS, de Pina-Costa A, Santos HFP, Calvet GA, Lupi O, Siqueira AM, Valls-de-Souza R, Valim C, Brasil P.

03-04-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/37011087/>

An epidemiological synthesis of emerging and re-emerging zoonotic disease threats in Cameroon, 2000-2022: a systematic review.

Tahmo NB, Wirsiy FS, Nnamdi DB, Tongo M, Lawler JV, Broadhurst MJ, Wondji CS, Brett-Major DM.

17-12-2022

IJID Reg.

<https://pubmed.ncbi.nlm.nih.gov/37009575/>

Introduction: Population factors such as urbanization, socio-economic, and environmental factors are driving forces for emerging/re-emerging zoonotic diseases in Cameroon. To inform preparedness and prioritization efforts, this study mapped out epidemiological data (including prevalence) of zoonotic diseases occurring in Cameroon between 2000 and 2022 by demographic factors. **Methods:** Following the PRISMA guidelines, a protocol was registered in the PROSPERO database (CRD42022333059). Independent reviewers searched the PubMed, Embase, CINAHL, Cochrane, and Scopus databases on May 30, 2022 for relevant articles; duplicates were removed, and the titles, abstracts, and full texts were screened to identify eligible articles. **Results:** Out of 4142 articles identified, 64 eligible articles were retrieved in the database search and an additional 12 from the cited literature ($N = 76$). Thirty-five unique zoonoses (viral, bacterial, and parasitic) were indexed, including Cameroon priority zoonoses: anthrax, bovine tuberculosis, Ebola and Marburg virus disease, highly pathogenic avian influenza, and rabies. The number of studies varied by region, ranging from 12 in the Far North to 32 in the Centre Region. The most reported were as follows: brucellosis (random-effects pooled estimate proportion (effect size), ES 0.05%, 95% confidence interval (CI) 0.03-0.07; $n = 6$), dengue (ES 0.13%, 95% CI 0.06-0.22; $n = 12$), avian and

swine influenza virus (ES 0.10%, 95% CI 0.04-0.20; $n = 8$), and toxoplasmosis (ES 0.49%, 95% CI 0.35-0.63; $n = 11$), although I^2 values were greater than 75%, thus there was high inter-study heterogeneity ($P < 0.01$). **Conclusions:** This understanding of the distribution of emerging and re-emerging zoonotic threats in Cameroon is vital to effective preventive and resource prioritization measures.

Temperature and sex shape Zika virus pathogenicity in the adult Brat cheesehead brain: A *Drosophila* model for virus-associated neurological diseases.

Tafesh-Edwards G, Kalukin A, Bunnell D, Chtarbanova S, Eleftherianos I.

16-03-2023

iScience.

<https://pubmed.ncbi.nlm.nih.gov/37009222/>

SENSITIVITY ANALYSIS FOR EVALUATING PRINCIPAL SURROGATE ENDPOINTS RELAXING THE EQUAL EARLY CLINICAL RISK ASSUMPTION.

Huang Y, Zhuang Y, Gilbert P.

Sept-2022

Ann Appl Stat.

<https://pubmed.ncbi.nlm.nih.gov/37008748/>

This article addresses the evaluation of post-randomization immune response biomarkers as principal surrogate endpoints of a vaccine's protective effect, based on data from randomized vaccine trials. An important metric for quantifying a biomarker's principal surrogacy in vaccine research is the vaccine efficacy curve, which shows a vaccine's efficacy as a function of potential biomarker values if receiving vaccine, among an 'early-always-at-risk' principal stratum of trial participants who remain disease-free at the time of biomarker measurement whether having received vaccine or placebo. Earlier work in principal surrogate evaluation relied on an 'equal-early-clinical-risk' assumption for identifiability of the vaccine curve, based on observed disease status at the time of biomarker measurement. This assumption is violated in the common setting that the vaccine has an early effect on the clinical endpoint before the biomarker is measured. In particular, a vaccine's early protective effect observed in two phase III dengue vaccine trials (CYD14/CYD15) has motivated our current research development. We relax the 'equal-early-clinical-risk' assumption and propose a new sensitivity analysis framework for principal surrogate evaluation allowing for early vaccine efficacy. Under this framework, we develop inference procedures for vaccine efficacy curve estimators based on the estimated maximum likelihood approach. We then use the proposed methodology to assess the surrogacy of post-randomization neutralization titer in the motivating dengue application.

Structural and immunological basis of cross-reactivity between dengue and Zika infections: Implications in serosurveillance in endemic regions.

Gaspar-Castillo C, Rodríguez MH, Ortiz-Navarrete V, Alpuche-Aranda CM, Martinez-Barnette J.

17-03-2023

Front Microbiol.

<https://pubmed.ncbi.nlm.nih.gov/37007463/>

Dengue and Zika are arthropod-borne viral diseases present in more than 100 countries around the world. In the past decade, Zika emerged causing widespread outbreaks in new regions, where dengue has been endemic-epidemic for a long period. The wide and extensive dissemination of the mosquito vectors, *Aedes aegypti*, and *Ae. albopictus*, favor the co-existence of both infections in the same regions. Together with an important proportion of asymptomatic infections, similar clinical manifestations, and a short time window for acute infection confirmatory tests, it is difficult to differentially estimate both dengue and Zika incidence and prevalence. DENV and ZIKV flavivirus share high structural similarity, inducing a cross-reactive immune response that leads to false positives in serological tests particularly in secondary infections. This results in overestimation of recent Zika outbreaks seroprevalence in dengue endemic regions. In this review, we address the biological basis underlying DENV and ZIKV structural homology; the structural and cellular basis of immunological cross reactivity; and the resulting difficulties in measuring dengue and Zika seroprevalence. Finally, we offer a perspective about the need for more research to improve serological tests performance.

Optical coherence tomography angiography features of dengue retinopathy manifesting as acute macular neuroretinopathy, branch vein vasculitis and neurosensory detachment.

Rajurkar K, Thakar M.

02-09-2022

Oman J Ophthalmol.

<https://pubmed.ncbi.nlm.nih.gov/37007231/>

Construction and immunogenicity of an mRNA vaccine against chikungunya virus.

Liu J, Lu X, Li X, Huang W, Fang E, Li W, Liu X, Liu M, Li J, Li M, Zhang Z, Song H, Ying B, Li Y.

15-03-2023

Front Immunol.

<https://pubmed.ncbi.nlm.nih.gov/37006310/>

Chikungunya fever (CHIKF) has spread to more than 100 countries worldwide, with frequent outbreaks in Europe and the Americas in recent years. Despite the relatively low lethality of infection, patients can suffer from long-term sequelae. Until now, no available vaccines have been approved for use; however, increasing attention is being paid to the development of vaccines against chikungunya virus (CHIKV), and the World Health Organization has included vaccine development in the initial blueprint deliverables. Here, we developed an mRNA vaccine using the nucleotide sequence encoding structural proteins of CHIKV. And immunogenicity was evaluated by neutralization assay, Enzyme-linked immunospot assay

and Intracellular cytokine staining. The results showed that the encoded proteins elicited high levels of neutralizing antibody titers and T cell-mediated cellular immune responses in mice. Moreover, compared with the wild-type vaccine, the codon-optimized vaccine elicited robust CD8⁺ T-cell responses and mild neutralizing antibody titers. In addition, higher levels of neutralizing antibody titers and T-cell immune responses were obtained using a homologous booster mRNA vaccine regimen of three different homologous or heterologous booster immunization strategies. Thus, this study provides assessment data to develop vaccine candidates and explore the effectiveness of the prime-boost approach.

Diagnostic and vaccine potential of Zika virus envelope protein (E) derivatives produced in bacterial and insect cells.

Lunardelli VAS, Almeida BDS, Apostolico JS, Rezende T, Yamamoto MM, Pereira SS, Bueno MFC, Pereira LR, Carvalho KI, Shessarenko RD, de Souza Ferreira LC, Boscardin SB, Rosa DS.

16-03-2023

Front Immunol.

<https://pubmed.ncbi.nlm.nih.gov/37006270/>

An effective live-attenuated Zika vaccine candidate with a modified 5' untranslated region.

Nazneen F, Thompson EA, Blackwell C, Bai JS, Huang F, Bai F.

01-04-2023

NPJ Vaccines.

<https://pubmed.ncbi.nlm.nih.gov/37005424/>

Zika virus (ZIKV) is a mosquito-transmitted flavivirus that has caused devastating congenital Zika syndrome (CZS), including microcephaly, congenital malformation, and fetal demise in human newborns in recent epidemics. ZIKV infection can also cause Guillain-Barré syndrome (GBS) and meningoencephalitis in adults. Despite intensive research in recent years, there are no approved vaccines or antiviral therapeutics against CZS and adult Zika diseases. In this report, we developed a novel live-attenuated ZIKV strain (named Z7) by inserting 50 RNA nucleotides (nt) into the 5' untranslated region (UTR) of a pre-epidemic ZIKV Cambodian strain, FSS13025. We used this particular ZIKV strain as it is attenuated in neurovirulence, immune antagonism, and mosquito infectivity compared with the American epidemic isolates. Our data demonstrate that Z7 replicates efficiently and produces high titers without causing apparent cytopathic effects (CPE) in Vero cells or losing the insert sequence, even after ten passages. Significantly, Z7 induces robust humoral and cellular immune responses that completely prevent viremia after a challenge with a high dose of an American epidemic ZIKV strain PRVABC59 infection in type I interferon (IFN) receptor A deficient (*Ifnar1*^{-/-}) mice. Moreover, adoptive transfer of plasma collected from Z7 immunized mice protects *Ifnar1*^{-/-} mice from ZIKV (strain PRVABC59) infection. These results suggest that modifying the ZIKV 5' UTR is a novel strategy to develop live-

attenuated vaccine candidates for ZIKV and potentially for other flaviviruses.

Novel development of Lecanicillium lecanii-based granules as a platform against malarial vector Anopheles culicifacies.

Sogan N, Kala S, Kapoor N, Nagpal BN, Ramlal A, Nautiyal A.

01-04-2023

World J Microbiol Biotechnol.

<https://pubmed.ncbi.nlm.nih.gov/37004584/>

Mosquitoes are infectious vectors for a wide range of pathogens and parasites thereby transmitting several diseases including malaria, dengue, Zika, Japanese encephalitis and chikungunya which pose a major public health concern. Mostly synthetic insecticides are usually applied as a primary control strategy to manage vector-borne diseases. However excessive and non-judicious usage of such chemically derived insecticides has led to serious environmental and health issues owing to their biomagnification ability and increased toxicity towards non-target organisms. In this context, many such bioactive compounds originating from entomopathogenic microbes serve as an alternative strategy and environmentally benign tool for vector control. In the present paper, the entomopathogenic fungus, *Lecanicillium lecanii* (LL) was processed to make the granules. Developed 4% LL granules have been characterized using the technique of Fourier transform infrared spectroscopy (FTIR) and scanning electron microscope (SEM). The developed formulation was also subjected to an accelerated temperature study at 40 °C and was found to be stable for 3 months. Further, GCMS of the *L. lecanii* was also performed to screen the potential biomolecules present. The developed formulation was found to be lethal against *Anopheles culicifacies* with an LC₅₀ value of 11.836 µg/mL. The findings from SEM and histopathology also substantiated the mortality effects. Further, the SEM EDX (energy dispersive X-ray) studies revealed that the treated larvae have lower nitrogen content which is correlated to a lower level of chitin whereas the control ones has higher chitin content and healthy membranes. The developed LL granule formulation exhibited high toxicity against *Anopheles* mosquitoes. The granule formulations can be used as an effective biocontrol strategy against malaria-causing mosquitoes.

Nasopharyngeal swabs as alternative specimens for the diagnosis of dengue virus infection.

Maia AC, de Souza Cardoso Quintão T, de Oliveira PM, Cassemiro ÉM, Alves DCC, de Melo Alves PP, Dos Anjos Pereira Martins F, Araujo ELL, da Costa Gurgel H, Noronha EF, Ramalho WM, Pereira AL, Slavov SN, de Araújo WN, Haddad R.

30-03-2023

J Infect.

<https://pubmed.ncbi.nlm.nih.gov/37003524/>

Hemocup blood feeder: An affordable and simplified blood-feeding device for maintenance of Aedes aegypti mosquito colonies in Sri Lanka.

Dilani PVD, Wickramasinghe PDSU, Lakshman GVC, Ranathunge T, Dassanayake RS, Silva Gunawardene YIN.
30-03-2023

Exp Parasitol.

<https://pubmed.ncbi.nlm.nih.gov/37003431/>

Dengue is a mosquito-borne viral disease mainly transmitted by *Aedes aegypti* and disease control is primarily reliant on mosquito vector control strategies. In the failure of conventional vector control strategies, new strategies are being developed which specifically require the maintenance of mosquito colonies in the laboratories. Blood-feeding is an essential part of the routine colony maintenance of *Ae. aegypti*. Therefore, the current study was focused on developing a simplified artificial membrane-feeding device, "Hemocup" feeder out of affordable material. viz., plastic cups, styrofoam insulation system, parafilm-M, and preheated water to facilitate the *Ae. aegypti* artificial blood feeding. The performance of the device was compared to that of a commercially available blood-feeding device, "Hemotek", by assessing the blood-feeding rate, fecundity, and egg hatchability. Similar blood feeding rates were observed for Hemocup and Hemotek methods (91.8 ± 1.6 and 94.3 ± 1.6 respectively; $p > 0.05$) as well as comparable fecundity between the two methods (20.8 ± 0.7 and 22.0 ± 1.5 respectively; $p > 0.05$). Furthermore, there was no statistically significant difference in egg hatchability between the two methods (91.9 ± 1.4 and 93.8 ± 1.4 , respectively; $p > 0.05$). The results indicate that this simple Hemocup blood-feeding system can be used for routine colonization of laboratory strains of *Ae. aegypti* and for mass-rearing purposes.

Clinical Profile of Pediatric Cases of Dengue during the 2019 Epidemic in Bangladesh: A Multicenter Cross-Sectional Study.

Yesmin S, Ahammad AM, Sarmin S, Rafi MA, Islam S, Hasan MJ.

Apr-2023

Mymensingh Med J.

<https://pubmed.ncbi.nlm.nih.gov/37002764/>

Detecting dengue fever in children using online Rasch analysis to develop algorithms for parents: An APP development and usability study.

Hu TY, Chow JC, Chien TW, Chou W.

31-03-2023

Medicine (Baltimore).

<https://pubmed.ncbi.nlm.nih.gov/37000053/>

Background: Dengue fever (DF) is a significant public health concern in Asia. However, detecting the disease using traditional dichotomous criteria (i.e., absent vs present) can be extremely difficult. Convolutional neural networks (CNNs) and artificial neural networks (ANNs),

due to their use of a large number of parameters for modeling, have shown the potential to improve prediction accuracy (ACC). To date, there has been no research conducted to understand item features and responses using online Rasch analysis. To verify the hypothesis that a combination of CNN, ANN, K-nearest-neighbor algorithm (KNN), and logistic regression (LR) can improve the ACC of DF prediction for children, further research is required.

Methods: We extracted 19 feature variables related to DF symptoms from 177 pediatric patients, of whom 69 were diagnosed with DF. Using the RaschOnline technique for Rasch analysis, we examined 11 variables for their statistical significance in predicting the risk of DF. Based on 2 sets of data, 1 for training (80%) and the other for testing (20%), we calculated the prediction ACC by comparing the areas under the receiver operating characteristic curve (AUCs) between DF + and DF- in both sets. In the training set, we compared 2 scenarios: the combined scheme and individual algorithms. **Results:** Our findings indicate that visual displays of DF data are easily interpreted using Rasch analysis; the k-nearest neighbors algorithm has a lower AUC (< 0.50); LR has a relatively higher AUC (0.70); all 3 algorithms have an almost equal AUC ($= 0.68$), which is smaller than the individual algorithms of Naive Bayes, LR in raw data, and Naive Bayes in normalized data; and we developed an app to assist parents in detecting DF in children during the dengue season. **Conclusion:** The development of an LR-based APP for the detection of DF in children has been completed. To help patients, family members, and clinicians differentiate DF from other febrile illnesses at an early stage, an 11-item model is proposed for developing the APP.

Influence of mosquito-borne biological agents on health risks among soldiers and military personnel.

Gajda E, Krzowski Ł, Kowalczyk K, Pabin A, Maculewicz E.

31-03-2023

Ann Agric Environ Med.

<https://pubmed.ncbi.nlm.nih.gov/36999849/>

Introduction and objective: Mosquitoes are the most important vector group for humans, and three genera - *Aedes*, *Anopheles* and *Culex*, are of greatest significance in the transmission of pathogens to humans and animals. The geographical expansion of vectors can lead to the spread diseases into new regions. Soldiers exercise in the field, participate in missions, or are stationed in Military Contingents located in different climatic conditions, which is directly related to exposure to mosquito-borne diseases.

Objective: The aim is to describe the role of mosquitoes in the transmission of selected pathogens of medical and epidemiological importance, which pose a new threat in Europe, pointing to soldiers and other military personnel as particularly vulnerable occupational groups. **Review methods:** PubMed and other online resources and publications were searched to evaluate scientific relevance. **Brief description of the state of knowledge.:** In recent years in Europe, attention has been drawn to emerging infectious diseases transmitted by mosquitoes, including malaria, Dengue fever, West Nile fever and Chikungunya fever. West Nile virus infections were

recorded in many European countries, including Greece, Italy, Germany and Austria. Soldiers, due to their tasks, are particularly vulnerable to vector-borne diseases. In order to reduce the exposure of soldiers to mosquito-borne diseases various protection measures are used. **Summary:** Some of vector-borne diseases belong to emerging infectious diseases and may pose a threat to public health. The burden on soldiers with these diseases can be significant, which is the reason why methods of surveillance and the control of vectors are being developed.

The anti-immune dengue subgenomic flaviviral RNA is present in vesicles in mosquito saliva and is associated with increased infectivity.

Yeh SC, Strilets T, Tan WL, Castillo D, Medkour H, Rey-Cadilhac F, Serrato-Pomar IM, Rachenne F, Chowdhury A, Chuo V, Azar SR, Singh MK, Hamel R, Missé D, Kini RM, Kenney LJ, Vasilakis N, Marti-Renom MA, Nir G, Pompon J, Garcia-Blanco MA.

30-03-2023

PLoS Pathog.

<https://pubmed.ncbi.nlm.nih.gov/36996041/>

Understanding antibody-dependent enhancement in dengue: Are afucosylated IgG1s a concern?

Teo A, Tan HD, Loy T, Chia PY, Chua CLL.

30-03-2023

PLoS Pathog.

<https://pubmed.ncbi.nlm.nih.gov/36996026/>

The protein disulfide isomerase inhibitor 3-methyltoxoflavin inhibits Chikungunya virus.

Puhl AC, Fernandes RS, Godoy AS, Gil LHV, Oliva G, Ekins S.

01-04-2023

Bioorg Med Chem.

<https://pubmed.ncbi.nlm.nih.gov/36940609/>

Chikungunya virus (CHIKV) is the etiological agent of chikungunya fever, a (re)emerging arbovirus infection, that causes severe and often persistent arthritis, as well as representing a serious health concern worldwide for which no antivirals are currently available. Despite efforts over the last decade to identify and optimize new inhibitors or to reposition existing drugs, no compound has progressed to clinical trials for CHIKV and current prophylaxis is based on vector control, which has shown limited success in containing the virus. Our efforts to rectify this situation were initiated by screening 36 compounds using a replicon system and ultimately identified the natural product derivative 3-methyltoxoflavin with activity against CHIKV using a cell-based assay (EC₅₀ 200 nM, SI = 17 in Huh-7 cells). We have additionally screened 3-methyltoxoflavin against a panel of 17 viruses and showed that it only additionally demonstrated inhibition of the yellow fever virus (EC₅₀ 370 nM, SI = 3.2 in Huh-7 cells). We have also showed that 3-methyltoxoflavin has excellent in vitro human and mouse

microsomal metabolic stability, good solubility and high Caco-2 permeability and it is not likely to be a P-glycoprotein substrate. In summary, we demonstrate that 3-methyltoxoflavin has activity against CHIKV, good in vitro absorption, distribution, metabolism and excretion (ADME) properties as well as good calculated physicochemical properties and may represent a valuable starting point for future optimization to develop inhibitors for this and other related viruses.

Standardized evaluation of Zika nucleic acid tests used in clinical settings and blood screening.

Stone M, Bakkour S, Grebe E, Emperador DM, Escadafal C, Deng X, Dave H, Kelly-Cirino C, Lackritz E, Rojas DP, Simmons G, Rabe IB, Busch MP.

17-03-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/36930653/>

The chaperone BiP promotes dengue virus replication and mosquito vitellogenesis in Aedes aegypti.

Yeh CT, Weng SC, Tsao PN, Shiao SH.

Apr-2023

Insect Biochem Mol Biol.

<https://pubmed.ncbi.nlm.nih.gov/36921733/>

Binding immunoglobulin protein (BiP, also known as GRP78), a chaperone and master regulator of the unfolded protein response (UPR) pathway, plays an essential role in several flavivirus infections, but its functional role in regulating dengue virus replication in the mosquito remains largely unknown. We here demonstrated the interaction between a dengue virus serotype 2 (DENV2) and BiP in *Aedes aegypti* and report the discovery of a novel functional role of BiP in mosquito vitellogenesis. Silencing *Ae. aegypti* BiP (AaBiP) expression resulted in the significant inhibition of DENV2 viral genome replication, viral protein production, and infectious viral particle biogenesis. Co-immunoprecipitation assays showed that the DENV2 non-structural protein 1 (NS1) interacts with the AaBiP protein, and silencing AaBiP expression led to enhanced DENV2 NS1 aggregation, indicating that AaBiP plays a role in viral protein stability. A kinetic study focusing on pulse treatment of MG132, a proteasome inhibitor, in AaBiP-silenced mosquitoes showed that DENV2 NS1 was drastically elevated, which further suggests that AaBiP-mediated viral protein degradation is mediated by proteasomal machinery. Silencing of AaBiP also resulted in a reduction in mosquito fertility and fecundity. Depletion of AaBiP inhibited mosquito vitellogenesis due to the reduction of vitellogenin mRNA and elevated aggregation of vitellogenin protein post blood meal, further suppressing ovary development and fecundity. Overall, our results suggest that AaBiP is a dual-function protein with roles in both the regulation of dengue virus replication and mosquito reproduction. Our findings will be useful in the establishment of more efficient strategies for vector-borne disease control.

Human microglial models to study host-virus interactions.

McMillan RE, Wang E, Carlin AF, Coufal NG.

May-2023

Exp Neurol.

<https://pubmed.ncbi.nlm.nih.gov/36907350/>

Generation of a thermostable, oral Zika vaccine that protects against virus challenge in non-human primates.

Bacon A, Teixeira M, Costa V, Bone P, Simmons J, Drew J.

06-04-2023

Vaccine.

<https://pubmed.ncbi.nlm.nih.gov/36894395/>

Here we report the development of a thermally stable, orally administered, candidate Zika vaccine using human serotype 5 adenovirus (AdHu5). We engineered AdHu5 to express the genes for the envelope and NS1 proteins of Zika virus. AdHu5 was formulated using a proprietary platform, OraPro, comprising a mix of sugars and modified amino acids that can overcome elevated temperatures (37 C), and an enteric coated capsule that protects the integrity of the AdHu5 from the acid in the stomach. This enables the delivery AdHu5 to the immune system of the small intestine. We show that oral delivery of AdHu5 elicited antigen-specific serum IgG immune responses in a mouse model and in a non-human primate model. Importantly, these immune responses were able reduce viral counts in mice and to prevent detectable viraemia in the non-human primates on challenge with live Zika virus. This candidate vaccine has significant advantages over many current vaccines that are maintained in a cold or ultra-cold chain and require parenteral administration.

N-sulfonyl peptide-hybrids as a new class of dengue virus protease inhibitors.

Behrouz S, Kühl N, Klein CD.

05-05-2023

Eur J Med Chem.

<https://pubmed.ncbi.nlm.nih.gov/36893626/>

Dengue virus (DENV) from the Flaviviridae family causes an epidemic disease that seriously threatens human life. The viral serine protease NS2B-NS3 is a promising target for drug development against DENV and other flaviviruses. We here report the design, synthesis, and in-vitro characterization of potent peptidic inhibitors of DENV protease with a sulfonyl moiety as N-terminal cap, thereby creating sulfonamide-peptide hybrids. The in-vitro target affinities of some synthesized compounds were in the nanomolar range, with the most promising derivative reaching a K_i value of 78 nM against DENV-2 protease. The synthesized compounds did not have relevant off-target activity nor cytotoxicity. The metabolic stability of compounds against rat liver microsomes and pancreatic enzymes was remarkable. In general, the integration of sulfonamide moieties at the N-terminus of peptidic inhibitors proved to be a promising and attractive strategy for further drug development against DENV infections.

Analysing inhibition of dengue virus in Wolbachia-infected mosquito cells following the removal of Wolbachia.

Hussain M, Etebari K, Asgari S.

Apr-2023

Virology.

<https://pubmed.ncbi.nlm.nih.gov/36889142/>

Comparative Efficacy of Mayaro Virus-Like Particle Vaccines Produced in Insect or Mammalian Cells.

Abbo SR, Nguyen W, Abma-Henkens MHC, van de Kamer D, Savelkoul NHA, Geertsema C, Le TTT, Tang B, Yan K, Dumenil T, van Oers MM, Suhrbier A, Pijlman GP.

30-03-2023

J Virol.

<https://pubmed.ncbi.nlm.nih.gov/36883812/>

Effect of the Tetravalent Dengue Vaccine TAK-003 on Sequential Episodes of Symptomatic Dengue.

Sáez-Llorens X, Biswal S, Borja-Tabora C, Fernando L, Liu M, Wallace D, Folschweiller N, Reynales H, LeFevre I; TIDES Study Group.

06-03-2023

Am J Trop Med Hyg.

<https://pubmed.ncbi.nlm.nih.gov/36878213/>

In the pivotal phase 3 efficacy trial ([NCT02747927](https://doi.org/10.1186/1745-6215-13-1)) of the TAK-003 dengue vaccine, 5 of 13,380 TAK-003 recipients and 13 of 6,687 placebo recipients experienced two episodes of symptomatic dengue between the first dose and the end of the study, ~57 months later (patients received the second dose 3 months after the first dose). Two of these participants experienced repeat infection with the same serotype (i.e., homotypic reinfection). In comparison with placebo, the relative risk of a subsequent episode of symptomatic dengue was 0.19 (95% CI, 0.07-0.54) in TAK-003 recipients. Based on the small number of subsequent episodes, these data suggest a potential incremental effect of TAK-003 beyond prevention of the first episode of symptomatic dengue after vaccination.

Prevalence and epidemiological aspects of Chikungunya fever in states of the Northeast region of Brazil: A systematic review.

Silva ADC, Silva ADC, de Castro PASV, Ávila IR, Bezerra JMT.

May-2023

Acta Trop.

<https://pubmed.ncbi.nlm.nih.gov/36868369/>

Chikungunya fever is a disease caused by the Chikungunya virus (CHIKV), which is transmitted through the bite of infected female hematophagous mosquitoes of the genus *Aedes* (Diptera: Culicidae). In the Americas, the first autochthonous cases of the disease were recorded in 2013. A year later, in 2014, the first records of the disease were acquired locally in Brazil, in the states of Bahia and Amapá. The present study aimed to carry out a systematic review of the literature on the prevalence and

epidemiological aspects of Chikungunya fever in states of the Northeast region of Brazil, between the years 2018 to 2022. This study was registered in the Open Science Framework (OSF) and in the International Prospective Register of Systematic Reviews (PROSPERO) and followed the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). The searches were carried out in the scientific electronic databases Literatura Latino-Americana e do Caribe em Ciências da Saúde (LILACS), U. S. National Library of Medicine (PubMed) and Scientific Electronic Library Online (SciELO), using descriptors cataloged in Descritores em Ciências da Saúde (DeCS) and Medical Subject Headings (MeSH) in Portuguese, English and Spanish. Gray literature was also searched by accessing Google Scholar to search for additional publications not captured in the selected electronic databases. Of the 19 studies included in the present systematic review, seven referred to the state of Ceará. Most cases of Chikungunya fever corresponded to the female gender (ranging from 7.5% to 100.0%), to the age group younger than 60 years (84.2%), to literate individuals (93.3%), belonging to the non-white race/color (95.21%) and blacks (100.0%), and residents of the urban area (range from 51.95% to 100.0%). As for laboratory characteristics, most notifications were diagnosed using clinical-epidemiological criteria (ranging from 71.21% to 90.35%). The epidemiological information about Chikungunya fever in the Northeast region of Brazil presented in this systematic review is useful to better understand the characteristics of the disease introduction process in the country. To this end, prevention and control strategies must be adopted, especially in the Northeast, as this region is most responsible for the number of cases of the disease in the country.

Impact of lockdown on cardiovascular disease hospitalizations in a Zero-COVID-19 country.

Moury PH, Ochida N, Motiejunaite J, Collart V, Série M, Gervolino S, Mangeas M, Bouvier JB, Couadau E, Mebazaa A, Dupont-Rouzeyrol M.

Apr-2023

Public Health.

<https://pubmed.ncbi.nlm.nih.gov/36867989/>

Key Residue in the Precursor Region of M Protein Contributes to the Neurovirulence and Neuroinvasiveness of the African Lineage of Zika Virus.

He MJ, Wang HJ, Yan XL, Lou YN, Song GY, Li RT, Zhu Z, Zhang RR, Qin CF, Li XF.

30-03-2023

J Virol.

<https://pubmed.ncbi.nlm.nih.gov/36840584/>

The Zika virus (ZIKV) represents an important global health threat due to its unusual association with congenital Zika syndrome. ZIKV strains are phylogenetically grouped into the African and Asian lineages. However, the viral determinants underlying the phenotypic differences between the lineages remain unknown. Here, multiple sequence alignment revealed a highly conserved residue

at position 21 of the premembrane (prM) protein, which is glutamic acid and lysine in the Asian and African lineages, respectively. Using reverse genetics, we generated a recombinant virus carrying an E21K mutation based on the genomic backbone of the Asian lineage strain FSS13025 (termed E21K). The E21K mutation significantly increased viral replication in multiple neural cell lines with a higher ratio of M to prM production. Animal studies showed E21K exhibited increased neurovirulence in suckling mice, leading to more severe defects in mouse brains by causing more neural cell death and destruction of hippocampus integrity. Moreover, the E21K substitution enhanced neuroinvasiveness in interferon alpha/beta (IFN- α/β) receptor knockout mice, as indicated by the increased mortality, and enhanced replication in mouse brains. The global transcriptional analysis showed E21K infection profoundly altered neuron development networks and induced stronger antiviral immune response than wild type (WT) in both neural cells and mouse brains. More importantly, the reverse K21E mutation based on the genomic backbone of the African strain MR766 caused less mouse neurovirulence. Overall, our findings support the 21st residue of prM functions as a determinant for neurovirulence and neuroinvasiveness of the African lineage of ZIKV. **IMPORTANCE** The suspected link of Zika virus (ZIKV) to birth defects led the World Health Organization to declare ZIKV a Public Health Emergency of International Concern. ZIKV has been identified to have two dominant phylogenetic lineages, African and Asian. Significant differences exist between the two lineages in terms of neurovirulence and neuroinvasiveness in mice. However, the viral determinants underlying the phenotypic differences are still unknown. Here, combining reverse genetics, animal studies, and global transcriptional analysis, we provide evidence that a single E21K mutation of prM confers to the Asian lineage strain FSS130125 significantly enhanced replication in neural cell lines and more neurovirulent and neuroinvasiveness phenotypes in mice. Our findings support that the highly conserved residue at position 21 of prM functions as a determinant of neurovirulence and neuroinvasiveness of the African lineage of ZIKV in mice.

Central nervous system manifestations of dengue infection: data from a tertiary care Centre in South India.

George JT, Lenin A, Koshy M, Vignesh CV, Sathyendra S.

31-03-2023

Postgrad Med J.

<https://pubmed.ncbi.nlm.nih.gov/36828393/>

Pathogen inactivation methods to prevent transfusion-transmissible arboviruses: A systematic review and meta-analysis.

Giménez-Richarte Á, Ortiz de Salazar MI, Giménez-Richarte MP, Larrea L, Arbona C, Marco P, Ramos-Rincón JM.

Apr-2023

Trop Med Int Health.

<https://pubmed.ncbi.nlm.nih.gov/36806816/>

Objective: Arboviruses are emerging as a relevant threat to transfusion safety. Pathogen inactivation methods (PIMs) may reduce the risk of transmission through transfusion, as long as they meet minimum standards for effectiveness. This study aims to assess the log reduction of viral load achieved with different PIMs, according to the blood product they are used on and the arbovirus targeted. **Methods:** Systematic literature review and meta-analysis. Searches were conducted in MEDLINE and Embase. The study protocol was registered in PROSPERO CRD42022312061. We selected records reporting the log reduction of viral load achieved with the main PIMs (amotosalen + UVA light [INTERCEPT], riboflavin + UV light [Mirasol], methylene blue + visible light/UVC light [THERAFLEX], solvent detergent, amustaline [INTERCEPT] and PEN110 [Inactine]), applied to any blood product (plasma, platelets, red blood cells or whole blood) and for any arbovirus. The log reduction of viral loads was assessed by obtaining the mean log reduction factor (LRF). We compared and classified the LRF of different techniques using statistical methods. **Results:** We included 59 publications reporting LRF results in 17 arboviruses. For 13 arboviruses, including Chikungunya virus, Dengue virus, West Nile virus and Zika virus, at least one of the methods achieves adequate or optimal log reduction of viral load-mean LRF ≥ 4 . The LRF achieved with riboflavin + UV light is inferior to the rest of the techniques, both overall and specifically for plasma, platelets preserved in platelet additive solution (PAS)/plasma, and red blood cells/whole blood. The LRF achieved using Mirasol is also lower for inactivating Chikungunya virus, Dengue virus and Zika virus. For West Nile virus, we found no significant differences. In plasma, the method that achieves the highest LRF is solvent/detergent; in platelets, THERAFLEX and INTERCEPT; and in red blood cells/whole blood, PEN110 (Inactine). **Conclusion:** Not all PIMs achieve the same LRF, nor is this equivalent between the different arboviruses or blood products. Overall, the LRFs achieved using riboflavin + UV light (Mirasol) are inferior to those achieved with the rest of the PIMs. Regarding the others, LRFs vary by arbovirus and blood product. In light of the threat of different arboviruses, blood establishments should have already validated PIMs and be logistically prepared to implement these techniques quickly.

Infections in travellers returning to the UK: a retrospective analysis (2015-2020).

Warner JC, Hatzioanou D, Osborne JC, Bailey DJ, Brooks TJG, Semper AE.
05-04-2023
J Travel Med.
<https://pubmed.ncbi.nlm.nih.gov/36708032/>

Analysis of cross-reactivity among flaviviruses using sera of patients with dengue showed the importance of neutralization tests with paired serum samples for the correct interpretations of serological test results for dengue.

Maeki T, Tajima S, Ando N, Wakimoto Y, Hayakawa K, Kutsuna S, Kato F, Taniguchi S, Nakayama E, Lim CK, Saijo M.

May-2023

J Infect Chemother.

<https://pubmed.ncbi.nlm.nih.gov/36702208/>

Dengue is a febrile illness caused by the dengue virus (DENV) that belongs to the genus *Flavivirus* in the family *Flaviviridae*. Cross-reactivity between flaviviruses poses a challenge while interpreting serological test results. In the present study, the cross-reactivity of sera of the patients with dengue, who traveled from Japan to DENV-endemic countries, was analyzed by using an enzyme-linked immunosorbent assay (ELISA) and neutralization test (NT). Sixteen serum samples were collected from patients with dengue and were tested for: i) IgM antibodies against Zika virus (ZIKV), West Nile virus (WNV), Japanese encephalitis virus (JEV), and tick-borne encephalitis virus (TBEV) using IgM ELISA, ii) IgG antibody against TBEV using IgG ELISA, and iii) neutralizing antibody against ZIKV, WNV, TBEV, and JEV. Among the 16 samples tested using ELISA, seven samples were IgM-positive for at least one of the other flaviviruses, and nine samples were IgG-positive for TBEV. Neutralizing antibody titers (NATs) against ZIKV, WNV, and TBEV were one-fourth or lower than those against the causative DENV in all samples. The NATs against JEV were one-fourth or lower than those against the causative DENV in six convalescent-phase serum sample among the seven convalescent-phase serum samples. The NAT against DENV of the residual one convalescent-phase serum was similar to that against JEV and that against JEV of its relevant acute-phase serum sample. These results showed that NTs with paired serum samples are important to correctly interpret the serological test results for DENV.

Chikungunya in returning travellers from Bali - A GeoSentinel case series.

Mayer AB, Consigny PH, Grobusch MP, Camprubí-Ferrer D, Huits R, Rothe C.

Mar-Apr 2023

Travel Med Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/36682574/>

Chikungunya: risks for travellers.

Simon F, Caumes E, Jelinek T, Lopez-Velez R, Steffen R, Chen LH.

05-04-2023

J Travel Med.

<https://pubmed.ncbi.nlm.nih.gov/36648431/>

Residual efficacy of selected larvicides against *Culex pipiens pipiens* (Diptera: Culicidae) under laboratory and semi-field conditions.

Sakka MK, Ioannou CS, Papadopoulos NT, Athanassiou CG.

Mar-2023

Environ Sci Pollut Res Int.

<https://pubmed.ncbi.nlm.nih.gov/36626059/>

Mosquitoes are a threat worldwide since they are vectors of important pathogens and parasites such as malaria, dengue, yellow fever, and West Nile. The residual toxicity of several commercial mosquito larvicides was evaluated for the control of *Culex pipiens pipiens* under controlled laboratory and semi-field conditions during late spring and summer of 2013. The evaluation included six different active ingredient formulations, i.e., diflubenzuron (Du-Dim), *Bacillus thuringiensis* var. *israelensis* (Bti) (Vectobac), spinosad (Mozkill), S-methoprene (Biopren), temephos (Abate), and polydimethylsiloxane (PDMS) (Aquatain), that are currently registered of and had been registered in the past for mosquito control. Under controlled laboratory conditions, the residual activity ranged from 1 week (S-methoprene) up to 2 months (spinosad, PDMS). Exposure of larvicides under semi-field conditions resulted in noticeable differences regarding their efficacy as compared to the laboratory bioassays. Exposure of S-methoprene, Bti, and spinosad, for up to 3 days, resulted in similar adult emergence to the controls. On the other hand, the residual efficacy of diflubenzuron, temephos, and PDMS ranged from 14 to 28 days, depending on the season of exposure. Longevity and fecundity of adults that had emerged from surviving larvae, in most of the cases tested, did not differ significantly from that of the controls. The results of the present study demonstrate the necessity of both field and laboratory studies to draw safe conclusions regarding the efficacy of larvicides against mosquitoes and the selection of the proper formulation for each application scenario. In addition, defining the seasonal variation in the residual toxicity of the tested formulations could be useful for improving mosquitoes' management programs.

Respiratory sequelae of dengue fever.

Mehmood A, Afzal MW, Ahmad M, Mufti M, Malik J, Zaidi SMJ.

Apr-2023

Trop Doct.

<https://pubmed.ncbi.nlm.nih.gov/36579820/>

Dengue outbreak amongst travellers returning from Cuba-GeoSentinel surveillance network, January-September 2022.

Díaz-Menéndez M, Angelo KM, de Miguel Buckley R, Bottieau E, Huits R, Grobusch MP, Gobbi FG, Asgeirsson H, Duvignaud A, Norman FF, Javelle E, Epelboin L, Rothe C, Chappuis F, Martinez GE, Popescu C, Camprubí-Ferrer D, Molina I, Odolini S, Barkati S, Kuhn S, Vaughan S, McCarthy A, Lago M, Libman MD, Hamer DH.

05-04-2023

J Travel Med.

<https://pubmed.ncbi.nlm.nih.gov/36573483/>

Increasing numbers of travellers returning from Cuba with dengue virus infection were reported to the GeoSentinel Network from June to September 2022, reflecting an ongoing local outbreak. This report demonstrates the importance of travellers as sentinels of arboviral outbreaks and highlights the need for early identification of travel-related dengue.

Varied presentations of congenital dengue infection in neonates.

Bhatter S, Jain J.

Apr-2023

Trop Doct.

<https://pubmed.ncbi.nlm.nih.gov/36691681/>

Dengue fever is a common viral infection in the tropics and is prevalent in Southeast Asia. Dengue infection is associated with increased morbidity and mortality in the perinatal period. Transplacental transfer of dengue infection is rare. Here we report of four such cases.

Pathogenesis of chronic chikungunya arthritis: Resemblances and links with rheumatoid arthritis.

Amaral JK, Bingham CO 3rd, Taylor PC, Vilá LM, Weinblatt ME, Schoen RT.

Mar-Apr 2023

Travel Med Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/36549417/>

Chikungunya virus (CHIKV) infection results from transmission by the mosquito vector. Following an incubation period of 5-7 days, patients develop an acute febrile illness, chikungunya fever (CHIKF), characterized by high fevers, maculopapular rash, headaches, polyarthritis/arthritis, myalgias, nausea, vomiting, and diarrhea. Joint pain is often severe, and most often involves the hands, the wrists, the ankles, and the metatarsal-phalangeal joints of the feet. Many patients recover within several weeks, but up to 50% develop chronic joint pain and swelling for more than 12 weeks, then we refer to these symptoms as chronic chikungunya arthritis (CCA). The pathogenesis of CCA is not well understood. In this article, we suggest that mesenchymal stem cells (MSCs) may play an important role in this pathogenesis. This heterogeneous group of multipotent cells, morphologically similar to fibroblasts, may undergo epigenetic changes capable of generating aberrant progenies. However, we believe that there is no need for a latent infection. In our pathogenic hypothesis, CHIKV infection of MSCs would cause epigenetic changes both in MSCs themselves and in their progenies, without the need for reactivation of dormant viruses.

Thermodynamic characterization of a macrocyclic Zika virus NS2B/NS3 protease inhibitor and its acyclic analogs.

Hammerschmidt SJ, Huber S, Braun NJ, Lander M, Steinmetzer T, Kersten C.

Apr-2023

Arch Pharm (Weinheim).

<https://pubmed.ncbi.nlm.nih.gov/36480352/>

Dengue and COVID-19 co-infections: an important consideration in the tropics.

Dalugama C, Seneviratne SL.

03-04-2023

Trans R Soc Trop Med Hyg.

<https://pubmed.ncbi.nlm.nih.gov/36479900/>

PCR investigation of infections in patients consulting at a healthcare centre over a four-year period during the Grand Magal of Touba.

Goumballa N, Sambou M, Samba DF, Bassene H, Bedotto M, Aidara A, Dieng M, Hoang VT, Parola P, Sokhna C, Gautret P.

Mar-Apr 2023

Travel Med Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/36470351/>

Background: Respiratory and gastrointestinal symptoms and febrile illness are the most common complaints among ill pilgrims attending the Grand Magal of Touba (GMT) in Senegal. **Methods:** Patients presenting with respiratory or gastrointestinal symptoms or febrile systemic illnesses were recruited between 2018 and 2021 at a healthcare centre close to Touba. Respiratory, gastrointestinal and blood samples were tested for potential pathogens using qPCR. **Results:** 538 patients were included. 45.5% of these were female, with a median age of 17 years. Of the 326 samples collected from patients with a cough, 62.8% tested positive for at least one virus, including influenza viruses (33.1%). A high positivity rate of bacterial carriage was observed for *Haemophilus influenzae* (72.7%), *Streptococcus pneumoniae* (51.2%) and *Moraxella catarrhalis* (46.0%). Of the 95 samples collected from patients with diarrhoea, 71.3% were positive, with high rates of bacterial carriage, ranging from 4.2% for *Tropheryma whippelii* to 45.3% for Enteropathogenic *Escherichia coli*. Of the 141 blood samples collected from patients with fever, 31.9% were positive including *Plasmodium falciparum* (21.3%), *Borrelia* sp. (5.7%) and dengue virus (5.0%). **Conclusion:** This study provides insight into the aetiology of most common infections at the GMT on which to base therapeutic options.

Recent Advances in Biosensors for Detection of COVID-19 and Other Viruses.

Patel SK, Surve J, Parmar J, Ahmed K, Bui FM, Al-Zahrani FA.

2023

IEEE Rev Biomed Eng.

<https://pubmed.ncbi.nlm.nih.gov/36197867/>

Dengue-related maculopathy.

Richier Q, Bataille N, Gauzère L, Safa I, Villeroy F, Raffray L.

05-04-2023

J Travel Med.

<https://pubmed.ncbi.nlm.nih.gov/36130206/>

Sublethal exposure to spinetoram impacts life history traits and dengue virus replication in *Aedes aegypti*.

Wang L, Pang Z, Chen Q, Song Z, Lu Y, Yang M, Huang J, Yu XQ, Wang X.

Apr-2023

Insect Sci.

<https://pubmed.ncbi.nlm.nih.gov/36069276/>

Insecticides are anthropogenic environmental stressors and also a common stressor for mosquito vectors. However, the use of insecticides is often guided by short-term efficacy, and the sublethal effect on their target or nontarget species has long been ignored. Here, we analyzed how sublethal exposure of the promising vector-control bioinsecticide spinetoram to *Aedes aegypti* larvae alter adult performance and susceptibility to dengue virus (DENV) infection. We found that the surviving adult mosquitoes were significantly smaller and exhibited weaker blood-feeding capacity than control females, apart from the extended immature development period. In terms of reproductive potential, although the F_0 generation produced a similar number of eggs and offspring during the first gonotrophic cycle, the survival rates of the F_1 generations were significantly lower as compared to the control group, suggesting transgenerational sublethal effects on the F_1 generation. Notably, surviving adult females had higher DENV-2 viral loads than the control group after spinetoram sublethal exposure. Mechanistically, transcriptomic analysis showed that inhibition of oxidative phosphorylation may function in stimulating DENV production in adult *Ae. aegypti*. In Aag2 cells, significant accumulation of apoptosis, mitochondrial reactive oxygen species production, and DENV-2 replication by spinetoram exposure consistently support our conclusion. Our study highlights the threat of sublethal spinetoram exposure on outbreaks of mosquito-borne viruses.

Analyzing implementation of public health interventions: A need for rigor, and the challenges of stakeholder involvement.

Ridde V, Carillon S, Desgrées du Lou A, Sombié I.

Apr-2023

Rev Epidemiol Sante Publique.

<https://pubmed.ncbi.nlm.nih.gov/35835715/>

Mosquito Larvicidal Activity of Compounds from Unripe Fruit Peel of Avocado (*Persea americana* Mill.).

Louis MRLM, Rani VP, Krishnan P, Reagan AD, Balakrishna K, Ignacimuthu S, Packiam SM, Maheswaran R, Shiota O.

Apr-2023

Appl Biochem Biotechnol.

<https://pubmed.ncbi.nlm.nih.gov/35201599/>

Challenges in diagnosing fever in traveler returning from tropical areas - is it dengue or chikungunya? Case report.

Bętkowska A, Hanke J, Krankowska D, Mikula T, Wiercińska-Drapała A.

2022

Przegl Epidemiol.

<https://pubmed.ncbi.nlm.nih.gov/37017189/>

Arthropod-borne viral infections caused by dengue virus (DENV) and chikungunya virus (CHIKV) are prevalent in the

same regions and are spread by the same mosquito type (*Aedes*) and have similar clinical manifestations. This study emphasized the challenges of diagnosing fever in a patient returning from a tropical area. We report a case of a 52-year-old patient who presented with fever, myalgia, and headache after travelling to Laos and Thailand. After ten days of the disease, the diagnosis of chikungunya was made. Recent travel history should be a standard part of assessment when consulting febrile patients and is essential for further diagnosis. Malaria should permanently be excluded from travellers returning from tropical regions with fever. In the differential diagnosis, dengue, chikungunya, and other mosquito-borne infections should be considered. Patients wishing to travel to such areas need to be educated beforehand on the necessary preventative measures.

Rage

Progress towards dog-mediated rabies elimination in PR China: a scoping review.

Shen T, Welburn SC, Sun L, Yang GJ.

06-04-2023

Infect Dis Poverty.

<https://pubmed.ncbi.nlm.nih.gov/37024944/>

Background: Rabies continues to be a serious threat to global public health endangering people's health and public health safety. In the People's Republic of China, multi-sectoral and comprehensive prevention and control strategies have aimed to extensively curb human rabies transmission. Here, we examine the current state of rabies infection in China, explore strategic interventions put in place in response to WHO's ambition of "Zero rabies deaths by 2030" and critically assess the constraints and feasibility of dog-mediated rabies elimination in China.

Methods: This study analyzed and evaluated the process towards dog-mediated rabies elimination in China from five perspectives: namely, human, dog, policy, challenge, and prospects. Evidence-based data on progress of dog-mediated rabies elimination in China was derived from a number of sources; a literature search was undertaken using PubMed, Web of Science and CNKI databases, distribution data for human rabies cases as derived from the Data-center of the China Public Health Science and policy and document data were obtained from official websites of the relevant China ministries and commissions. **Results:** The incidence of human rabies cases in China have shown a downward trend year-on-year since 2007. Implementation of a government-led, multi-sectoral "One Health" approach to combating rabies has driven down the total number of rabies deaths nationwide to around 200 in 2020. The number of provincial-level administrative divisions (PLADs) reporting human cases of rabies has also decreased to 21 in 2020, 13 of which reported less than 10 cases. Furthermore, the number of outpatient visits seeking rabies post-exposure prophylaxis has risen dramatically over the past two decades, with demand being 15 times higher than it was initially. There remain however, significant gaps in rabies elimination outcomes across the different regions of China. To date

the target of achieving a canine rabies vaccination rate of > 75% has not been met. The challenges of rabies immunization of dogs and dog management in underdeveloped cities and rural areas need to be addressed together with more effective animal surveillance and rabies risk from and too wildlife and livestock. **Conclusions:** The Chinese government-led, multi-sectoral "One Health" approach to combating rabies and has made significant progress over the past decade. Development and adoption of more cost-effective One Health strategies can achieve more nationally beneficial rabies elimination outcomes. The ambitious target of "Zero rabies deaths by 2030" can be met through establishment of long-lasting herd immunity in dogs by means of dog mass vaccination campaigns, dog population management, epidemiological surveillance and the application of large-scale oral rabies vaccine to eliminate rabies in wild animals coupled with deployment of cost-effective human post-exposure prophylaxis, and community education.

Increase in rabies cases during COVID-19 pandemic: Is there a connection?

Rasizadeh R, Hossein Bannazadeh Baghi.

31-03-2023

J Infect Dev Ctries.

<https://pubmed.ncbi.nlm.nih.gov/37023440/>

Single-Atom Nanocatalytic Therapy for Suppression of Neuroinflammation by Inducing Autophagy of Abnormal Mitochondria.

Li B, Bai Y, Yion C, Wang H, Su X, Feng G, Guo M, Peng W, Shen B, Zheng B.

05-04-2023

ACS Nano.

<https://pubmed.ncbi.nlm.nih.gov/37018124/>

Bif-1c Attenuates Viral Proliferation by Regulating Autophagic Flux Blockade Induced by the Rabies Virus CVS-11 Strain in N2a Cells.

Hou P, Guo Y, Jin H, Sun J, Bai Y, Li W, Li L, Cao Z, Wu F, Zhang H, Li Y, Yang S, Xia X, Huang P, Wang H.

04-04-2023

Microbiol Spectr.

<https://pubmed.ncbi.nlm.nih.gov/37014208/>

Bax-interacting factor-1 (Bif-1) is a multifunctional protein involved in apoptosis, autophagy, and mitochondrial morphology. However, the associations between Bif-1 and viruses are poorly understood. As discrete Bif-1 isoforms are selectively expressed and exert corresponding effects, we evaluated the effects of neuron-specific/ubiquitous Bif-1 isoforms on rabies virus (RABV) proliferation. First, infection with the RABV CVS-11 strain significantly altered Bif-1 expression in mouse neuroblastoma (N2a) cells, and Bif-1 knockdown in turn promoted RABV replication. Overexpression of neuron-specific Bif-1 isoforms (Bif-1b/c/e) suppressed RABV replication. Moreover, our study showed that Bif-1c colocalized with LC3 and partially alleviated the incomplete autophagic flux induced by

RABV. Taken together, our data reveal that neuron-specific Bif-1 isoforms impair the RABV replication process by abolishing autophagosome accumulation and blocking autophagic flux induced by the RABV CVS-11 strain in N2a cells. **IMPORTANCE** Autophagy can be triggered by viral infection and replication. Autophagosomes are generated and affect RABV replication, which differs by viral strain and infected cell type. Bax-interacting factor-1 (Bif-1) mainly has a proapoptotic function but is also involved in autophagosome formation. However, the association between Bif-1-involved autophagy and RABV infection remains unclear. In this study, our data reveal that a neuron-specific Bif-1 isoform, Bif-1c, impaired viral replication by unchoking autophagosome accumulation induced by RABV in N2a cells to a certain extent. Our study reveals for the first time that Bif-1 is involved in modulating autophagic flux and plays a crucial role in RABV replication, establishing Bif-1 as a potential therapeutic target for rabies.

Safety of purified Vero cell rabies vaccine manufactured in Pakistan: A comparative analysis of intradermal and intramuscular routes.

Ali W, Ismail Tajik M, Ali I, Gul A, Khan JZ.

03-04-2023

Curr Med Res Opin.

<https://pubmed.ncbi.nlm.nih.gov/37011066/>

An epidemiological synthesis of emerging and re-emerging zoonotic disease threats in Cameroon, 2000-2022: a systematic review.

Tahmo NB, Wirsiy FS, Nnamdi DB, Tongo M, Lawler JV, Broadhurst MJ, Wondji CS, Brett-Major DM.

17-12-2023

IJID Reg.

<https://pubmed.ncbi.nlm.nih.gov/37009575/>

Introduction: Population factors such as urbanization, socio-economic, and environmental factors are driving forces for emerging/re-emerging zoonotic diseases in Cameroon. To inform preparedness and prioritization efforts, this study mapped out epidemiological data (including prevalence) of zoonotic diseases occurring in Cameroon between 2000 and 2022 by demographic factors. **Methods:** Following the PRISMA guidelines, a protocol was registered in the PROSPERO database (CRD42022333059). Independent reviewers searched the PubMed, Embase, CINAHL, Cochrane, and Scopus databases on May 30, 2022 for relevant articles; duplicates were removed, and the titles, abstracts, and full texts were screened to identify eligible articles. **Results:** Out of 4142 articles identified, 64 eligible articles were retrieved in the database search and an additional 12 from the cited literature ($N = 76$). Thirty-five unique zoonoses (viral, bacterial, and parasitic) were indexed, including Cameroon priority zoonoses: anthrax, bovine tuberculosis, Ebola and Marburg virus disease, highly pathogenic avian influenza, and rabies. The number of studies varied by region, ranging from 12 in the Far North to 32 in the Centre Region. The most reported were as follows: brucellosis

(random-effects pooled estimate proportion (effect size), ES 0.05%, 95% confidence interval (CI) 0.03-0.07; $n = 6$), dengue (ES 0.13%, 95% CI 0.06-0.22; $n = 12$), avian and swine influenza virus (ES 0.10%, 95% CI 0.04-0.20; $n = 8$), and toxoplasmosis (ES 0.49%, 95% CI 0.35-0.63; $n = 11$), although I^2 values were greater than 75%, thus there was high inter-study heterogeneity ($P < 0.01$). **Conclusions:** This understanding of the distribution of emerging and re-emerging zoonotic threats in Cameroon is vital to effective preventive and resource prioritization measures.

Trachome

A Virtual Reading Center Model Using Crowdsourcing to Grade Photographs for Trachoma: Validation Study.

Brady CJ, Cockrell RC, Aldrich LR, Wolle MA, West SK.

06-04-2023

J Med Internet Res.

<https://pubmed.ncbi.nlm.nih.gov/37023420/>

Background: As trachoma is eliminated, skilled field graders become less adept at correctly identifying active disease (trachomatous inflammation-follicular [TF]). Deciding if trachoma has been eliminated from a district or if treatment strategies need to be continued or reinstated is of critical public health importance. Telemedicine solutions require both connectivity, which can be poor in the resource-limited regions of the world in which trachoma occurs, and accurate grading of the images. **Objective:** Our purpose was to develop and validate a cloud-based "virtual reading center" (VRC) model using crowdsourcing for image interpretation. **Methods:** The Amazon Mechanical Turk (AMT) platform was used to recruit lay graders to interpret 2299 gradable images from a prior field trial of a smartphone-based camera system. Each image received 7 grades for US \$0.05 per grade in this VRC. The resultant data set was divided into training and test sets to internally validate the VRC. In the training set, crowdsourcing scores were summed, and the optimal raw score cutoff was chosen to optimize kappa agreement and the resulting prevalence of TF. The best method was then applied to the test set, and the sensitivity, specificity, kappa, and TF prevalence were calculated. **Results:** In this trial, over 16,000 grades were rendered in just over 60 minutes for US \$1098 including AMT fees. After choosing an AMT raw score cut point to optimize kappa near the World Health Organization (WHO)-endorsed level of 0.7 (with a simulated 40% prevalence TF), crowdsourcing was 95% sensitive and 87% specific for TF in the training set with a kappa of 0.797. All 196 crowdsourced-positive images received a skilled overread to mimic a tiered reading center and specificity improved to 99%, while sensitivity remained above 78%. Kappa for the entire sample improved from 0.162 to 0.685 with overreads, and the skilled grader burden was reduced by over 80%. This tiered VRC model was then applied to the test set and produced a sensitivity of 99% and a specificity of 76% with a kappa of 0.775 in the entire set. The prevalence estimated by the VRC was 2.70% (95% CI 1.84%-3.80%) compared to the ground truth prevalence of 2.87% (95% CI 1.98%-4.01%). **Conclusions:** A VRC model

using crowdsourcing as a first pass with skilled grading of positive images was able to identify TF rapidly and accurately in a low prevalence setting. The findings from this study support further validation of a VRC and crowdsourcing for image grading and estimation of trachoma prevalence from field-acquired images, although further prospective field testing is required to determine if diagnostic characteristics are acceptable in real-world surveys with a low prevalence of the disease.

Targeted mass azithromycin distribution for trachoma: a community-randomized trial (TANA II).

Mahmud H, Haile BA, Tadesse Z, Gebresillasie S, Shiferaw A, Zerihun M, Liu Z, Callahan EK, Cotter SY, Varnado NE, Oldenburg CE, Porco TC, Lietman TM, Keenan JD.

Apr-2023

Clin Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/37021692/>

Ulcère de Buruli

Buruli Ulcer a Diagnostic Challenge-A Report from Non-Endemic Area.

Lahiri K, Dhar S, Saha A.

Nov-Dec 2022

Indian J Dermatol.

<https://pubmed.ncbi.nlm.nih.gov/36998861/>

Buruli ulcer caused by *Mycobacterium ulcerans* subsp. *shinshuense*: A case report.

Fujimori T, Hagiya H, Iio K, Yamasaki O, Miyamoto Y, Hoshino Y, Kakehi A, Okura M, Minabe H, Yokoyama Y, Otsuka F, Higashikage A.

May-2023

J Infect Chemother.

<https://pubmed.ncbi.nlm.nih.gov/36813163/>

Buruli ulcer is the third most common mycobacterial infection worldwide and is mainly diagnosed in tropical regions. Globally, this progressive disease is caused by *Mycobacterium ulcerans*; however, *Mycobacterium ulcerans* subsp. *shinshuense*, an Asian variant, has been exclusively identified in Japan. Because of insufficient clinical cases, the clinical features of *M. ulcerans* subsp. *shinshuense*-associated Buruli ulcer remain unclear. A 70-year-old Japanese woman presented with erythema on her left backhand. The skin lesion deteriorated without an apparent etiology of inflammation, and she was referred to our hospital 3 months after disease onset. A biopsy specimen was incubated in 2% Ogawa medium at 30 °C. After 66 days, we detected small yellow-pigmented colonies, suggesting scotochromogens. Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI Biotyper; Bruker Daltonics, Billerica, MA, USA) indicated that the organism was *Mycobacterium pseudoshottsii* or *Mycobacterium marinum*. However, additional PCR testing for the insertion sequence 2404 (IS2404) was positive, suggesting that the pathogen was

either *M. ulcerans* or *M. ulcerans* subsp. *shinshuense*. Further examination by 16S rRNA sequencing analysis, focusing on nucleotide positions 492, 1247, 1288, and 1449-1451, we finally identified the organism as *M. ulcerans* subsp. *shinshuense*. The patient was successfully treated with 12 weeks of clarithromycin and levofloxacin treatment. Mass spectrometry is the latest microbial diagnostic method; however, it cannot be used to identify *M. ulcerans* subsp. *shinshuense*. To accurately detect this enigmatic pathogen and uncover its epidemiology and clinical characteristics in Japan, more accumulation of clinical cases with accurate identification of the causative pathogen is essential.

Lèpre

Leprosy & Broken Bacilli on Slit Skin Smear.

Sukanya G, Manoharan K, Logeswari PT, Naidu DK.

06-04-2023

QJM.

<https://pubmed.ncbi.nlm.nih.gov/37021961/>

Bacterial Lesions of the Oral Mucosa.

Cabido LF, Romañach MJ.

May-2023

Oral Maxillofac Surg Clin North Am.

<https://pubmed.ncbi.nlm.nih.gov/37019503/>

High prevalence of olfactory impairment among leprosy patients: A cross-sectional study.

Kondo RN, Araújo MCP, Ramos PM, Miot HA, Fornazieri MA.

05-04-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/37018206/>

Background: The effect of leprosy on the sense of smell is not yet fully established. Studies that have relied only on patients' perceptions may have under- or over-estimated the change in smell perception. A validated and psychophysical method is necessary to avoid these errors in assessment. **Objectives:** This study aimed to validate the existence of olfactory involvement in leprosy patients. **Methods:** A cross-sectional, controlled study was conducted, in which individuals with leprosy (exposed individuals) and individuals without leprosy (control patients) were recruited. For each exposed individual, we selected two control patients. A total of 108 patients (72 control patients and 36 exposed individuals) with no history of infection with the new coronavirus (COVID-19) took the University of Pennsylvania Smell Identification Test (UPSIT). **Results:** Most exposed individuals had olfactory dysfunction [$n = 33$, 91.7% (CI 95%: 77.5%-98.3%)] when compared with the control patients [$n = 28$, 38.9% (CI 95%: 27.6%-51.1%)], but only two (5.6%) had olfactory complaints. The olfactory function was significantly worse among exposed individuals [UPSIT leprosy = 25.2 (CI 95%: 23.1-27.3) when compared with the UPSIT control patients = 34.1 (CI 95%: 33.0-35.3);

$p < 0.001$]. The risk of olfactory loss was higher among the exposed individuals [OR: 19.5 (CI 95%: 5.18-105.70; $p < 0.001$)]. **Conclusions:** Olfactory dysfunction was highly prevalent among exposed individuals, although they had little or no self-knowledge of the disorder. The results show that it is important to assess the sense of smell in exposed individuals.

Leprosy reactions after SARS-COV2 (COVID-19) infection.

Gutiérrez-Villarreal IM, Ocampo-Candiani J, Villarreal-Martinez A, Gomez-Flores M, Fernández LT, Rodríguez-Tamez G, Pérez-Garza DM, González-Martínez G, Yamalliel-Ortega LA, Chavez-Alvarez S.

05-04-2023

J Eur Acad Dermatol Venereol.

<https://pubmed.ncbi.nlm.nih.gov/37016975/>

A comparative study of modulatory interaction between cytokines and apoptotic proteins among Scleroderma patients with and without pulmonary involvement.

Khadilkar P, Chougule D, Tipnis T, Khopkar U, Nadkar M, Rajadhyaksha A, Kini S, Kharkar V, Athvale A, Athvale T, Madkaikar M, Pradhan V.

01-04-2023

Cytokine.

<https://pubmed.ncbi.nlm.nih.gov/37011542/>

Background: Interstitial lung disease (ILD) and pulmonary arterial hypertension (PAH) are the most eminent forms of pulmonary involvement in Scleroderma. In this study we investigate the interaction between cytokines and apoptotic proteins in treatment naïve Scleroderma (SSc) patients with and without pulmonary involvement.

Methods: Newly diagnosed treatment naïve Scleroderma (SSc) patients ($n = 100$) and healthy controls ($n = 100$) were enrolled. Patients were classified as ILD-SSc, PAH-SSc and non-pulmonary SSc (np-SSc). Study variables like mRSS score, autoantibody profile, serum cytokines, serum TGF- β (1,2,3) and apoptotic proteins were assessed for these patients. **Results:** Scleroderma patients showed elevated levels of serum cytokines, but significantly lower IL-22 and TGF- β 1 when compared to healthy controls ($p < 0.05$). Apoptotic proteins were significantly elevated among Scleroderma patients, but the patient groups also showed significant lower caspase 1/3/9 levels when compared to healthy controls ($p < 0.05$). ILD-SSc patients reported higher mRSS score ($p = 0.0436$) when compared with PAH-SSc and np-SSc. In ILD-SSc patients, finger tightening ($p = 0.0481$) and calcinosis/lesions ($p = 0.0481$) were significant clinical presentations whereas, digital ulcers were significantly prominent in np-SSc patients ($p = 0.0132$). Elevated TGF- β 3 levels ($p = 0.02$) in SSC-ILD and reduced IL-4 levels ($p = 0.02$) in SSC-PAH were significant cytokines as compared to np-SSc. Significant correlations were obtained among serum cytokines and apoptotic proteins in Scleroderma patients with and without pulmonary involvement. ($p < 0.05$) **CONCLUSION:** Our study highlights the correlation between mRSS score, cytokines and apoptotic proteins in SSc patients with pulmonary

involvement. A longitudinal follow up in these patients with assessment of these immunological parameters may be helpful in monitoring the disease.

Determinant factors of leprosy-related disability; comparison of acceleration failure time and parametric shared frailty models.

Masresha BM, Yesuf KM, Moyehodie YA, Biresaw HB, Mulugeta SS, Addisia GD.

03-04-2023

PLoS One.

<https://pubmed.ncbi.nlm.nih.gov/37011051/>

Background: Leprosy is an illness persisting for a long time or constantly recurring brought about by Mycobacterium leprae. The collusion of the causing agent with Schwann cells leads to incapability of being changed loss of fringe nerve tissue; followed by incapacity and that is not restricted to actual powerlessness yet additionally makes a negative picture, prompting segregation and social disgrace against the altered people also, their families.

Methods: The analysis of this study comprises 205 samples of patients at All African TB and Leprosy Rehabilitation and Training Centre from January 2015 up to December 2019 G.C who were taking medication for leprosy and who possess all necessary data. Territorial conditions in the region of the patients were utilized as a clustering impact in all frailty models. Acceleration failure time models and parametric shared frailty models with Weibull and log-strategic patterns were utilized to dissect hazard factors related to disability ensued by leprosy. All fitted models were looked at by utilizing AIC. **Results:** From that of 205, 69(33.7%) experienced at least one kind of disability grade during treatment taking. In light of AIC, log-logistic-gamma shared frailty model was the final best fitting model and also there was considerable variation among patients. The final model showed the age of patients, symptom duration, treatment category of patients, and sensory loss were found to be the most significant determinants of leprosy disability. **Conclusion:** In this investigation, there is proof of heterogeneity at the group level and disability was related to the age of patients, symptom duration, treatment category of patient, what's more, sensory loss subsequently, uncommon consideration ought to be given to these huge indicators, which eventually diminish the event of disability. To lessen the patient-related postponement, the program should lay more noteworthy accentuation on bringing issues to light in the local area by zeroing in on key messages like indications, inability result of the late discovery, accessibility of free treatment what's more, accessibility of disease care in general wellbeing office.

Small Finger Proximal Intraphalangeal Joint Chronic Arthritis Secondary to Leprosy: A Case Report.

Elbayer AM, Ibrahim MM, Alharami S, Wani I, Elhessy AH.

30-03-2023

Cureus.

<https://pubmed.ncbi.nlm.nih.gov/37009364/>

The Association of Depression, Loneliness, and Internet Addiction Levels in Male Bachelor of Medicine, Bachelor of Surgery (MBBS) Students With Androgenetic Alopecia Male Pattern Baldness in a Medical College in Kolar, India.

Prasanna H, T S R, K SK, Kk A, Kiran M, Reddy M.

28-02-2023

Cureus.

<https://pubmed.ncbi.nlm.nih.gov/37007329/>

Introduction The genetically determined progressive process that causes a gradual conversion of terminal hair into vellus hair is known as androgenetic alopecia (AGA). AGA male pattern baldness is very common among male medical students whose self-image is severely deteriorated by AGA and this affects the quality of their professional career. Hence, the assessment of the association of depression, loneliness, and internet addiction levels of male Bachelor of Medicine, Bachelor of Surgery (MBBS) students with AGA male pattern baldness is essential to improving academic and professional performance. **Aims and objectives** The aim of this study is to evaluate the effects of AGA male pattern baldness and its severity on depression, loneliness, and internet addiction levels of male medical students in Kolar. **Materials and methods** This questionnaire-based cross-sectional study was conducted among 100 male MBBS students from Sri Devaraj Urs Medical College in Kolar with AGA male pattern baldness of varying grades. The participants were selected through simple random sampling from July 2022 to November 2022 with their prior informed consent. Students' AGA severity was evaluated clinically using the Norwood-Hamilton Classification. Their levels of depression, loneliness, and internet addiction were assessed using the standardized Beck Depression Inventory (BDI) scale, University of Carolina Los Angeles - Loneliness Scale (UCLA-LS), and Young Internet Addiction Test - Short Form (YIAT-SF), respectively, and one-way analysis of variance (ANOVA) was used to ascertain the statistical significance between the means of BDI, UCLA-LS, and YIAT-SF with the severity of AGA. Chi-square/Fisher Exact test was used to find the significance of study parameters on a categorical scale between two or more groups. Significance was assessed at a 5% level of significance. **Results** The mean of BDI (17.38, 25.11, 34.62, 41.25, 51.00), UCLA-LS (18.72, 27.51, 36.69, 43.5, 49.00), and YIAT-SF (20.51, 31.77, 50.31, 60.25, 72.00) scores in each of the AGA grades from Grade I to Grade V in our study showed that these scores increase along with an increase in the severity of AGA and are statistically significant. The frequency distribution of male medical students with varied degrees of AGA and the level of depression, loneliness, and internet addiction levels assessed by the BDI, UCLA-LS, and YIAT-SF showed a robust and statistically significant association between the severity of AGA and the severity of depression, loneliness, and internet addiction levels. **Conclusion** The current study showed that there is a statistically significant association of depression, loneliness, and internet addiction levels in male MBBS students with AGA male pattern baldness.

Atypical Presentations of Myocardial Infarction: A Systematic Review of Case Reports.

Khan IA, Karim HMR, Panda CK, Ahmed G, Nayak S.

26-02-2023

Cureus.

<https://pubmed.ncbi.nlm.nih.gov/36999116/>

A Case of Familial Lichen Nitidus with Atypical Morphology.

Gupta SK, Dhiman A, Shukla R.

Nov-Dec 2022

Indian J Dermatol.

<https://pubmed.ncbi.nlm.nih.gov/36998897/>

The Mystery of an Asymptomatic Peri-Orbital Subcutaneous Nodule in a Patient from Western India.

Bindu R, Bhosale A, Awake P.

Nov-Dec 2022

Indian J Dermatol.

<https://pubmed.ncbi.nlm.nih.gov/36998896/>

Myiasis as a Rare Complication of Neglected Pemphigus Vulgaris: Two Cases.

Singh A, Kumar TS, Ganguly S, Reddy MPS.

Nov-Dec 2022

Indian J Dermatol.

<https://pubmed.ncbi.nlm.nih.gov/36998895/>

Oral and Systemic Manifestations in Leprosy a Hospital Based Study with Literature Review.

Vohra P.

Nov-Dec 2022

Indian J Dermatol.

<https://pubmed.ncbi.nlm.nih.gov/36998854/>

Introduction: Leprosy is a chronic granulomatous disease of the peripheral nerve and muscle of upper respiratory tract. Consequence to the neighbouring primary site, oral lesions have been seen in 20-60% of patients with leprosy mainly lepromatous leprosy. The lepromatous nodules may be infective and may lead to the spread of disease and hence require proper diagnosis. **Aim:** To assess oral lesion in leprosy patients. To assess the disease and the occurrence of oral lesion according to age and gender. To detect any primary lesion in oral cavity and compare these lesions in duration to study. **Material and methods:** One hundred patients with leprosy were examined and their oral manifestations were recorded. **Results:** It was found that 70 (70%) leprosy patients showed oral manifestations. Eighteen (25%) had chronic generalized periodontitis, 9 (12.8%) cases of oral melanosis, 7 (10%) atrophy of papillae and loss of taste sensation each, 6 (8.5%) complained of aphthous and candidiasis each, 5 (7.14%) depigmentation and 4 (5.71%) smokers palate, oral submucous fibrosis and fissured tongue. **Conclusion:** Our clinical findings are in conjugation with previous

studies; however, as per the review of literature, this is the first study worldwide where we have examined 100 cases of leprosy which has not been documented till date. We suggest that the lesser incidence of oral lesions is observed recently compared to older reports because of more effective present treatment which is initiated earlier.

A Clinical Study of Efficacy of Autologous Platelet-Rich Fibrin (PRF) in Chronic Non-Healing Ulcers.

Madhu M, Hulmani M, Naveen Kumar AC, Kumar VJ.

Nov-Dec 2022

Indian J Dermatol.

<https://pubmed.ncbi.nlm.nih.gov/36998844/>

Prevalence of Anxiety and Depression among People Living with Leprosy and its Relationship with Leprosy-Related Stigma.

Sharma P, Shakya R, Singh S, Bhandari AR, Shakya R, Amatya A, Joshi C, Gurung G.

Nov-Dec 2022

Indian J Dermatol.

<https://pubmed.ncbi.nlm.nih.gov/36998835/>

Background: Leprosy, a chronic infectious disease, is associated with a high risk of psychiatric disorders. **Aims and objectives:** We aim to estimate the prevalence of anxiety and depressive symptoms among people living with leprosy at a special community residence in Nepal. We also aimed to find the correlation between anxiety and depression. **Materials and methods:** This is a cross-sectional descriptive study conducted in a community of people with leprosy staying at a centre in Nepal using all enumerative sampling. The semi-structured schedule, hospital anxiety and depression scale and stigma assessment and reduction of impact (SARI) stigma scale were applied among 119 participants. **Results:** About 10.1% ($n = 12$) and 12.6% ($n = 15$) of participants scored above the threshold score indicative of definitive clinically significant anxiety and depression symptoms. In multivariable analysis, leprosy-related stigma and attribution of leprosy to bad deeds were significant correlates of anxiety; whereas leprosy-related stigma and duration of stay at the centre were significant correlates of depression. **Conclusion:** The prevalence of depression and anxiety symptoms among people living with leprosy is higher than that in the general population. Stigma is a significant correlation for both. It is important to screen for mental health issues while managing patients with leprosy and implement strategies aimed at leprosy-related stigma reduction.

Cutaneous Metal Hypersensitivity Syndrome in Total Knee Arthroplasty with Titanium-Coated Implant.

Prasanna S, Rane M, Singh S, Kharkar V.

Nov-Dec 2022

Indian J Dermatol.

<https://pubmed.ncbi.nlm.nih.gov/36998832/>

Skin Lesion in Haematological Malignancy-How Dermatology Can Save the Life of a Patient.

Gorai S, Das K, Chakrapani A, Lahiri K, Bhattacharyya S.

Nov-Dec 2022

Indian J Dermatol.

<https://pubmed.ncbi.nlm.nih.gov/36998819/>

Successful Treatment of Recurrent Oral and Genital Ulcers in Behcet's Disease with Rituximab.

Mohta A, Jain SK, Mehta RD.

Nov-Dec 2022

Indian J Dermatol.

<https://pubmed.ncbi.nlm.nih.gov/36998818/>

B lymphocytes deficiency results in altered immune response and increased susceptibility to Mycobacterium leprae in a murine leprosy model.

Azevedo MCS, Marques H, Binelli LS, Malange MSV, Devides AC, Fachin LRV, Soares CT, Belone AFF, Rosa PS, Garlet GP, Trombone APF.

May-2023

Cytokine.

<https://pubmed.ncbi.nlm.nih.gov/36996537/>

Leprosy is a chronic and infectious disease that primarily affects the skin and peripheral nervous system, presenting a wide spectrum of clinical forms with different degrees of severity. The distinct host immune response patterns developed in the response to the bacillus *Mycobacterium leprae*, the leprosy etiologic agent, are associated with the spectral clinical forms and outcome of the disease. In this context, B cells are allegedly involved in the disease immunopathogenesis, usually as antibody-producing cells, but also as potential effector or regulatory elements. In order to determine the regulatory B cells role in experimental leprosy, this study evaluated the outcome of *M. leprae* infection in B cell deficient mice (BKO) and WT C57Bl/6 control, by means of microbiological/bacilloscopic, immunohistochemical and molecular analysis, performed 8 months after *M. leprae* inoculation. The results demonstrated that infected BKO showed a higher bacilli number when compared with WT animals, demonstrating the importance of these cells in experimental leprosy. The molecular analysis demonstrates that the expression of IL-4, IL-10 and TGF- β was significantly higher in the BKO footpads when compared to WT group. Conversely, there was no difference in IFN- γ , TNF- α and IL-17 expression levels in BKO and WT groups. IL-17 expression was significantly higher in the lymph nodes of WT group. The immunohistochemical analysis revealed that M1 (CD80 $^{+}$) cells counts were significantly lower in the BKO group, while no significant difference was observed to M2 (CD206 $^{+}$) counts, resulting a skewed M1/M2 balance. These results demonstrated that the absence of B lymphocytes contribute to the persistence and multiplication of *M. leprae*, probably due to the increased expression of the IL-4, IL-10 and TGF- β cytokines, as well

as a decrease in the number of M1 macrophages in the inflammatory site.

Genetic diversity of *Mycobacterium leprae* in the state of São Paulo, an area of low-leprosy incidence in Brazil.

Finardi AJ, Oliveira NG, Moraes EB, Batista LCF, Bortolomai BE, Suffys PN, Baptista IMFD.

27-03-2023

Rev Soc Bras Med Trop.

<https://pubmed.ncbi.nlm.nih.gov/36995787/>

Background: Brazil has the second largest number of leprosy cases worldwide, and the state of São Paulo has been considered non-endemic since 2006. **Methods:** We analyzed 16 variable number tandem repeats loci and three single nucleotide polymorphisms loci of *Mycobacterium leprae* (M. leprae) in 125 clinical isolates from patients in different municipalities in the state. **Results:** The clustering pattern of M. leprae indicated that the transmission of leprosy persisted in the state and included scenarios of intra-extra-familial transmission in areas with low endemicity. **Conclusions:** A significantly active circulation of M. leprae was observed. Therefore, surveillance and control measures must be implemented.

Buruli ulcer caused by *Mycobacterium ulcerans* subsp. *shinshuense*: A case report.

Fujimori T, Hagiya H, Iio K, Yamasaki O, Miyamoto Y, Hoshino Y, Kakehi A, Okura M, Minabe H, Yokoyama Y, Otsuka F, Higashikage A.

May-2023

J Infect Chemother.

<https://pubmed.ncbi.nlm.nih.gov/36813163/>

Efficacy of autologous platelet-rich plasma therapy versus topical Minoxidil in men with moderate androgenetic alopecia: a randomized open-label trial.

Balasundaram M, Kumari R, Ramassamy S.

Dec-2023

J Dermatol Treat.

<https://pubmed.ncbi.nlm.nih.gov/36800229/>

Background: Platelet-rich plasma (PRP) is an adjunctive treatment in androgenetic alopecia (AGA). Its role as a monotherapy, when compared to FDA-approved therapies in moderate grades of androgenetic alopecia is not established. **Objectives:** We sought to study the efficacy and safety of standardized non-activated PRP preparation against topical minoxidil in AGA. **Methods:** Men aged 20-50 with Grade III and IV (Modified Hamilton-Norwood) AGA were randomized to receive 5% Minoxidil (×6 months) or PRP injections (monthly ×3). The primary endpoints were global photographic assessment at week 24, change in target area hair counts, density, and anagen hair at week 12. Other outcomes were subjects' satisfaction and adverse events. **Results:** In total, 64 participants were randomized. At week 24, 56% responded to Minoxidil arm and 38% to PRP ($p = 0.124$). There was a significant increase in target area hair count

and density at week 12 within the groups. The difference between the groups was not statistically significant. Adverse events occurred in 53% and 37% of the PRP and minoxidil groups, respectively. Patient satisfaction was better with Minoxidil. **Conclusion:** PRP is effective in the treatment of moderate grades of androgenetic alopecia in men, although perhaps not different from minoxidil. Side effects occur more frequently with PRP.

Seventy years of evidence on the efficacy and safety of drugs for treating leprosy: a network meta-analysis.

Yang J, Kong J, Li B, Ji Z, Liu A, Chen J, Liu M, Fan Y, Peng L, Song J, Wu X, Gao L, Ma W, Dong Y, Luo S, Bao F.

Apr-2023

J Infect.

<https://pubmed.ncbi.nlm.nih.gov/36796681/>

Core single nucleotide polymorphism analysis reveals transmission of *Mycobacterium marinum* between animal and environmental sources in two aquaria.

Komine T, Srivorakul S, Yoshida M, Tanaka Y, Sugimoto Y, Inohana M, Fukano H, Hoshino Y, Kurata O, Wada S.

May-2023

J Fish Dis.

<https://pubmed.ncbi.nlm.nih.gov/36727551/>

Mycobacterium marinum is a slow-growing, photochromogenic nontuberculous mycobacterium, which can cause mycobacteriosis in various animals, including humans. Several cases of fish mycobacteriosis have been reported to date. *Mycobacterium marinum* has also been isolated from aquatic environmental sources such as water, sand, biofilms, and plants in the natural environments. Hence, we hypothesized that a wide variety of sources could be involved in the transmission of M. marinum. In this study, we tested this hypothesis by isolating M. marinum from various sources such as fish, invertebrates, seagrass, periphytons, biofilms, sand, and/or water in two aquaria in Japan and conducting a phylogenetic analysis based on single-nucleotide polymorphisms (SNPs) using whole-genome sequences of the isolated strains. The analysis revealed that the strains from animal and environmental sources belonged to the same clusters. This molecular-based study epidemiologically confirmed that various sources, including fish, invertebrates, and environmental sources, could be involved in transmission of M. marinum in a closed-rearing environment. This is the first report where M. marinum was isolated from different sources, and various transmission routes were confirmed in actual cases, which provided essential information to improve the epidemiology of M. marinum.

Point counting-serial image index: A new scoring system for melasma.

Srishti D, Chethana SG, Kanthraj GR, Betkerur JB.

Jan-Mar 2023

Indian J Dermatol Venereol Leprol.

<https://pubmed.ncbi.nlm.nih.gov/36688879/>

Hyperfunction variant rs708035 of interleukin 1 receptor-associated kinases 2 gene involved in the predisposition of leprosy infection.

Saleem S, Zia M, Siddiqui F, Ghouri M, Kulsoom U, Kawal S, Fatima S, Zehra S.

Apr-2023

J Gene Med.

<https://pubmed.ncbi.nlm.nih.gov/36670053/>

Background: Mycobacterium leprae (slow-growing bacteria) is the etiological agent for leprosy infection, which is a chronic granulomatous disease. Symptoms initiate with the loss of sensation in the affected areas, which can lead to severe injuries, cuts and burns. IRAK2 (interleukin-1 receptor-associated kinases 2) is reported to function in the regulation of the NFκB pathway. The frequency of the IRAK2 polymorphism (rs708035) was unknown in the Pakistani population. Therefore, the study was designed to identify the role of the rs708035 SNP (single nucleotide polymorphism) in susceptibility to leprosy. **Methodology:** The case-control study was designed, and participants were selected by Ridley-Jopling Classification. Blood samples from healthy individuals and patients were collected after ethical approval. Genomic DNA was extracted for the amplification of selected polymorphisms by tetra-primer amplification refractory mutation system polymerase chain reaction. The desired products were observed via agarose gel (2.5%) electrophoresis followed by data analysis using bioinformatics tools (SNP Stats and SHEsis) and statistical tests (odds ratio, OR, and chi square). **Results:** The study revealed that the mutant genotype (TT) was found to be frequent among cases (22.80%) in comparison with the controls (1.66%). The SNP rs708035 was significantly associated with the progression of leprosy ($\chi^2 = 17.62$, $p < 0.0001$). The targeted SNP significantly increases the risk of leprosy 2.3 times (OR = 2.3119, 95% CI 1.2729-4.1989, $p < 0.01$). The genetic model also confirms the significant association of the A/T genotype with leprosy in the over-dominant model (OR = 2.83, 95% CI 1.16-6.89, $p < 0.001$). **Conclusions:** The study revealed a significant association of the targeted SNP with leprosy and provided baseline data regarding the association of rs708035. The current research could be utilized for the preparation of biomarkers by considering a larger sample size. **Highlights:** The patients suffering from leprosy faced various comorbidities, including hypertension and diabetes. The study reports for the first time a significant association of interleukin 1 receptor associated kinases 2 (IRAK2) single nucleotide polymorphism (SNP) rs708035 among the Pakistani population (Karachi). The current study provides baseline data to develop diagnostic biomarkers for early detection of leprosy.

Lepromatous leprosy presenting with erythema nodosum leprosum mimicking Bechet's disease.

Quintarelli L, Magnaterra E, Maglie R, Corrà A, Ruffo di Calabria V, Aimo C, Mariotti EB, Verdelli A, Maio V, Antiga E, Caproni M.

Mar-Apr 2023

Travel Med Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/36528249/>

Role of molecular approaches to distinguish post kala-azar dermal leishmaniasis from leprosy: A case study.

Roy S, Roy M, Nath S, Chaudhuri SJ, Ghosh MK, Mukherjee S, Chatterjee M.

Jan-Mar 2023

Indian J Dermatol Venereol Leprol.

<https://pubmed.ncbi.nlm.nih.gov/36461804/>

Efficacy of fixed duration multidrug therapy for the treatment of multibacillary leprosy: A prospective observational study from Northern India.

Singh I, Ahuja M, Lavania M, Pathak VK, Turankar RP, Singh V, Sengupta U, Das L, Kumar A, Saini GB.

Jan-Mar 2023

Indian J Dermatol Venereol Leprol.

<https://pubmed.ncbi.nlm.nih.gov/36331863/>

Background: In endemic regions of several countries, the prevalence of leprosy has not come down to the level of elimination. On the contrary, new cases are being detected in large numbers. Clinically, it is frequently noted that despite completion of multibacillary multidrug therapy for 12 months, the lesions remain active, especially in cases with high bacteriological indices.

Aim: The present study focused on finding out the viable number of Mycobacterium leprae during the 12-month regimen of multibacillary multidrug therapy, at six and 12 months intervals and, attempting to determine their role in disease transmission. **Methods:** Seventy eight cases of multibacillary leprosy cases were recruited from leprosy patients registered at The Leprosy Mission hospitals at Shahdara (Delhi), Naini (Uttar Pradesh) and Champa (Chhattisgarh), respectively. Slit skin smears were collected from these patients which were transported to the laboratory for further processing. Ribonucleic acid was extracted by TRIzol method. Total Ribonucleic acid was used for real-time reverse transcription-polymerase chain reaction (two-step reactions). A standard sample with a known copy number was run along with unknown samples for a reverse transcription-polymerase chain reaction. Patients were further assessed for their clinical and molecular parameters during 6th month and 12th month of therapy. **Results:** All 78 new cases showed the presence of a viable load of bacilli at the time of recruitment, but we were able to follow up only on 36 of these patients for one year. Among these, using three different genes, 20/36 for *esxA*, 22/36 for *hsp18* and 24/36 for 16S rRNA cases showed viability of *M. leprae* at the time of completion of 12 months of multidrug therapy treatment. All these positive patients were histopathologically active and had bacillary indexes ranging between 3+ and 4+. Patients with a high copy number of the Mycobacterium leprae gene, even after completion of treatment as per WHO recommended fixed-dose multidrug therapy, indicated the presence of live bacilli. **Limitations:** Follow up for one year was difficult, especially in Delhi because of the

migratory nature of the population. Patients who defaulted for scheduled sampling were not included in the study. **Conclusion:** The presence of a viable load of bacilli even after completion of therapy may be one of the reasons for relapse and continued transmission of leprosy in the community.

Classic Kaposi sarcoma in Eastern India.

Darung I, Shah N, Ghosh A, Kamgo L, Kavishwar V.

Jan-Mar 2023

Indian J Dermatol Venereol Leprol.

<https://pubmed.ncbi.nlm.nih.gov/36331842/>

Early detection of sensory nerve function impairment in leprosy under field conditions.

John AS, Govindharaj P.

Jan-Mar 2023

Indian J Dermatol Venereol Leprol.

<https://pubmed.ncbi.nlm.nih.gov/35841354/>

Aim: To assess the fine sensation of palms and soles in field conditions, to enable early detection of nerve function impairment before the loss of protective sensation, thus preventing the development of disability. **Methods:** A cross-sectional descriptive study was conducted at seven tertiary referral hospitals located in different states in India. This study included all newly diagnosed patients affected by leprosy, who were registered during the period between March 2011 and April 2012. A detailed history was taken along with charting and voluntary muscle testing /sensory testing (VMT/ST) for the diagnosed patients. The sensation was measured using 0.2 gm Semmes-Weinstein filaments for palms and 4 gm for soles first, followed by 2 gm Semmes-Weinstein filaments for palms and 10 gm for soles. **Results:** Among the 374 patients, 106 were identified with sensory nerve function impairment. Of the 106 patients, 84 were identified with absence of both fine and protective sensation and 22 patients had a loss of fine touch sensation with protective sensation intact. **Limitation:** This study was conducted only among patients who were newly diagnosed with leprosy. Hence, future longitudinal studies in a larger population will add more validity to the study. **Conclusion:** The patients who had loss of fine sensation would have been missed by the normal leprosy programme protocol which uses 2 gm and 10 gm filaments for testing sensory loss before initiating steroid therapy. Further research is needed to determine whether testing for fine sensation with 0.2 gm Semmes-Weinstein filaments for palms and 4 gm for soles can be introduced at all specialized leprosy centres to detect nerve function impairment at an earlier stage followed by steroid therapy.

Intravenous pulsed corticosteroids for leprosy neuritis: Logical or irrational?

Mehta H, Narang T, Dogra S, Kumar B.

Jan-Mar 2023

Indian J Dermatol Venereol Leprol.

<https://pubmed.ncbi.nlm.nih.gov/35593278/>

Single-nucleotide polymorphism and haplotype analysis of macrophage migration inhibitory factor gene and its correlation with serum macrophage migration inhibitory factor levels in North Indian psoriatic patients with moderate disease severity: A cross-sectional study.

Chhabra S, Banerjee N, Narang T, Sood S, Bishnoi A, Goel S, Bansal F, Singh S, Priyanka K, Minz RW, Dogra S.

Jan-Mar 2023

Indian J Dermatol Venereol Leprol.

<https://pubmed.ncbi.nlm.nih.gov/34114423/>

Background: Psoriasis is associated with significant morbidity and impaired quality of life. Identification of the host genes that influence disease susceptibility and can potentially guide future, targeted therapy is the need of the hour. **Aims:** The aim of the study was to investigate the associations of macrophage migration inhibitory factor (MIF) gene polymorphisms, that is, a 5-8-CATT tetra nucleotide repeats at -794 (-794*CATT5-8) and a single-nucleotide polymorphism at -173 (-173*G/C) with the risk of chronic plaque psoriasis and to observe the correlation, if any, of disease determinants with genetic functional variants and circulating MIF levels. **Methods:** Five hundred and seventeen individuals (265 psoriasis patients and 252 controls) were genotyped for MIF gene polymorphisms. Data were analyzed with respect to disease susceptibility, serum MIF levels, disease severity, age at onset, disease duration and presence of comorbidities. **Results:** The presence of co-morbidities was more frequently noted in patients with late onset disease ($P = 0.01$). No statistically significant differences were observed either in genotype ($P = 0.680$) or allele frequency ($P = 0.69$) with respect to distribution of MIF-173*G/C polymorphism between patients and controls. The frequencies of genotypes -794*CATT 5/7 and 7/7 were significantly lower in patients ($P = 0.027^*$ and 0.038^* , respectively). CATT*5/MIF-173*C haplotype occurred at a higher frequency in patients (odds ratio 3.03, 95% confidence intervals 1.09-8.47, $P = 0.02$). The mean serum MIF levels were significantly higher in patients as compared to controls ($P < 0.001$). The presence of either extended MIF -794*CATT repeats or C allele did not reveal any significant association with serum MIF levels or age at onset. Analysis of effect of various disease determinants revealed no significant association with genetic variants and serum MIF levels. **Limitations:** The lesional expression of MIF could not be studied. **Conclusion:** Our results showed that CATT*5/MIF-173*C haplotype is associated with increased susceptibility to psoriasis vulgaris.

Hemorrhagic herpes Zoster: A rare presentation.

Fernandes S, D'Souza M, Nandakishore B.

Jan-Mar 2023

Indian J Dermatol Venereol Leprol.

<https://pubmed.ncbi.nlm.nih.gov/33666058/>

Trypanosomes (trypanosomiasis) et maladie de Chagas

Effective drug discovery in Chagas disease.

Tarleton RL.

04-04-2023

Trends Parasitol.

<https://pubmed.ncbi.nlm.nih.gov/37024318/>

The Chagas field has gone >50 years without tangible progress toward new therapies. My colleagues and I have recently reported on a benzoxaborole compound that achieves consistent parasitological cure in experimentally infected mice and in naturally infected non-human primates (NHPs). While these results do not assure success in human clinical trials, they significantly de-risk this process and form a strong justification for such trials. Highly effective drug discovery depends on a solid understanding of host and parasite biology and excellent knowledge in designing and validating chemical entities. This opinion piece seeks to provide perspectives on the process that led to the discovery of AN15368, with the hope that this will facilitate the discovery of additional clinical candidates for Chagas disease.

Evaluation of the antiparasitic and antifungal activities of new synthetic piperlongumine-type cinnamide derivatives: booster effect by halogen substituents.

Khan TA, Al Nasr IS, Koko WS, Ma J, Eckert S, Brehm L, Ben Said RS, Daoud I, Hanachi R, Rahali S, van de Sande W, Ersfeld K, Schobert R, Biersack B.

06-04-2023

ChemMedChem.

<https://pubmed.ncbi.nlm.nih.gov/37021847/>

A series of synthetic N-acylpyrrolidone and -piperidone derivatives of the natural alkaloid piperlongumine were prepared and tested for their activities against *Leishmania* major and *Toxoplasma gondii* parasites. Replacement of one of the aryl meta-methoxy groups by halogens such as chlorine, bromine and iodine led to distinctly increased antiparasitic activities. For instance, the new bromo- and iodo-substituted compounds 3b/c and 4b/c showed strong activity against *L. major* promastigotes ($IC_{50} = 4.5-5.8 \mu M$). Their activities against *L. major* amastigotes were moderate. In addition, the new compounds 3b, 3c, and 4a-c exhibited high activity against *T. gondii* parasites ($IC_{50} = 2.0-3.5 \mu M$) with considerable selectivities when taking their effects on non-malignant Vero cells into account. Notable antitrypanosomal activity against *Trypanosoma brucei* was also found for 4b. Antifungal activity against *Madurellamycetomatis* was observed for compound 4c at higher doses. Quantitative structure-activity relationship (QSAR) studies were carried out, and docking calculations of test compounds bound to tubulin revealed binding differences between the 2-pyrrolidone and 2-piperidone

derivatives. Microtubules-destabilizing effects were observed for 4b in *T. b. brucei* cells.

Antiprotozoal compounds from *Mikania periplocifolia*.

Laurella LC, Elso OG, Rodriguez RN, Viecez JM, Alonso MR, Bontempi EJ, Malchiodi E, Catalán CAN, Cazorla SI, Sülsen VP.

03-04-2023

Fitoterapia.

<https://pubmed.ncbi.nlm.nih.gov/37019368/>

Chagas disease, African trypanosomiasis and Leishmaniasis are neglected parasitic diseases which affect millions of people worldwide. In a previous work, we report the antiprotozoal activity of the dichloromethane extract of *Mikania periplocifolia* Hook. & Arn. (Asteraceae). The aim of this work was to isolate and identify the bioactive compounds present in the extract. The fractionation of the dichloromethane extract has led to the isolation of the sesquiterpene lactone miscandenin and the flavonoid onopordin, together with the sesquiterpene lactones mikanolide, dihydromikanolide and deoxymikanolide, which have previously shown antiprotozoal activity. Miscandenin and onopordin were assayed in vitro against *Trypanosoma cruzi*, *T. brucei* and *Leishmania braziliensis*. Miscandenin was active against *T. cruzi* trypomastigotes and amastigotes with IC_{50} values of 9.1 and 7.7 $\mu g/ml$, respectively. This sesquiterpene lactone and the flavonoid onopordin showed activity against *T. brucei* trypomastigotes ($IC_{50} = 0.16$ and 0.37 $\mu g/ml$) and *L. braziliensis* promastigotes ($IC_{50} = 0.6$ and 1.2 $\mu g/ml$), respectively. The CC_{50} values on mammalian cells were 37.9 and 53.4 $\mu g/ml$ for miscandenin and onopordin, respectively. Besides, the pharmacokinetic and physicochemical properties of miscandenin were assessed in silico, showing a good drug-likeness profile. Our results highlight this compound as a promising candidate for further preclinical studies in the search of new drugs for the treatment of trypanosomiasis and leishmaniasis.

Anxiety, depression, and memory loss in Chagas disease: a puzzle far beyond neuroinflammation to be unpicked and solved.

Lannes-Vieira J, Vilar-Pereira G, Barrios LC, Silva AA.

03-04-2023

Mem Inst Oswaldo Cruz.

<https://pubmed.ncbi.nlm.nih.gov/37018799/>

Mental disorders such as anxiety, depression, and memory loss have been described in patients with chronic Chagas disease (CD), a neglected tropical disease caused by the protozoan parasite *Trypanosoma cruzi*. Social, psychological, and biological stressors may take part in these processes. There is a consensus on the recognition of an acute nervous form of CD. In chronic CD patients, a neurological form is associated with immunosuppression and neurobehavioural changes as sequelae of stroke. The chronic nervous form of CD has been refuted, based on the absence of histopathological lesions and neuroinflammation; however, computed tomography shows brain atrophy. Overall, in preclinical models of

chronic *T. cruzi* infection in the absence of neuroinflammation, behavioural disorders such as anxiety and depression, and memory loss are related to brain atrophy, parasite persistence, oxidative stress, and cytokine production in the central nervous system. Interferon-gamma (IFN γ)-bearing microglial cells are colocalised with astrocytes carrying *T. cruzi* amastigote forms. In vitro studies suggest that IFN γ fuels astrocyte infection by *T. cruzi* and implicate IFN γ -stimulated infected astrocytes as sources of TNF and nitric oxide, which may also contribute to parasite persistence in the brain tissue and promote behavioural and neurocognitive changes. Preclinical trials in chronically infected mice targeting the TNF pathway or the parasite opened paths for therapeutic approaches with a beneficial impact on depression and memory loss. Despite the path taken, replicating aspects of the chronic CD and testing therapeutic schemes in preclinical models, these findings may get lost in translation as the chronic nervous form of CD does not fulfil biomedical model requirements, as the presence of neuroinflammation, to be recognised. It is hoped that brain atrophy and behavioural and neurocognitive changes are sufficient traits to bring the attention of researchers to study the biological and molecular basis of the central nervous system commitment in chronic CD.

Proximity-Dependent Biotinylation and Identification of Flagellar Proteins in *Trypanosoma cruzi*.

Won MM, Baublis A, Burleigh BA.

05-04-2023

mSphere.

<https://pubmed.ncbi.nlm.nih.gov/37017578/>

The *Trypanosoma cruzi* Antigen and Epitope Atlas: antibody specificities in Chagas disease patients across the Americas.

Ricci AD, Bracco L, Salas-Sarduy E, Ramsey JM, Nolan MS, Lynn MK, Altcheh J, Ballering GE, Torrico F, Kesper N, Villar JC, Marcipar IS, Marco JD, Agüero F.

03-04-2023

Nat Commun.

<https://pubmed.ncbi.nlm.nih.gov/37012236/>

During an infection the immune system produces pathogen-specific antibodies. These antibody repertoires become specific to the history of infections and represent a rich source of diagnostic markers. However, the specificities of these antibodies are mostly unknown. Here, using high-density peptide arrays we examined the human antibody repertoires of Chagas disease patients. Chagas disease is a neglected disease caused by *Trypanosoma cruzi*, a protozoan parasite that evades immune mediated elimination and mounts long-lasting chronic infections. We describe a proteome-wide search for antigens, characterised their linear epitopes, and show their reactivity on 71 individuals from diverse human populations. Using single-residue mutagenesis we revealed the core functional residues for 232 of these epitopes. Finally, we show the diagnostic performance of identified antigens on challenging samples. These datasets

enable the study of the Chagas antibody repertoire at an unprecedented depth and granularity, while also providing a rich source of serological biomarkers.

Proteomic analysis defines the interactome of telomerase in the protozoan parasite, *Trypanosoma brucei*.

Davis JA, Reyes AV, Nitika, Saha A, Wolfgeher DJ, Xu SL, Truman AW, Li B, Chakrabarti K.

16-04-2023

Front Cell Dev Biol.

<https://pubmed.ncbi.nlm.nih.gov/37009488/>

PREVALENCE AND RISK FACTORS ASSOCIATED WITH NATURAL INFECTION BY *Trypanosoma evansi* IN CAMPEIRO HORSES.

Golombieski L, Bassi das Neves G, Casa MDS, Costa GCS, Miletto LC, Saito ME, Fonteque JH.

31-03-2023

J Equine Vet Sci.

<https://pubmed.ncbi.nlm.nih.gov/37004780/>

Campeiro horse is a breed locally adapted to the Santa Catarina plateau region and its main characteristic is the gait, it is known as "Marchador das Araucárias". It is a breed considered in danger of extinction, being fundamental the search for the preservation of this important genetic resource. Surra, caused by the protozoan *Trypanosoma evansi*, is among the diseases that affect horses. However, there are no data on the prevalence of infection in Campeiro horses. This study aimed to determine the prevalence of *T. evansi* in Campeiro horses, correlate hematology and serum biochemistry, and identify possible risk factors. Blood samples were collected by venipuncture of 214 Campeiro horses, 50 males and 164 females, aged between three months and 27 years, from 16 properties located in the States of Santa Catarina, Rio Grande do Sul, and Paraná. An epidemiological questionnaire was carried out with the owners to analyze the associated risk factors. The blood samples were submitted to PCR, IFAT, complete blood count, and serum biochemistry. The prevalence was 14% of positive animals by PCR and 59% by IFAT. There was an increase in hematocrit, and in the number of basophils, a decrease in plasmatic fibrinogen, and in the enzymatic activity of ALT, AST, and urea, and an increase in CK and creatinine in positive animals, which is possibly unrelated to the infection. The data obtained through the epidemiological questionnaires showed no difference. Therefore, *T. evansi* is present in the South of Brazil, with a high prevalence in Campeiro horses.

Role of the RNA-binding protein ZC3H41 in the regulation of ribosomal protein messenger RNAs in trypanosomes.

Ceballos-Pérez G, Rico-Jiménez M, Gómez-Liñán C, Estévez AM.

31-03-2023

Parasit Vectors.

<https://pubmed.ncbi.nlm.nih.gov/37004055/>

Trypanosoma cruzi: Does the intake of nanoencapsulated benznidazole control acute infections?

Dutra da Silva A, Fracasso M, Bottari NB, Gundel S, Ourique AF, Assmann CE, Ferreira DASP, Castro MFV, Reichert KP, de Souza LAF, da Veiga ML, da Rocha MIUM, Monteiro SG, Morsch VM, Chitolina Schetinger MR, da Silva AS.

29-03-2023

Exp Parasitol.

<https://pubmed.ncbi.nlm.nih.gov/37001581/>

Chagas Disease (CD) affects around eight million people worldwide. It is considered a neglected disease that presents few treatment options with efficacy only in the acute phase. Nanoparticles have many positive qualities for treating parasite infections and may be effectively and widely employed in clinical medicine. This research aimed to evaluate the nanoencapsulated benznidazole treatment in animals experimentally infected with *Trypanosoma cruzi*. To analyze the treatment efficacy, we evaluated survival during thirty days, parasitemia, genotoxicity, and heart and liver histopathology. Thirty-five female Swiss mice were organized into seven groups characterizing a dose curve: A - Negative control (uninfected animals), B - Positive control (infected animals), C - Benznidazole (BNZ) 100 mg/kg (infected animals), D - 5 mg/kg Benznidazole nanocapsules (NBNZ) (infected animals), E - 10 mg/kg Benznidazole nanocapsules (infected animals), F - 15 mg/kg Benznidazole nanocapsules (infected animals), G - 20 mg/kg Benznidazole nanocapsules (infected animals). The animals were infected with the Y strain of *T. cruzi* intraperitoneally. The treatment was administered for eight days by oral gavage. It was possible to observe that the treatment with the highest NBNZ dose presented efficacy similar to the standard benznidazole drug. The 20 mg/kg NBNZ dose was able to reduce parasitemia, increase survival, and drastically reduce heart and liver tissue damage compared to the 100 mg/kg BNZ dose. Moreover, it showed a lower DNA damage index than the BNZ treatment. In conclusion, the nanoencapsulation of BNZ promotes an improvement in parasite proliferation control with a five times smaller dose relative to the standard dose of free BNZ, thus demonstrating to be a potential innovative therapy for CD.

Structural basis for guide RNA selection by the RESC1-RESC2 complex.

Dolce LG, Nesterenko Y, Walther L, Weis F, Kowalinski E.
31-03-2023

Nucleic Acids Res.

<https://pubmed.ncbi.nlm.nih.gov/36999600/>

Kinetoplastid parasites, such as trypanosomes or leishmania, rely on RNA-templated RNA editing to mature mitochondrial cryptic pre-mRNAs into functional protein-coding transcripts. Processive pan-editing of multiple editing blocks within a single transcript is dependent on the 20-subunit RNA editing substrate binding complex (RESC) that serves as a platform to orchestrate the interactions between pre-mRNA, guide RNAs (gRNAs), the catalytic RNA editing complex (RECC), and a set of RNA

helicases. Due to the lack of molecular structures and biochemical studies with purified components, neither the spacio-temporal interplay of these factors nor the selection mechanism for the different RNA components is understood. Here we report the cryo-EM structure of *Trypanosoma brucei* RESC1-RESC2, a central hub module of the RESC complex. The structure reveals that RESC1 and RESC2 form an obligatory domain-swapped dimer. Although the tertiary structures of both subunits closely resemble each other, only RESC2 selectively binds 5'-triphosphate-nucleosides, a defining characteristic of gRNAs. We therefore propose RESC2 as the protective 5'-end binding site for gRNAs within the RESC complex. Overall, our structure provides a starting point for the study of the assembly and function of larger RNA-bound kinetoplast RNA editing modules and might aid in the design of anti-parasite drugs.

Immunodominant surface epitopes power immune evasion in the African trypanosome.

Gkeka A, Aresta-Branco F, Triller G, Vlachou EP, van Straaten M, Lilic M, Olinares PDB, Perez K, Chait BT, Blatnik R, Ruppert T, Verdi JP, Stebbins CE, Papavasiliou FN.

28-03-2023

Cell Rep.

<https://pubmed.ncbi.nlm.nih.gov/36943866/>

The African trypanosome survives the immune response of its mammalian host by antigenic variation of its major surface antigen (the variant surface glycoprotein or VSG). Here we describe the antibody repertoires elicited by different VSGs. We show that the repertoires are highly restricted and are directed predominantly to distinct epitopes on the surface of the VSGs. They are also highly discriminatory; minor alterations within these exposed epitopes confer antigenically distinct properties to these VSGs and elicit different repertoires. We propose that the patterned and repetitive nature of the VSG coat focuses host immunity to a restricted set of immunodominant epitopes per VSG, eliciting a highly stereotyped response, minimizing cross-reactivity between different VSGs and facilitating prolonged immune evasion through epitope variation.

Leishmaniose

Evaluation of the antiparasitic and antifungal activities of new synthetic piperlongumine-type cinnamide derivatives: booster effect by halogen substituents.

Khan TA, Al Nasr IS, Koko WS, Ma J, Eckert S, Brehm L, Ben Said RS, Daoud I, Hanachi R, Rahali S, van de Sande W, Ersfeld K, Schobert R, Biersack B.

06-04-2023

ChemMedChem.

<https://pubmed.ncbi.nlm.nih.gov/37021847/>

A series of synthetic N-acylpiperidone and -piperidone derivatives of the natural alkaloid piperlongumine were

prepared and tested for their activities against *Leishmania* major and *Toxoplasma gondii* parasites. Replacement of one of the aryl meta-methoxy groups by halogens such as chlorine, bromine and iodine led to distinctly increased antiparasitic activities. For instance, the new bromo- and iodo-substituted compounds 3b/c and 4b/c showed strong activity against *L. major* promastigotes (IC₅₀ = 4.5-5.8 µM). Their activities against *L. major* amastigotes were moderate. In addition, the new compounds 3b, 3c, and 4a-c exhibited high activity against *T. gondii* parasites (IC₅₀ = 2.0-3.5 µM) with considerable selectivities when taking their effects on non-malignant Vero cells into account. Notable antitrypanosomal activity against *Trypanosoma brucei* was also found for 4b. Antifungal activity against *Madurellamyces tomentosus* was observed for compound 4c at higher doses. Quantitative structure-activity relationship (QSAR) studies were carried out, and docking calculations of test compounds bound to tubulin revealed binding differences between the 2-pyrrolidone and 2-piperidone derivatives. Microtubules-destabilizing effects were observed for 4b in *T. b. brucei* cells.

Pediatric lymphatic leishmaniasis: a case report.

Kindie EA, Yefter ET, Alemu BA, Gurji TB, Tadesse AK.

06-04-2023

J Med Case Rep.

<https://pubmed.ncbi.nlm.nih.gov/37020261/>

Background: There are three main forms of leishmaniasis: visceral (the most serious form because it is almost always fatal without treatment), cutaneous (the most common, usually causing skin ulcers), and mucocutaneous (affecting mouth, nose, and throat). Leishmaniasis is caused by protozoan parasites, which are transmitted by the bite of infected female phlebotomine sandflies. The disease affects some of the world's poorest people and is associated with malnutrition, population displacement, poor housing, a weak immune system, and lack of financial resources. An estimated 700,000 to 1 million new cases occur annually. Only a small fraction of those infected by parasites causing leishmaniasis will eventually develop the disease. We report a case of exclusive lymph node involvement in leishmaniasis, presenting as localized lymphadenopathies. The diagnosis of lymphatic leishmaniasis was confirmed by the presence of *Leishmania donovani* bodies in fine needle aspiration cytology, and positive anti-rK39 antibodies. The bone marrow aspiration was negative for *Leishmania donovani* bodies. Abdominal ultrasound was done and there was no organomegaly. Furthermore, localized lymphadenopathies may provide a diagnostic challenge by clinically mimicking a lymphoma or other causes of lymphadenopathy. Due to its rarity and its tendency to pose a clinical diagnostic challenge, we decided to report a case of lymphatic leishmaniasis. **Case presentation:** A 12-year-old Amara male patient presented to the University of Gondar comprehensive specialized hospital, Northwestern Ethiopia, with six discrete right lateral cervical lymphadenopathies, the largest measuring 3 × 2 cm², with no cutaneous lesion. Fine needle aspiration cytology confirmed the diagnosis of leishmaniasis in lymph node, and he was put on sodium stibogluconate (20 mg/kg

body weight/day) and paromomycin (15 mg/kg body weight/day) injections, which are given intramuscularly for 17 days. Having completed his medication at the University of Gondar comprehensive specialized hospital, he had a smooth course and was discharged with appointment scheduled for follow-up after 3 months.

Conclusion: In the clinical evaluation of a patient with isolated lymphadenopathies, leishmaniasis must be considered as a differential diagnosis in immunocompetent subjects in endemic areas for early diagnostic workup and management.

Antiprotozoal compounds from *Mikania periplocifolia*.

Laurella LC, Elso OG, Rodríguez RN, Viecez JM, Alonso MR, Bontempi EJ, Malchiodi E, Catalán CAN, Cazorla SI, Sülsen VP.

03-04-2023

Fitoterapia.

<https://pubmed.ncbi.nlm.nih.gov/37019368/>

The role of sand flies as vectors of viruses other than phleboviruses.

Jancarova M, Polanska N, Volf P, Dvorak V.

Apr-2023

J Gen Virol.

<https://pubmed.ncbi.nlm.nih.gov/37018120/>

Molecular Diagnosis of Leishmaniasis in Spain: Development and Validation of Ready-To-Use Gel-Form Nested and Real-Time PCRs To Detect *Leishmania* spp.

Chicharro C, Nieto J, Miguelañez S, Garcia E, Ortega S, Peña A, Rubio JM, Flores-Chavez M.

04-04-2023

Microbiol Spectr.

<https://pubmed.ncbi.nlm.nih.gov/37014253/>

Leishmaniasis is an endemic parasitic disease in at least 98 countries. In Spain, it is considered a zoonosis caused by *Leishmania infantum*, with an annual incidence of 0.62 cases/100,000 inhabitants. The predominant clinical manifestations are the cutaneous (CL) and visceral forms (VL), and the diagnosis is performed by parasitological, serological, and molecular tests. At the WHO Collaborating Center for Leishmaniasis (WHOCCLeish), routine diagnostic tests are based on a nested PCR (Ln-PCR), culture, and serological tests. To simplify our PCR protocol, we aimed to develop and validate a ready-to-use nested gel-form PCR (LeishGelPCR) and a duplex real-time PCR (qPCR) that allowed simultaneous detection of *Leishmania* and mammalian DNA as an internal control (Leish-qPCR). Clinical validation was performed in 200 samples from the WHOCCLeish collection; 92 and 85 out of 94 and 87 samples were positive by LeishGelPCR and Leish-qPCR, respectively, showing a sensitivity of 98% in both approaches. The specificity was 100% for LeishGelPCR and 98% for Leish-qPCR. The limits of detection of both protocols were similar (0.5 and 0.2 parasites/reaction). Parasite loads in VL and CL forms were similar, although high loads were observed when invasive samples were

tested. In conclusion, LeishGelPCR and Leish-qPCR showed excellent performance in the diagnosis of leishmaniasis. These new forms of 18S rRNA gene PCR are equivalent to Ln-PCR and can be introduced in the algorithm for CL and VL diagnosis. **IMPORTANCE** Although the gold standard for diagnosis of leishmaniasis is the microscopic observation of amastigotes, molecular techniques are becoming a cost-efficient alternative. Currently, PCR is a routine resource that is used in many reference microbiology laboratories. In this article, we have described two ways to improve the reproducibility and usability of the molecular detection of *Leishmania* spp. These new approaches could be introduced even in middle- and low-resource laboratories; one is a ready-to-use gel-form system of a nested PCR and the other is a real-time PCR. We show why molecular diagnosis is the best methodology to confirm a clinical suspicion of leishmaniasis with higher sensitivity than traditional methods, thus facilitating early diagnosis and timely treatment of human leishmaniasis.

A systematic review of peptide-based serological tests for the diagnosis of leishmaniasis.

Pagniez J, Petitdidier E, Parra-Zuleta O, Pissarra J, Bras-Gonçalves R.

2023

Parasite.

<https://pubmed.ncbi.nlm.nih.gov/37010451/>

Serological methods should meet the needs of leishmaniasis diagnosis due to their high sensitivity and specificity, economical and adaptable rapid diagnostic test format, and ease of use. Currently, the performances of serological diagnostic tests, despite improvements with recombinant proteins, vary greatly depending on the clinical form of leishmaniasis and the endemic area. Peptide-based serological tests are promising as they could compensate for antigenic variability and improve performance, independently of *Leishmania* species and subspecies circulating in the endemic areas. The objective of this systematic review was to inventory all studies published from 2002 to 2022 that evaluate synthetic peptides for serological diagnosis of human leishmaniasis and also to highlight the performance (e.g., sensitivity and specificity) of each peptide reported in these studies. All clinical forms of leishmaniasis, visceral and tegumentary, and all *Leishmania* species responsible for these diseases were considered. Following PRISMA statement recommendations, 1,405 studies were identified but only 22 articles met the selection criteria and were included in this systematic review. These original research articles described 77 different peptides, of which several have promising performance for visceral or tegumentary leishmaniasis diagnosis. This review highlights the importance of and growing interest in synthetic peptides used for serological diagnosis of leishmaniasis, and their performances compared to some widely used tests with recombinant proteins.

A short-term method to evaluate anti-leishmania drugs by inhibition of stage differentiation in *Leishmania mexicana* using flow cytometry.

Teh-Poot CF, Dzul-Huchim VM, Mercado JM, Villanueva-Lizama LE, Bottazzi ME, Jones KM, Tsai FTF, Cruz-Chan JV.

31-03-2032

Exp Parasitol.

<https://pubmed.ncbi.nlm.nih.gov/37004860/>

Leishmania infantum infection after visiting southern Spain in patients on biological treatment; an observational, longitudinal, cohort study.

Hammarström H, Moreno J, Dotevall L, Calander AM.

29-03-2023

Travel Med Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/37001789/>

Putrescine supplementation shifts macrophage L-arginine metabolism related-genes reducing *Leishmania amazonensis* infection.

Zanatta JM, Acuña SM, de Souza Angelo Y, de Almeida Bento C, Peron JPS, Stolf BS, Muxel SM.

31-03-2023

PLoS One.

<https://pubmed.ncbi.nlm.nih.gov/37000792/>

Leishmania is a protozoan that causes leishmaniasis, a neglected tropical disease with clinical manifestations classified as cutaneous, mucocutaneous, and visceral leishmaniasis. In the infection context, the parasite can modulate macrophage gene expression affecting the microbicidal activity and immune response. The metabolism of L-arginine into polyamines putrescine, spermidine, and spermine reduces nitric oxide (NO) production, favoring *Leishmania* survival. Here, we investigate the effect of supplementation with L-arginine and polyamines in infection of murine BALB/c macrophages by *L. amazonensis* and in the transcriptional regulation of genes involved in arginine metabolism and proinflammatory response. We showed a reduction in the percentage of infected macrophages upon putrescine supplementation compared to L-arginine, spermidine, and spermine supplementation. Unexpectedly, deprivation of L-arginine increased nitric oxide synthase (Nos2) gene expression without changes in NO production. Putrescine supplementation increased transcript levels of polyamine metabolism-related genes Arg2, ornithine decarboxylase (Odc1), Spermidine synthase (SpdS), and Spermine synthase (SpmS), but reduced Arg1 in *L. amazonensis* infected macrophages, while spermidine and spermine promoted opposite effects. Putrescine increased Nos2 expression without leading to NO production, while L-arginine plus spermine led to NO production in uninfected macrophages, suggesting that polyamines can induce NO production. Besides, L-arginine supplementation reduced IL-1b during infection, and L-arginine or L-arginine plus putrescine increased Mcp1 at 24h of infection, suggesting that polyamines availability can interfere with cytokine/chemokine production. Our data showed that putrescine shifts L-arginine-metabolism related-genes on BALB/c macrophages and affects infection by *L. amazonensis*.

Correction: DNA replication protein Cdc45 directly interacts with PCNA via its PIP box in *Leishmania donovani* and the Cdc45 PIP box is essential for cell survival.

Yadav A, Sharma V, Pal J, Gulati P, Goel M, Chandra U, Bansal N, Saha S.

31-03-2023

PLoS Pathog.

<https://pubmed.ncbi.nlm.nih.gov/37000714/>

Structural basis for guide RNA selection by the RESC1-RESC2 complex.

Dolce LG, Nesterenko Y, Walther L, Weis F, Kowalinski E.

31-03-2023

Nucleic Acids Res.

<https://pubmed.ncbi.nlm.nih.gov/36999600/>

Kinetoplastid parasites, such as trypanosomes or leishmania, rely on RNA-templated RNA editing to mature mitochondrial cryptic pre-mRNAs into functional protein-coding transcripts. Processive pan-editing of multiple editing blocks within a single transcript is dependent on the 20-subunit RNA editing substrate binding complex (RESC) that serves as a platform to orchestrate the interactions between pre-mRNA, guide RNAs (gRNAs), the catalytic RNA editing complex (RECC), and a set of RNA helicases. Due to the lack of molecular structures and biochemical studies with purified components, neither the spacio-temporal interplay of these factors nor the selection mechanism for the different RNA components is understood. Here we report the cryo-EM structure of *Trypanosoma brucei* RESC1-RESC2, a central hub module of the RESC complex. The structure reveals that RESC1 and RESC2 form an obligatory domain-swapped dimer. Although the tertiary structures of both subunits closely resemble each other, only RESC2 selectively binds 5'-triphosphate-nucleosides, a defining characteristic of gRNAs. We therefore propose RESC2 as the protective 5'-end binding site for gRNAs within the RESC complex. Overall, our structure provides a starting point for the study of the assembly and function of larger RNA-bound kinetoplast RNA editing modules and might aid in the design of anti-parasite drugs.

Can domestic dogs be considered a good reservoir of *Leishmania* (L.) infantum chagasi in an endemic area of nonulcerated cutaneous leishmaniasis in Southern Honduras?

Segura GBR, Ochoa WHS, Matta VLRD, Martínez M, Tercero CR, Gonzalez RR, Pacheco CMS, Flores GVA, Silveira FT, Henriquez MMR, Laurenti MD.

24-03-2023

Rev Inst Med Trop Sao Paulo.

<https://pubmed.ncbi.nlm.nih.gov/36995877/>

Dogs are considered to be the main domestic reservoir associated with the transmission of *Leishmania* (L.) infantum chagasi to humans in endemic areas of visceral leishmaniasis in America. However, little is known about the role of canines as a source of infection in endemic

areas of nonulcerated cutaneous leishmaniasis (NUCL). Therefore, the objective of the present study was to investigate the role of dogs as a possible reservoir of the parasite in Southern Honduras. Dogs (n = 107) living with individuals affected by NUCL were clinically examined and biological material was collected for parasitological and immunological diagnosis. Most animals showed a healthy appearance and a few presented slight weight loss (64%), alopecia (7%), onychogryphosis (5%) and skin lesions (1%). The overall seroprevalence of *Leishmania* infection based on the DDP® quick test and/or in-house ELISA serological test was 41%. The presence of the parasite's DNA was confirmed in 94% of the dogs; however, the average parasite load in the buffy coat was low at 6.09 parasites/μL, ranging between 0.221 and 50.2. The skin of seropositive dogs examined by histopathology using paraffin sections stained by hematoxylin and immunohistochemistry did not show cutaneous lesions or parasite amastigotes. Based on the absence of parasites in the skin and the low parasite load detected in the buffy coat, it seems that the dog does not represent a good source of infection for the vector in the endemic area of NUCL transmission in Southern Honduras. Other domestic and/or wild animals should be investigated.

DC-SIGN receptor is expressed by cells from cutaneous leishmaniasis lesions and differentially binds to *Leishmania* (Viannia) braziliensis and L. (Leishmania) amazonensis promastigotes.

Mendes-Aguiar CO, Kitahara-Oliveira MY, de Almeida ACO, Pereira-Oliveira M, de Oliveira Neto MP, Pirmez C, Sampaio EP, Gomes-Silva A, Da-Cruz AM.

27-03-2023

Mem Inst Oswaldo Cruz.

<https://pubmed.ncbi.nlm.nih.gov/36995847/>

Blood parasite load by qPCR as therapeutic monitoring in visceral leishmaniasis patients in Brazil: a case series study.

Aquino SR, Diniz LFB, Nunes SLP, Silva RLO, Gouveia GV, Gouveia JJS, Sales KGDS, Dantas-Torres F, Carmo RFD.

27-03-2023

Rev Soc Bras Med Trop.

<https://pubmed.ncbi.nlm.nih.gov/36995785/>

Background: This study aimed to describe the kinetics of *Leishmania* parasite load determined using kinetoplast DNA (kDNA)-based quantitative polymerase chain reaction (qPCR) in visceral leishmaniasis (VL) patients. **Methods:** Parasite load in blood was assessed by qPCR at five time points, up to 12 months post-diagnosis. Sixteen patients were followed up. **Results:** A significant reduction in the parasite load was observed after treatment ($P < 0.0001$). One patient had an increased parasite load 3 months post-treatment and relapsed clinically at month six. **Conclusions:** We have described the use of kDNA-based qPCR in the post-treatment follow-up of VL cases.

Design, synthesis, and repurposing of O⁶-aminoalkyl-sulfuretin analogs towards discovery of potential lead compounds as antileishmanial agents.

Hassan AHE, Phan TN, Moon S, Lee CH, Kim YJ, Cho SB, El-Sayed SM, Choi Y, No JH, Lee YS.

05-05-2023

Eur J Med Chem.

<https://pubmed.ncbi.nlm.nih.gov/36944273/>

Selective whole-genome amplification reveals population genetics of *Leishmania braziliensis* directly from patient skin biopsies.

Pilling OA, Reis-Cunha JL, Grace CA, Berry ASF, Mitchell MW, Yu JA, Malekshahi CR, Krespan E, Go CK, Lombana C, Song YS, Amorim CF, Lago AS, Carvalho LP, Carvalho EM, Brisson D, Scott P, Jeffares DC, Beiting DP.

20-03-2023

PLoS Pathog.

<https://pubmed.ncbi.nlm.nih.gov/36940219/>

Development of a microemulsion loaded with epoxy- α -lapachone against *Leishmania (Leishmania) amazonensis* murine infection.

Peixoto JF, Gonçalves-Oliveira LF, Souza-Silva F, Côrtes LMC, Dias-Lopes G, Cardoso FO, Santos RO, Patricio BFC, Nicoletti CD, Lima CGS, Calabrese KDS, Moreira DL, Rocha HVA, da Silva FC, Ferreira VF, Alves CR.

05-04-2023

Int J Pharm.

<https://pubmed.ncbi.nlm.nih.gov/36934883/>

Epoxy- α -lapachone (ELAP), an oxirane-functionalized molecule synthesized from naturally occurring lapachol, has shown promising activity against murine infection with *Leishmania (Leishmania) amazonensis*. Herein, we report the successful development of oil-in-water-type (o/w) microemulsions (ME) loaded with ELAP (ELAP-ME) using Capmul MCM, Labrasol, and PEG 400. Stability studies revealed that ELAP-ME (100 μ g/mL of ELAP), which was comprised of globule size smaller than 120.4 ± 7.7 nm, displayed a good stability profile over 73 days. ELAP-ME had an effect in BALB/c mice infected with *L. (L.) amazonensis*, causing reductions in paw lesions after two weeks of treatment (~2-fold) when compared to untreated animals. Furthermore, there was also a reduction in the parasite load both in the footpad (60.3%) and in the lymph nodes (31.5%). Based on these findings, ELAP-ME emerges as a promising treatment for tegumentary leishmaniasis.

Synthesis, characterization, antioxidant and antiparasitic activities new naphthyl-thiazole derivatives.

Santos NFN, Junior NDSB, de Oliveira JF, Duarte DMFA, Dos Santos Soares JC, Clara Marques DS, da Silva Santos AC, Nogueira F, Alves Pereira VR, Alves de Lima MC, da Cruz Filho IJ.

May-2023

Exp Parasitol.

<https://pubmed.ncbi.nlm.nih.gov/36907541/>

Sequence analysis of SWEET transporters from trypanosomatids and evaluation of its expression in *Trypanosoma cruzi*.

Osorio-Méndez JF, Téllez GA, Zapata-López D, Echeverry S, Castaño JC.

May-2023

Exp Parasitol.

<https://pubmed.ncbi.nlm.nih.gov/36878387/>

Evaluation of immunomodulatory potential of recombinant histidyl-tRNA synthetase (rLdHisRS) protein of *Leishmania donovani* as a vaccine candidate against visceral leishmaniasis.

Kushwaha V, Capalash N.

May-2023

Acta Trop.

<https://pubmed.ncbi.nlm.nih.gov/36878386/>

Visceral leishmaniasis is neglected tropical protozoan disease caused by *Leishmania donovani* and are associated with high fatality rate in developing countries since prophylactic vaccines are not available. In the present study, we evaluated the immunomodulatory potential of *L. donovani* histidyl-tRNA synthetase (LdHisRS) and predicted the epitopes using immunoinformatic tools. Histidyl-tRNA synthetase (HisRS) is a class IIa aminoacyl t-RNA synthetase enzyme (aaRS) required for histidine incorporation into proteins during protein synthesis. The recombinant LdHisRS protein (rLdHisRS) was expressed in *E. coli* BL-21 cells, and its immunomodulatory role was assessed in J774A.1 murine macrophage and in BALB/c mice, respectively. LdHisRS specifically stimulated and triggered enhance cell proliferation, nitric oxide release and IFN- γ (70%; $P < 0.001$), and IL-12 (55.37%; $P < 0.05$) cytokine release in vitro, whereas BALB/c mice immunized with rLdHisRS show higher NO release (80.95%; $P < 0.001$), higher levels of Th1 cytokines IFN- γ (14%; $P < 0.05$), TNF- α (34.93%; $P < 0.001$), and IL-12 (28.49%; $P < 0.001$) and robust IgG ($p < 0.001$) and IgG2a ($p < 0.001$) production. We also identified 20 Helper T-lymphocytes (HTLs), 30 cytotoxic T lymphocytes (CTLs), and 18 B-cell epitopes from HisRS protein of *L. donovani*. All these epitopes can be further used to make a multiepitope vaccine against *L. donovani*.

Alpha-galactosylceramide as adjuvant induces protective cell-mediated immunity against *Leishmania mexicana* infection in vaccinated BALB/c mice.

Diupotex M, Zamora-Chimal J, Cervantes-Sarabia RB, Salaiza-Suazo N, Becker I.

Apr-2023

Cell Immunol.

<https://pubmed.ncbi.nlm.nih.gov/36870122/>

Adjuvants represent a promising strategy to improve vaccine effectiveness against infectious diseases such as

leishmaniasis. Vaccination with the invariant natural killer T cell ligand α -galactosylceramide (α GalCer) has been used successfully as adjuvant, generating a Th1-biased immunomodulation. This glycolipid enhances experimental vaccination platforms against intracellular parasites including *Plasmodium yoelii* and *Mycobacterium tuberculosis*. In the present study, we assessed the protective immunity induced by a single-dose intraperitoneal injection of α GalCer (2 μ g) co-administrated with a lysate antigen of amastigotes (100 μ g) against *Leishmania mexicana* infection in BALB/c mice. The prophylactic vaccination led to 5.0-fold reduction of parasite load at the infection site, compared to non-vaccinated mice. A predominant pro-inflammatory response was observed in challenged vaccinated mice, represented by a 1.9 and 2.8-fold-increase of IL-1 β and IFN- γ producing cells, respectively, in the lesions, and by 23.7-fold-increase of IFN- γ production in supernatants of restimulated splenocytes, all compared to control groups. The co-administration of α GalCer also stimulated the maturation of splenic dendritic cells and modulated a Th1-skewed immune response, with high amounts of IFN- γ production in serum. Furthermore, peritoneal cells of α GalCer-immunized mice exhibited an elevated expression of Ly6G and MHCII. These findings indicate that α GalCer improves protection against cutaneous leishmaniasis, supporting evidence for its potential use as adjuvant in *Leishmania*-vaccines.

The enemy within: lipid asymmetry in intracellular parasite-host interactions.

Fraser M, Matuschewski K, Maier AG.

31-03-2023

Emerg Top Life Sci.

<https://pubmed.ncbi.nlm.nih.gov/36820809/>

Role of Brazilian bats in the epidemiological cycle of potentially zoonotic pathogens.

Castelo-Branco DSCM, Nobre JA, Souza PRH, Diógenes EM, Guedes GMM, Mesquita FP, Souza PFN, Rocha MFG, Sidrim JJC, Cordeiro RA, Montenegro RC.

Apr-2023

Microb Pathog.

<https://pubmed.ncbi.nlm.nih.gov/36804526/>

Bats (Chiroptera) are flying mammals of great biodiversity and habits. These characteristics contribute for them being natural reservoirs and part of the epidemiological cycle of several potentially zoonotic pathogens, such as viruses, protozoa, fungi and bacteria. Brazil hosts approximately 15% of the world's bat diversity, with 181 distinct species, 68 genera and 9 families. About 60% of infectious diseases in humans are of zoonotic origin and, in the last decades, the detection of zoonotic pathogens in bats and their environment has been reported, such as Rabies virus (RABV) and *Histoplasma capsulatum*. Thus, the aim of this work was to review the reports of zoonotic pathogens associated with bats in Brazil in the past ten years. We reviewed the main pathogenic microorganisms described and the species of bats most frequently involved in the epidemiological cycles of these zoonotic agents. The

obtained data show an upward trend in the detection of zoonotic pathogens in Brazilian bats, such as RABV, *Bartonella* sp., *Histoplasma capsulatum* and *Leishmania* spp., with emphasis on the bat species *Artibeus lituratus*, *Carollia perspicillata*, *Desmodus rotundus* and *Molossus molossus*. These findings highlight the importance of monitoring bat-associated microorganisms to early identify pathogens that may threaten bat populations, including potentially zoonotic microorganisms, emphasizing the importance of the One Health approach to prevent and mitigate the risks of the emergence of zoonotic diseases.

Immunoproteomics approach for the discovery of antigens applied to the diagnosis of canine visceral leishmaniasis.

Costa SS, Santos LMO, Freire LC, Tedeschi ALF, Ribeiro NR, Queiroz MHR, Neto EB, Pimenta DC, Galvani NC, Luiz GP, de Oliveira ME, de Ávila RAM, Carvalho AMRS, Brigido BVS, Reis AB, Fernandes APSM, Coelho EAF, Roatt BM, Menezes-Souza D, Duarte MC.

May-2023

Acta Trop.

<https://pubmed.ncbi.nlm.nih.gov/36787861/>

In the present study, an immunoproteomic approach using *Leishmania infantum* parasites isolated from naturally infected dogs from an endemic region of the disease, was carried out to identify new antigens to be used in the diagnosis of canine visceral leishmaniasis (CVL). Protein extracts, obtained from parasites isolated from asymptomatic (CanLA) and symptomatic (CanLS) dogs, were used to perform the two-dimensional gels. Western Blotting assays were carried out by employing a pool of sera from dogs with visceral leishmaniasis (CanLA or CanLS), healthy dogs from an endemic area, or dogs with similar diseases associated with cross-reactions (babesiosis and ehrlichiosis). With these results, it was possible to exclude the spots that showed a cross-reactivity of the sera from groups of healthy dogs, and those with babesiosis or ehrlichiosis. Taken together, 20 proteins were identified, 15 of which have already been described in the literature and 5 of which are hypothetical. An immunogenomic screen strategy was applied to identify conserved linear B-cell epitopes in the identified hypothetical proteins. Two peptides were synthesized and tested in ELISA experiments as a proof of concept for the validation of our immunoproteomics findings. The results demonstrated that the antigens presented sensitivity and specificity values ranging from 81.93% to 97.59% and 78.14 to 85.12%, respectively. As a comparative antigen, a preparation of a *Leishmania* extract showed sensitivity and specificity values of 75.90% and 74.88%, respectively. The present study was able to identify proteins capable of being used for the serodiagnosis of canine visceral leishmaniasis.

Natural products derived steroids as potential anti-leishmanial agents; disease prevalence, underlying mechanisms and future perspectives.

Elawad MA, Elkhalfa MEM, Hamdoon AAE, Salim LHM, Ahmad Z, Ayaz M.

May-2023

Steroids.

<https://pubmed.ncbi.nlm.nih.gov/36764565/>

Co-occurrence of mucosal leishmaniasis caused by *Leishmania infantum* and mucosal-associated lymphoid tissue lymphoma.

Beudet H, L'Ollivier C, Bouabdallah R, Campana F, Bagonchy A, Lepidi H, Parola P, Cassir N.

Mar-apr-2023

Travel Med Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/36528250/>

Poor adherence is a major barrier to the proper treatment of cutaneous leishmaniasis: A case-control field assessment in Iran.

Bamorovat M, Sharifi I, Agha Kuchak Afshari S, Karamoozian A, Tahmouresi A, Heshmatkhah A, Salarkia E, Khosravi A, Hakimi Parizi M, Barghi M.

Apr-2023

Int J Parasitol Drugs Drug Resist.

<https://pubmed.ncbi.nlm.nih.gov/36525935/>

Leishmaniasis is an overlooked, poverty-stricken, and complex disease with growing social and public health problems. In general, leishmaniasis is a curable disease; however, there is an expansion of unresponsive cases to treatment in cutaneous leishmaniasis (CL). One of the effective and ignored determinants in the treatment outcome of CL is poor treatment adherence (PTA). PTA is an overlooked and widespread phenomenon to proper *Leishmania* treatment. This study aimed to explore the effect of poor adherence in unresponsiveness to treatment in patients with anthroponotic CL (ACL) by comparing conventional statistical modalities and machine learning analyses in Iran. Overall, 190 cases consisting of 50 unresponsive patients (case group), and 140 responsive patients (control group) with ACL were randomly selected. The data collecting form that included 25 queries (Q) was recorded for each case and analyzed by R software and genetic algorithm (GA) approaches. Complex treatment regimens (Q11), cultural and lay views about the disease and therapy (Q8), life stress, hopelessness and negative feelings (Q22), adverse effects of treatment (Q13), and long duration of the lesion (Q12) were the most prevalent significant variables that inhibited effective treatment adherence by the two methods, in decreasing order of significance. In the inherent algorithm approach, similar to the statistical approach, the most significant feature was complex treatment regimens (Q11). Providing essential knowledge about ACL and treatment of patients with chronic diseases and patients with misconceptions about chemical drugs are important issues directly related to the disease's unresponsiveness. Furthermore, early detection of patients to prevent the long duration of the disease and the process of treatment, efforts to minimize side effects of treatment, induction of positive thinking, and giving

hope to patients with stress and anxiety by medical staff, and family can help patients adhere to the treatment.

Thiophene derivatives activity against the protozoan parasite *Leishmania infantum*.

Bigot S, Leprohon P, Vasquez A, Bhadoria R, Skouta R, Ouellette M.

Apr-2023

Int J Parasitol Drugs Drug Resist.

<https://pubmed.ncbi.nlm.nih.gov/36525934/>

Visceral leishmaniasis in a patient with systemic lupus erythematosus: Dilemma in diagnosis and management.

Akkuzu G, Ozkara S, Ozgur DS, Karaalioglu B, Yildirim F, Ayer M, Bes C.

Apr-2023

Int J Rheum Dis.

<https://pubmed.ncbi.nlm.nih.gov/36502503/>

Patients with systemic lupus erythematosus (SLE) have an increased risk of bacterial, viral, fungal or parasitic infections, especially if they are receiving immunosuppressive therapy. Leishmaniasis is a group of diseases caused by intracellular flagellate protozoan parasites belonging to the genus *Leishmania*. We present a 48-year-old female patient, diagnosed with SLE many years ago, who presented with high fever and pancytopenia. We thought that the patient's hematologic findings were related to SLE hematologic involvement. However, we investigated other possible causes when there was no response to drugs for the treatment of SLE. A second bone marrow biopsy showed *Leishmania* amastigotes and the patient was diagnosed with leishmaniasis. The patient was treated with liposomal amphotericin-B (treatment completed at 40 days). She showed rapid clinical improvement and showed no signs of disease after 4 months.

Cysticercose

Prevalence and Associated Risk Factors of *Cysticercosis bovis* in Bishoftu Municipal Abattoir, Central Ethiopia.

Fesseha H, Asefa I.

26-03-2023

Environ Health Insights.

<https://pubmed.ncbi.nlm.nih.gov/37007220/>

Background: *Cysticercus bovis* has zoonotic implications with economic losses from organ contamination and treatment costs. In developing countries such as Ethiopia, where hygienic standards are low and residents customarily eat raw or undercooked meat, the disease is prevalent. **Methods:** A cross-sectional study was carried out from December 2021 to June 2022 to determine the prevalence of *Cysticercus bovis* in cattle slaughtered at the Bishoftu municipal abattoir, in central Ethiopia. Study populations for the active abattoir survey were cattle presented to the abattoir for slaughtering and routine

meat inspection conditions. The organ namely the tongue, masseter muscle, liver, and triceps muscle were inspected for the presence of *C. bovis*. **Results:** From a total of 330 cattle, 14 were found to be positive for *C. bovis*, with an overall prevalence of 4.24%. Based on the origin of the animals, the highest prevalence was recorded at Adama (7.27%), followed by Bishoftu (5.45%), Mojo (5.45%), Borana (3.63%), Dukem (3.63%), and Kaliti (0.00%). Similarly, out of 111 adults and 219 old-aged cattle slaughtered and examined at the abattoir, 4.5% and 4.11% were positive for *C. bovis*, respectively. Among tested independent variables, sex, body condition score, age, and origin of animals had no relationships with the prevalence of *C. bovis*. From the detected organ, the tongue ranks first for the highest number of cysts, followed by the masseter muscle, liver, and triceps muscle, with total cysts of 6, 4, 3, and 1, respectively. **Conclusion:** *C. bovis* is a prevalent zoonotic parasite disease that causes carcass condemnation; an enhanced understanding of the health consequences of teniasis is required to protect the community.

Prolonged Albendazole Therapy for Neurocysticercosis in Children: Author's Reply.

Kleebayoon A, Kaushik JS.

15-04-2023

Indian Pediatr.

<https://pubmed.ncbi.nlm.nih.gov/37002851/>

Prolonged Albendazole Therapy for Neurocysticercosis in Children.

Kleebayoon A, Wiwanitkit V.

15-04-2023

Indian Pediatr.

<https://pubmed.ncbi.nlm.nih.gov/37002850/>

Calcified Neurocysticercosis: Not So "Inactive" After All!

Udani V.

15-03-2023

Indian Pediatr.

<https://pubmed.ncbi.nlm.nih.gov/37002841/>

The epidemiology of human *Taenia solium* infections: A systematic review of the distribution in Eastern and Southern Africa.

Zulu G, Stelzle D, Mwape KE, Welte TM, Strømme H, Mubanga C, Mutale W, Abraham A, Hachangu A, Schmidt V, Sikasunge CS, Phiri IK, Winkler AS.

31-03-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/37000841/>

Background: *Taenia solium* is a tapeworm that causes taeniosis in humans and cysticercosis in humans and pigs. Within Eastern and Southern Africa (ESA), information on the presence of human taeniosis and cysticercosis seems scarce. This systematic review aimed to describe the current information available and gaps in the

epidemiology of human *T. solium* infections in ESA.

Methods/principle findings: Scientific literature published between 1st January 2000 and 20th June 2022 in international databases [MEDLINE (Ovid), Embase (Ovid), Global Health (Ovid), Scopus (Elsevier), African Index Medicus (via WHO Global Index Medicus), and Open Grey] was systematically reviewed for ESA. The study area included 27 countries that make up the ESA region. Information on either taeniosis, cysticercosis or NCC was available for 16 of 27 countries within the region and a total of 113 reports were retained for the review. Most case reports for cysticercosis and NCC were from South Africa, while Tanzania had the most aggregated cysticercosis reports. Eleven countries reported on NCC with seven countries reporting data on NCC and epilepsy. Unconfirmed human *T. solium* taeniosis cases were reported in nine countries while two countries (Madagascar and Zambia) reported confirmed *T. solium* cases. The cysticercosis seroprevalence ranged between 0.7-40.8% on antigen (Ag) ELISA and between 13.1-45.3% on antibody (Ab) ELISA. Based on immunoblot tests the Ab seroprevalence was between 1.7-39.3%, while the proportion of NCC-suggestive lesions on brain CT scans was between 1.0-76% depending on the study population. The human taeniosis prevalence based on microscopy ranged between 0.1-14.7%. Based on Copro Ag-ELISA studies conducted in Kenya, Rwanda, Tanzania, and Zambia, the highest prevalence of 19.7% was reported in Kenya. **Conclusions:** Despite the public health and economic impact of *T. solium* in ESA, there are still large gaps in knowledge about the occurrence of the parasite, and the resulting One Health disease complex, and monitoring of *T. solium* taeniosis and cysticercosis is mostly not in place.

Radiological Outcome of Neurocysticercosis in Children Six Months After Diagnosis - A Single Center Study.

Shanmugavel P, Sehgal R, Misra RN.

15-04-2023

Indian Pediatr.

<https://pubmed.ncbi.nlm.nih.gov/36604933/>

Objective: To assess proportion and predictors of lesion calcification in children aged 2-12 years with neurocysticercosis at six months follow up. **Methods:** Children aged between 2 and 12 years with Neurocysticercosis diagnosed on MRI brain were initially included and followed up for 6 months. Repeat CECT brain at 6 months was done to find if the lesion persisted/calcified/ resolved. **Results:** 16 out of 30 patients (53.3%) had calcification at six months follow up. Perilesional edema at the initial stage of the presentation was significantly associated with calcification at 6 months ($P=0.042$). **Conclusions:** Perilesional edema at the time of presentation was significantly associated with calcification in children with neurocysticercosis, six months after diagnosis.

Value of whole-body MRI for the assessment of response to albendazole in

disseminated neurocysticercosis: a prospective follow-up study.

Wangda K, Kumar N, Garg RK, Malhotra HS, Rizvi I, Uniyal R, Pandey S, Malhotra KP, Verma R, Sharma PK, Parihar A, Jain A.

03-04-2023

Trans R Soc Trop Med Hyg.

<https://pubmed.ncbi.nlm.nih.gov/36259415/>

Background: Disseminated neurocysticercosis is defined as simultaneous involvement of the brain (≥ 3 cysts) and at least one additional body site/organ. We aimed to identify disseminated cystic lesions in other body parts and investigate the effect of albendazole. **Methods:** We enrolled patients with multiple (≥ 3) neurocysticercosis brain lesions. Whole-body MRI (short tau inversion recovery coronal sequences) was performed to assess the number of lesions in the brain and other body parts at baseline and 3 months after albendazole therapy. **Results:** We screened 35 patients with multiple brain neurocysticercosis. In 13 patients, whole-body MRI demonstrated disseminated neurocysticercosis lesions. Ten patients were treated with albendazole. We excluded three patients. Brain MRI showed a mean lesion count of 163.6 ± 193.8 . Whole-body MRI (excluding the brain) showed a mean lesion count of 629.9 ± 486.1 . After albendazole therapy, the lesion load of the brain reduced significantly (163.6 ± 193.8 to 99 ± 178.3 ; $p=0.008$). Similarly, whole-body MRI showed a significant reduction in extracerebral neurocysticercosis lesion load (629.9 ± 486.1 to 183.4 ± 301.9 ; $p=0.005$). Three patients had complete resolution, five patients showed $\geq 50\%$ reduction and two patients had $<50\%$ reduction in extracerebral lesion load. **Conclusion:** Whole-body MRI should routinely be performed in multiple neurocysticercosis lesions of the brain. Albendazole treatment leads to a remarkable reduction in neurocysticercosis lesions throughout the body.

Dracunculose

Unusual cutaneous manifestations of dracunculiasis: Two rare case reports.

Darkase BA, Ratnaprkhi T, Bhatt K, Khopkar U.

Jan-Mar 2023

Indian J Dermatol Venereol Leprol.

<https://pubmed.ncbi.nlm.nih.gov/33969654/>

A nematode parasite, *Dracunculus medinensis*, causes dracunculiasis. Despite being non-fatal, this condition causes significant morbidity. Dracunculiasis is considered an eradicated disease in India since 1999. We report two cases that document the unusual linear morphea-like morphology of the calcified *D. medinensis* and the rare periorbital location of the worm. The cases presented here are rare and a diagnostic challenge, considering the eradicated status of dracunculiasis.

Echinococcoses

Identification of Omega-class glutathione transferases in helminths of the Taeniidae family.

Miles S, Mourglia-Ettlin G, Fernández V.

Apr-2023

Mol Biochem Parasitol.

<https://pubmed.ncbi.nlm.nih.gov/37024059/>

Molecular and immunological diagnosis of cystic echinococcosis from different hosts in the Gaza Strip, Palestine.

Al-Hindi AI, Bodell T, Alshmmari A.

16-03-2023

Parasite Epidemiol Control.

<https://pubmed.ncbi.nlm.nih.gov/37021323/>

The aim of the present study was to determine the molecular characteristics of *Echinococcus granulosus* sensu lato from faecal samples of dogs and the hydatid cyst from liver of bovine, camel, cattle, and sheep and the immunodiagnosis of Hydatid cyst in human sera samples from the Gaza Strip, in Palestine. A total of 38 faecal samples were collected near farms and local markets where stray dogs were grouping there. Post-slaughtering, the livers of the bovine, camel, cattle, and sheep were examined for cysts. Where 30 suspected hydatid cysts were collected, the number and size of cysts in each liver were recorded. For serology, 23 sera specimens were collected from farmers within the Gaza Strip. According to hospital records in Gaza, 12 patients had attended three different hospitals and had tested positive for hydatid cyst/cystic echinococcosis by CT scans and histopathology. ELISA results from the 23 human patients showed that 3/23 (13%) tested positive for hydatid disease. Of the 30 bovine and cattle harboring cysts, 14/30 (46.6%) were positive for hydatid cyst/cystic echinococcosis of which 23 (76.7%) were males and 7 (23.3%) were females. The present study shows that 6/38 (15.7%) were positive for *E. granulosus* sensu lato from faecal analysis in dogs. Subsequent sequencing of both dogs and cattle confirmed infection by the G1 strain. The cattle/dog strain (G1) of *E. granulosus* sensu lato suggests that this infection is cosmopolitan in its distribution. It is concluded that the detection of hydatid cyst/cystic echinococcosis in the examined hosts either human or animals should be considered among physicians and a large sample size is recommended in future research.

Alveolar echinococcosis in solid organ transplant recipients: a case series from two national cohorts.

Marquis B, Demonmerot F, Richou C, Thiéfin G, Millon L, Wallon M, Vuitton DA, Grall-Jezequel A, Grenouillet F, Epaulard O, Gervais P, Manuel O, Bresson-Hadni S; Swiss Transplant Cohort Study; FrancEchino Network.

2023

Parasite.

<https://pubmed.ncbi.nlm.nih.gov/37010450/>

Alveolar echinococcosis (AE) is a severe parasitic infection caused by the ingestion of *Echinococcus multilocularis* eggs. While higher incidence and faster evolution have been reported in immunosuppressed patients, no studies have been performed specifically on AE in transplant patients. We searched for all de novo AE cases diagnosed between January 2008 and August 2018 in solid organ transplant (SOT) recipients included in the Swiss Transplant Cohort Study and the FrancEchino Registry. Eight cases were identified (kidney = 5, lung = 2, heart = 1, liver = 0), half of which were asymptomatic at diagnosis. AE diagnosis was difficult due to the low sensitivity (60%) of the standard screening serology (Em2+) and the frequently atypical radiological presentations. Conversely, *Echinococcus* Western blot retained good diagnostic performances and was positive in all eight cases. Five patients underwent surgery, but complete resection could only be achieved in one case. Moreover, two patients died of peri-operative complications. Albendazole was initiated in seven patients and was well tolerated. Overall, AE regressed in one, stabilized in three, and progressed in one case, and had an overall mortality of 37.5% (3/8 patients). Our data suggest that AE has a higher mortality and a faster clinical course in SOT recipients; they also suggest that the parasitic disease might be due to the reactivation of latent microscopic liver lesions through immune suppression. Western blot serology should be preferred in this population. Finally, surgery should be considered with caution, because of its low success rate and high mortality, and conservative treatment with albendazole is well tolerated.

Monoclonal antibody-based localization of major diagnostic antigens in metacestode tissue, excretory/secretory products, and extracellular vesicles of *Echinococcus* species.

Kronenberg PA, Reinehr M, Eichenberger RM, Hasler S, Laurimäe T, Weber A, Deibel A, Müllhaupt B, Gottstein B, Müller N, Hemphill A, Deplazes P.

16-03-2023

Front Cell Infect Microbiol.

<https://pubmed.ncbi.nlm.nih.gov/37009502/>

Exploring the genetic diversity of genotypes G8 and G10 of the *Echinococcus canadensis* cluster in Europe based on complete mitochondrial genomes (13 550 - 13 552 bp).

Laurimäe T, Kinkar L, Moks E, Bagrade G, Saarma U.

03-04-2023

Parasitology.

<https://pubmed.ncbi.nlm.nih.gov/37005069/>

NOTCH signaling inhibition after DAPT treatment exacerbates alveolar echinococcosis hepatic fibrosis by blocking M1 and enhancing M2 polarization.

Li B, Wang L, Qi X, Liu Y, Li J, Lv J, Zhou X, Cai X, Shan J, Ma X.

May-2023

FASEB J.

<https://pubmed.ncbi.nlm.nih.gov/37002884/>

Alveolar echinococcosis (AE) is a lethal helminthic liver disease caused by persistent infection with *Echinococcus multilocularis* (*E. multilocularis*). Although more and more attention has been paid to the macrophages in *E. multilocularis* infection, the mechanism of macrophage polarization, a critical player in liver immunity, is seldom studied. NOTCH signaling is involved in cell survival and macrophage-mediated inflammation, but the role of NOTCH signaling in AE has been equally elusive. In this study, liver tissue samples from AE patients were collected and an *E. multilocularis* infected mouse model with or without blocking NOTCH signaling was established to analyze the NOTCH signaling, fibrotic and inflammatory response of the liver after *E. multilocularis* infection. Changes in polarization and origin of hepatic macrophages were analyzed by flow cytometry. In vitro qRT-PCR and Western blot assays were performed to analyze key receptors and ligands in NOTCH signaling. Our data demonstrated that hepatic fibrosis develops after AE, and the overall blockade of NOTCH signaling caused by DAPT treatment exacerbates the levels of hepatic fibrosis and alters the polarization and origin of hepatic macrophages. Blocking NOTCH signaling in macrophages after *E. multilocularis* infection downregulates M1 and upregulates M2 expression. The downregulation of NTCH3 and DLL3 in the NOTCH signaling pathway is significant. Therefore, NOTCH3/DLL3 may be the key pathway in NOTCH signaling regulating macrophage polarization affecting fibrosis caused by AE.

High potency of magnetic iron oxide nanoparticles covered by piroctone olamine against cystic echinococcosis.

Raziani Y, Cheraghipour K, Shakibaie M, Ghasemian Yadegari J, Mahmoudvand H.

May-2023

Biomed Pharmacother.

<https://pubmed.ncbi.nlm.nih.gov/36940617/>

This study examined the synthesis of magnetic iron oxide nanoparticles coated with PO (FOMNPsP) and assessed their in vitro, ex vivo, and in vivo effects against cystic echinococcosis. The FOMNPsP was synthesized through the alkalization of iron ions in a deoxygenated form. In vitro and ex vivo protoscolicidal effects of FOMNPsP (100-400 µg/mL) were evaluated on hydatid cyst protoscoleces by the eosin exclusion test for 10-60 min. The effect of FOMNPsP on caspase-3 gene expression and exterior ultra-structural of protoscoleces was assessed by real-time PCR and scanning electron microscopy (SEM), respectively. In vivo effects were assessed by evaluating the number, size, and weight of hydatid cysts among infected mice. The FOMNPsP size was < 55 nm, and the most frequent particles were in the 15-20 nm range. In vitro and ex vivo assays revealed that the highest protoscolicidal effect was observed at 400 µg/mL with 100% lethality. After exposure of protoscoleces with FOMNPsP, the level of gene expression of caspase-3 was

dose-dependently increased ($p < 0.05$). By SEM, the FOMNPsP-treated protoscoleces showed wrinkles and bulges resulting from the formation of blebs. FOMNPsP significantly decreased ($p < 0.01$) the mean number, size, and weight of the hydatid cyst. FOMNPsP revealed the potent protoscolicidal traits through disrupting the cell wall and apoptosis induction. The results also indicated the promising effect of FOMNPsP in controlling hydatid cysts in the animal model. Although FOMNPsP is safe for human normal cells, more investigations are required to clarify its toxicity and precise mechanisms of action.

Cystic echinococcosis in donkeys in eastern Africa.

Mulinge E, Zeyhle E, Mbae C, Gitau L, Kaburu T, Magambo J, Mackenstedt U, Romig T, Kern P, Wassermann M.

Apr-2023

Parasitology.

<https://pubmed.ncbi.nlm.nih.gov/36843475/>

Cystic echinococcosis (CE) is endemic in humans and domestic animals in eastern Africa. All the species of the *Echinococcus granulosus* sensu lato complex have been reported in this region except for *E. equinus*, possibly due to the small number of studies involving equids. This study reports the frequency of different *Echinococcus* species in donkeys from eastern Africa. A total of 5961 donkeys were examined during meat inspection in 3 slaughterhouses in Kenya. Identification of *Echinococcus* spp. was achieved through polymerase chain reaction-restriction fragment-length polymorphism and sequencing of the mitochondrial nicotinamide adenine dinucleotide (NADH) dehydrogenase subunit 1 gene. The prevalence of CE was 5.7% (337/5961). The 263 genotyped cysts belonged to *E. equinus* ($n = 163$), *E. granulosus* sensu stricto ($n = 70$), *E. canadensis* (G6/7) ($n = 26$) and *E. ortleppi* ($n = 4$). One donkey harboured a metacestode of *Spirometra theileri*. All *E. equinus* cases, except 2, originated from southern Ethiopia, whereas the other species were more evenly distributed across the study area. Most of the cysts belonging to *E. equinus* were fertile (111/163), while those of the other species were non-fertile. This is the first report of *Echinococcus* spp. in donkeys from sub-Saharan Africa and the first confirmation of *E. equinus* in East Africa. The frequent fertility of *E. equinus* cysts in donkeys affirms their suitability as intermediate hosts of this species, while low frequency and cyst fertility suggest a marginal role of donkeys in the transmission of *E. granulosus* s. s., *E. canadensis* (G6/7) and *E. ortleppi*.

Current and future distribution of a parasite with complex life cycle under global change scenarios: *Echinococcus multilocularis* in Europe.

Cenni L, Simoncini A, Massetti L, Rizzoli A, Haufler HC, Massolo A.

May-2023

Glob Chang Biol.

<https://pubmed.ncbi.nlm.nih.gov/36815401/>

Current status of cystic echinococcosis control in the Falkland Islands: has elimination been achieved?

West D, Pointing S, Randhawa HS, Mastin A, Rogan MT.

Apr-2023

Parasitology.

<https://pubmed.ncbi.nlm.nih.gov/36760183/>

Research progress in the proteomics of *Echinococcus multilocularis* and alveolar echinococcosis.

Pang MQ, Liu CC, Shi DL, Fan HN.

Apr-2023

Asian J Surg.

<https://pubmed.ncbi.nlm.nih.gov/36334997/>

[Robotic Left Hepatectomy Using the Glissonean Pedicle Approach for the Treatment of Caroli's Syndrome].

Birgin E, Reissfelder C, Rahbari NN.

Apr-2023

Zentralbl Chir.

<https://pubmed.ncbi.nlm.nih.gov/36104087/>

Background: Caroli's syndrome is a rare disease characterised by non-obstructive dilation of intrahepatic bile ducts, hepatic fibrosis, and an increased risk of developing cholangiocarcinoma. Minimally invasive liver resection has recently been increasingly adopted for the treatment of patients with localised Caroli's syndrome. However, robot-assisted liver resection for the treatment of Caroli's syndrome has not been published. **Materials and methods:** We report a case of a 72-year-old Asian female who was referred to our hospital with multifocal cystic dilation of liver segments II, III, and IV. She had no family history of congenital cysts. Her past medical history was uneventful except for an open appendectomy. The liver function tests were normal, with a negative echinococcus serology test. On MRI, the biliary anatomy at the hilum and right liver appeared to be regular. Therefore, a robotic left hepatectomy was carried out for the unilobar involvement of Caroli's syndrome using the Da Vinci Xi-system. **Results:** We performed a Glissonean pedicle approach while preserving the caudate lobe. After removing surgical adhesions from the anterior abdominal wall using robotic scissors, a routine cholecystectomy was performed. An aberrant left hepatic artery arising from the left gastric artery was clipped and divided. The left portal pedicle was controlled after lowering the hilar plate. The ischemic demarcation line on the liver surface was followed after clamping the left pedicle, and parenchymal dissection was performed using Maryland bipolar forceps. A Pringle manoeuvre was not applied. The left pedicle and the left hepatic vein were transected using a GIA stapling device while the middle hepatic vein was preserved. Indocyanine green fluorescence imaging confirmed adequate perfusion of the remnant liver tissue including the caudate lobe. The specimen was placed in an extraction bag and removed via a Pfannenstiel incision. The total operation time was 239 min, including a total blood loss of 100 ml. The postoperative course was uneventful. The patient was discharged on postoperative

day 5. On 6 months follow-up, the patient had normal liver function and no signs of recurrent disease. **Conclusion:** Robotic left hepatectomy using an extrahepatic Glissonean pedicle approach is technically feasible.

Case Series of Cystic Echinococcosis Over a Twelve-year Period at Sultan Qaboos University Hospital, Oman.

Hassan KS, Al Balushi A; Prashanth Kumar P1; Wazir HB, Al Adawi B.
31-03-2023
Oman Med J.
<https://pubmed.ncbi.nlm.nih.gov/37009206/>

Investigation of the mechanism of action of mefloquine and derivatives against the parasite *Echinococcus multilocularis*.

Memedovski R, Preza M, Müller J, Kämpfer T, Rufener R, de Souza MVN, da Silva ET, de Andrade GF, Braga S, Uldry AC, Buchs N, Heller M, Lundström-Stadelmann B.
Apr-2023
Int J Parasitol Drugs Drug Resist.
<https://pubmed.ncbi.nlm.nih.gov/36921443/>

Contrast-enhanced ultrasound (CEUS) in patients with metastasis-like hepatic alveolar echinococcosis: a cohort study.

Schweizer M, Schmidberger J, Schlingeloff P, Kratzer W.
Mar-2023
J Ultrasound.
<https://pubmed.ncbi.nlm.nih.gov/35597873/>

Purpose: Hepatic alveolar echinococcosis (HAE) of the metastasis-like pattern, according to the Echinococcus Ulm classification, is usually discovered as an incidental finding, and the diagnostic differentiation from "true metastases" is difficult. The aim of this study was to investigate whether lesions of the "metastasis-like pattern" in HAE show a typical contrast behavior that can be used for differentiation from metastasis in malignancies. **Methods:** This prospective clinical study included 11 patients with histologically confirmed HAE of the metastasis-like pattern (7 female and 4 male; mean age, 57.1 years; mean disease duration, 59.5 months), who had been examined by B-scan sonography and CEUS, from the National Echinococcosis Registry Germany. **Results:** On contrast-enhanced sonography, 11/11 reference lesions showed annular rim enhancement in the arterial and portal venous phases. Throughout the entire 4-min study period, none of the reference lesions showed central contrast enhancement-i.e., all exhibited a complete "black hole sign". A small central scar was seen in 81.8% of cases. **Conclusion:** In clinically unremarkable patients with incidentally detected metastasis-like lesions of the liver, contrast-enhanced sonographic detection of rim enhancement without central contrast uptake (black hole sign) should be considered evidence supporting a diagnosis of hepatic alveolar echinococcosis with a rare metastasis-like pattern. This can help to differentiate HAE from metastases, especially in high-endemic areas.

Trématodoses d'origine alimentaire (clonorchiasse, opisthorchiasse, fasciolase et paragonimose

Praziquantel - 50 years of research.

Waechtler A, Cezanne B, Maillard D, Sun R, Wang S, Wang J, Harder A.
03-04-2023
ChemMedChem.
<https://pubmed.ncbi.nlm.nih.gov/37009677/>

Investigations on Praziquantel (PZQ) started fifty years ago by a joint cooperation between Bayer AG and Merck KGaA. Until today PZQ is the drug of choice for schistosomiasis in human medicine and used in many combinations with antinematode drugs in veterinary medicine. The Sm.TRPM PZQ, a Ca²⁺-permeable transient receptor potential (TRP) channel, has been discovered as primary target of PZQ during the last decade. Furthermore, there is a short overview of routes of large-scale synthesis of racemic and pure R-PZQ. Until now racemic PZQ is used in veterinary and human medicine. In 2012 the Pediatric Praziquantel Consortium started PZQ chemistry and process development of pure R-PZQ for human application. It is hoped that R-PZQ will become available for pediatric use soon. The knowledge of the binding pocket of PZQ in Sm.TRPM PZQ allows to design synthesis of PZQ-derivatives of the next generation for a target-site directed screening. A similar screening should also be started for *Fasciola hepatica* TRPM PZQ.

New challenges in cholangiocarcinoma candidates for elective surgery: harnessing the microbiome dysbiosis.

Re OL, López-López V, Balaguer-Román A, Martínez-Sánchez MA, Eshmuminov D, Llamaza-Torres CJ, Miura K, Baroja-Mazo A, Ramírez P, Robles-Campos R, Ramos-Molina B.
31-03-2023
Langenbecks Arch Surg.
<https://pubmed.ncbi.nlm.nih.gov/37000331/>

Case Report: Reemerging Paragonimiasis in Umphang District, Thailand.

Hanprom J, Lapphra K, Tontiwattanasap W, Papwijitsil R, Copeland K, Chokephaibulkit K.
27-02-2023
Am J Trop Med Hyg.
<https://pubmed.ncbi.nlm.nih.gov/36848893/>

Paragonimiasis is a food-born zoonotic parasitosis caused by *Paragonimus* spp. Six cases of reemerging paragonimiasis within the Karan hill-tribe near the Thai-Myanmar border were evaluated to review clinical

manifestations, predisposing factors, and treatment regimens. All patients tested positive for paragonimiasis eggs and presented with an array of symptoms, including chronic cough, hemoptysis, peripheral eosinophilia, and thoracic radiograph abnormalities. All fully recovered after a 2- to 5-day course of 75 to 80 mg/kg/day praziquantel. We conclude that paragonimiasis should be considered during differential diagnoses to promote early treatment and to prevent misdiagnosis of reemerging or sporadic cases. This applies particularly to endemic regions and high-risk groups known to habitually consume raw or undercooked intermediate or paratenic hosts.

Genome-wide exploration reveals distinctive northern and southern variants of *Clonorchis sinensis* in the Far East.

Kinkar L, Korhonen PK, Saarma U, Wang T, Zhu XQ, Harliwong I, Yang B, Fink JL, Wang D, Chang BCH, Chelomina GN, Koehler AV, Young ND, Gasser RB.

May-2023

Mol Ecol Resour.

<https://pubmed.ncbi.nlm.nih.gov/36727564/>

Clonorchis sinensis is a carcinogenic liver fluke that causes clonorchiasis—a neglected tropical disease (NTD) affecting ~35 million people worldwide. No vaccine is available, and chemotherapy relies on one anthelmintic, praziquantel. This parasite has a complex life history and is known to infect a range of species of intermediate (freshwater snails and fish) and definitive (piscivorous) hosts. Despite this biological complexity and the impact of this biocarcinogenic pathogen, there has been no previous study of molecular variation in this parasite on a genome-wide scale. Here, we conducted the first extensive nuclear genomic exploration of *C. sinensis* individuals ($n = 152$) representing five distinct populations from mainland China, and one from Far East Russia, and revealed marked genetic variation within this species between "northern" and "southern" geographical regions. The discovery of this variation indicates the existence of biologically distinct variants within *C. sinensis*, which may have distinct epidemiology, pathogenicity and/or chemotherapeutic responsiveness. The detection of high heterozygosity within *C. sinensis* specimens suggests that this parasite has developed mechanisms to readily adapt to changing environments and/or host species during its life history/evolution. From an applied perspective, the identification of invariable genes could assist in finding new intervention targets in this parasite, given the major clinical relevance of clonorchiasis. From a technical perspective, the genomic-informatic workflow established herein will be readily applicable to a wide range of other parasites that cause NTDs.

Filariose lymphatique

Circulation of West Nile virus in mosquitoes approximate to the migratory bird stopover in West Coast Malaysia.

Natasha JA, Yasmin AR, Sharma RSK, Nur-Fazila SH, Nur-Mahiza MI, Arshad SS, Mohammed HO, Kumar K, Loong SK, Ahmad Khusaini MKS.

06-04-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/37023172/>

Being a tropical country with a conducive environment for mosquitoes, mosquito-borne illnesses such as dengue, chikungunya, lymphatic filariasis, malaria, and Japanese encephalitis are prevalent in Malaysia. Recent studies reported asymptomatic infection of West Nile virus (WNV) in animals and humans, but none of the studies included mosquitoes, except for one report made half a century ago. Considering the scarcity of information, our study sampled mosquitoes near migratory bird stopover wetland areas of West Coast Malaysia located in the Kuala Gula Bird Sanctuary and Kapar Energy Venture, during the southward migration period in October 2017 and September 2018. Our previous publication reported that migratory birds were positive for WNV antibody and RNA. Using a nested RT-PCR analysis, WNV RNA was detected in 35 (12.8%) out of 285 mosquito pools consisting of 2,635 mosquitoes, most of which were *Culex* spp. (species). Sanger sequencing and phylogenetic analysis revealed that the sequences grouped within lineage 2 and shared 90.12%-97.01% similarity with sequences found locally as well as those from Africa, Germany, Romania, Italy, and Israel. Evidence of WNV in the mosquitoes substantiates the need for continued surveillance of WNV in Malaysia.

Acceptability of test and treat with doxycycline against Onchocerciasis in an area of persistent transmission in Massangam Health District, Cameroon.

Nditanchou R, Dixon R, Atekem K, Akongo S, Biholong B, Ayisi F, Nwane P, Wilhelm A, Basnet S, Selby R, Wanji S, Bakajika D, Oye J, Kamgno J, Boakye D, Schmidt E, Senyonjo L.

05-04-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/37018235/>

The main onchocerciasis elimination strategy is annual Community-Directed Treatment with ivermectin (CDTi). However, as a response to persistent high infection prevalence in Massangam Health District in Cameroon, two rounds of alternative treatments including biannual CDTi, ground larviciding and test and treat with doxycycline (TTd) were implemented. This led to a significant prevalence reduction from 35.7% to 12.3% ($p < 0.001$) as reported by Atekem and colleagues. Here we report on the acceptability of TTd component based on qualitative and quantitative data. The TTd involved microscopic examination for microfilaria in skin biopsy and those infected were offered doxycycline 100 mg daily for 35 days by community-directed distributors (CDDs). Participation level was significantly high with 54% of eligible population (age > 8 , not pregnant, not breastfeeding, not severely ill,) participating in the test in each round, increasing to 83% over the two rounds. Factors associated with non-participation included mistrust, being female; being younger than 26 years; short stay in the community; and belonging to semi-nomadic

sub population due to their remote and disperse settlement, discrimination, their non selection as CDD, and language and cultural barriers. Treatment coverage was high -71% in round 1 and 83% in round 2. People moving away between testing and treatment impacted treatment coverage. Some participants noted mismatch between symptoms and test result; and that ivermectin is better than doxycycline, while others favoured doxycycline. CDD worried about work burden with unmatching compensation. Overall, TTd participation was satisfactory. But can be improved through reinforcing sensitisation, reducing time between test and treatment; combining TTd and CDTi in one outing; augmenting CDDs compensation and/or weekly visit; exploring for frequently excluded populations and adapting strategies to reach them; and use of a sensitive less invasive test.

Mathematical study of the dynamics of lymphatic filariasis infection via fractional-calculus.

Alshehri A, Shah Z, Jan R.

2023

Eur Phys J Plus.

<https://pubmed.ncbi.nlm.nih.gov/37008752/>

The infection of lymphatic filariasis (LF) is the primary cause of poverty and disability in individuals living with the disease. Many organizations globally are working toward mitigating the disease's impact and enhancing the quality of life of the affected patients. It is paramount to inspect the transmission pattern of this infection to provide effective interventions for its prevention and control. Here, we formulate an epidemic model for the progression process of LF with acute and chronic infection in the fractional framework. The basic concept of the novel Atangana-Baleanu operator is presented for the analysis of suggested system. We determine the basic reproduction number of the system via the approach of next-generation matrix and investigate the equilibria of the system for stability analysis. We have shown the impact of input factors on the outcomes of reproduction parameter with the help of partial rank correlation coefficient approach and visualize the most critical factors. To conceptualize the time series analysis of the suggested dynamics, we propose utilizing a numerical approach. The solution pathways of the system are illustrated to demonstrate how different settings affect the system. We demonstrate the dynamics of the infection numerically to educate the policy makers and health authorities about the mechanisms necessary for management and control.

Global Health Impact: A Model to Alleviate the Burden and Expand Access to Treatment of Neglected Tropical Diseases.

Hassoun N, Cosler L.

27-02-2023

Am J Trop Med Hyg.

<https://pubmed.ncbi.nlm.nih.gov/36848896/>

Mycétome

Evaluation of the antiparasitic and antifungal activities of new synthetic piperlongumine-type cinnamide derivatives: booster effect by halogen substituents.

Khan TA, Al Nasr IS, Koko WS, Ma J, Eckert S, Brehm L, Ben Said RS, Daoud I, Hanachi R, Rahali S, van de Sande W, Ersfeld K, Schobert R, Biersack B.

06-04-2023

ChemMedChem.

<https://pubmed.ncbi.nlm.nih.gov/37021847/>

A series of synthetic N-acylpyrrolidone and -piperidone derivatives of the natural alkaloid piperlongumine were prepared and tested for their activities against *Leishmania* major and *Toxoplasma gondii* parasites. Replacement of one of the aryl meta-methoxy groups by halogens such as chlorine, bromine and iodine led to distinctly increased antiparasitic activities. For instance, the new bromo- and iodo-substituted compounds 3b/c and 4b/c showed strong activity against *L. major* promastigotes (IC₅₀ = 4.5-5.8 µM). Their activities against *L. major* amastigotes were moderate. In addition, the new compounds 3b, 3c, and 4a-c exhibited high activity against *T. gondii* parasites (IC₅₀ = 2.0-3.5 µM) with considerable selectivities when taking their effects on non-malignant Vero cells into account. Notable antitrypanosomal activity against *Trypanosoma brucei* was also found for 4b. Antifungal activity against *Madurellamycetomatis* was observed for compound 4c at higher doses. Quantitative structure-activity relationship (QSAR) studies were carried out, and docking calculations of test compounds bound to tubulin revealed binding differences between the 2-pyrrolidone and 2-piperidone derivatives. Microtubules-destabilizing effects were observed for 4b in *T. b. brucei* cells.

Fungal infections in Algeria.

Aissat FZ, Denning DW.

02-04-2023

Mycoses.

<https://pubmed.ncbi.nlm.nih.gov/37005355/>

Comparing the performance of the common used eumycetoma diagnostic tests.

Siddig EE, Nyuykonge B, Mhmoud NA, Abdallah OB, Bahar MEN, Ahmed ES, Nyaoke B, Zijlstra EE, Verbon A, Bakhiet SM, Fahal AH, van de Sande WWJ.

May-2023

Mycoses.

<https://pubmed.ncbi.nlm.nih.gov/36583225/>

Objectives: Mycetoma is a neglected tropical implantation disease caused by 70 different infectious agents. Identifying the causative organism to the species level is essential for appropriate patient management. Ultrasound, histopathology, culture and two species-specific PCRs are most the commonly used methods for species identification in endemic regions. The aim of this

study was to compare the diagnostic performance of these commonly used assays using sequencing of barcoding genes as the gold standard. **Methods:** This descriptive cross-sectional study was conducted at the Mycetoma Research Centre, University of Khartoum, Sudan. It included 222 patients suspected of fungal mycetoma caused by *Madurella mycetomatis*. **Results:** 154 (69.3%) were correctly identified by ultrasound, histology, culture and both species-specific PCRs. In 60 patients, at least one of the diagnostic tests failed to identify *M. mycetomatis*. Five patients had no evidence of eumycetoma, and for three, only the ultrasound was indicative of mycetoma. The two species-specific PCRs were the most sensitive and specific methods, followed by culture and histology. Ultrasound was the least specific as it only allowed differentiation between actinomycetoma and eumycetoma. The time to result was 9.38 minutes for ultrasound, 3.76 hours for PCR, 8.5 days for histopathology and 21 days for grain culturing. **Conclusion:** Currently, PCR directly on DNA isolated from grains is the most rapid and reliable diagnostic tool to identify *M. mycetomatis* eumycetoma.

Fungal and bacterial mycetoma in migrants from Haiti: A case series.

Hulin M, Lamoureux C, Sainte-Rose V, Drak Alsibai K, Demar M, Couppe P, Blaizot R.

Mar-Apr 2023

Travel Med Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/36539021/>

Introduction: Invasive and superficial fungal infections are increasingly reported in Algeria, testifying to the increase in their frequency in parallel with the increase in risk factors and the availability of diagnostic means, at least in university hospitals (CHU). The latter, located in the major northern cities, are equipped with high-performance diagnostic tools compared to hospitals in the interior of the country. **Methods:** A comprehensive search of published and grey literature was undertaken. Prevalence and incidence of discrete fungal diseases were estimated using a deterministic modelling approach based on populations at risk. Population (2021) and major underlying disease risk groups were obtained from UNAIDS, WHO Tuberculosis and the international transplant registries as well as published data for asthma and COPD. The health service profile was summarised from national documentation. **Results:** Among the 43.6 million, including 12.9 million children, living in Algeria, the most prevalent fungal diseases are tinea capitis (>1.5 million), recurrent vaginal candidiasis (>500,000) and allergic fungal lung and sinus disorders (>110,000) and chronic pulmonary aspergillosis (>10,000). Life-threatening invasive fungal infection incidence includes 774 *Pneumocystis pneumonia* in AIDS, 361 cryptococcal meningitis, 2272 candidaemia and 2639 invasive aspergillosis cases. Fungal keratitis probably affects >6000 eyes each year. **Conclusions:** Fungal infections are underestimated in Algeria because they are sought in patients with risk factors only after bacterial infections when they should be sought in parallel. The diagnosis is only accessible in hospitals in large cities and the work

carried out in mycology is rarely published, making the estimation of the burden of these conditions difficult.

Onchocercose

Case definitions for onchocerciasis-associated epilepsy and nodding syndrome: A focused review.

Van Cutsem G, Siewe Fodjo JN, Dekker MCJ, Amaral LJ, Njamnshi AK, Colebunders R.

31-03-2023

Seizure.

<https://pubmed.ncbi.nlm.nih.gov/37023626/>

Design of a multi-epitopic vaccine against Epstein-Barr virus via computer-based methods.

Larijani A, Kia-Karimi A, Roostaei D.

14-03-2023

Front Immunol.

<https://pubmed.ncbi.nlm.nih.gov/36999015/>

Background: Scientific findings have shown that Epstein-Barr virus (EBV) plays a key role in the development of some tumor diseases. Therefore, this study intends to take a practical step in controlling the pathogenicity of this virus by designing an effective vaccine based on the virus Capsid Envelope and Epstein-Barr nuclear immunogen (EBNA) Proteins Epitopes. Currently, there are no effective drugs or vaccines to treat or prevent EBV infection. So, we applied a computer-based strategy to design an epitope vaccine. **Results:** We designed a powerful multi-epitope peptide vaccine against EBV using in silico analysis. The vaccine is made up of 844 amino acids derived from three different types of proteins (Envelope, Capsid, EBNA) found in two different viral strains. responses. These epitopes have a high immunogenic capacity and are not likely to cause allergies. To enhance the vaccine immunogenicity, we used rOv-ASP-1, a recombinant *Onchocerca volvulus* activation associated protein-1, as an adjuvant and linked it to the vaccine's N and C terminus. The physicochemical and immunological properties of the vaccine structure were evaluated. The proposed vaccine was stable, with a stability index of 33.57 and a pI of 10.10, according to bioinformatic predictions. Docking analysis revealed that the vaccine protein binds correctly with immunological receptors. **Conclusion:** Our results demonstrated that the multi-epitope vaccine might be potentially immunogenic and induce humoral and cellular immune responses against EBV. This vaccine can interact appropriately with immunological receptors. Also, it has a high-quality structure and suitable characteristics such as high stability.

Schistosomiasis

Urinary interleukins (IL)-6 and IL-10 in schoolchildren from an area with low prevalence of *Schistosoma haematobium* infections in coastal Kenya.

Njaanake KH, Omondi J, Mwangi I, Jaoko WG, Anzala O.
05-04-2023

PLOS Glob Public Health.

<https://pubmed.ncbi.nlm.nih.gov/37018184/>

Repetitive Schistosoma Exposure Causes Perivascular Lung Fibrosis and Persistent Pulmonary Hypertension.

Kumar R, Lee MH, Kassa B, Fonseca Balladares DC, Mickael C, Sanders L, Andruska A, Kumar M, Spiekerkoetter E, Bandeira A, Stenmark KR, Tudor RM, Graham BB.

04-04-2023

Clin Sci (Lond).

<https://pubmed.ncbi.nlm.nih.gov/37014925/>

Pulmonary hypertension (PH) can occur as a complication of schistosomiasis. In humans, schistosomiasis-PH persists despite anti-helminthic therapy and parasite eradication. We hypothesized that persistent disease arises as a consequence of exposure repetition. Methods: Following intraperitoneal sensitization, mice were experimentally exposed to *Schistosoma* eggs by intravenous injection, either once or three times repeatedly. The phenotype was characterized by right heart catheterization and tissue analysis. Results: Following intraperitoneal sensitization, a single intravenous *Schistosoma* egg exposure resulted in a PH phenotype that peaked at 7 to 14 days, followed by spontaneous resolution. Three sequential exposures resulted in a persistent PH phenotype. Inflammatory cytokines were not significantly different between mice exposed to one or three egg doses, but there was an increase in perivascular fibrosis in those who received three egg doses. Significant perivascular fibrosis was also observed in autopsy specimens from patients who died of this condition. Conclusions: Repeatedly exposing mice to schistosomiasis causes a persistent PH phenotype, accompanied by perivascular fibrosis. Perivascular fibrosis may contribute to the persistent schistosomiasis-PH observed in humans with this disease.

Pulmonary inflammation promoted by type-2 dendritic cells is a feature of human and murine schistosomiasis.

Houlder EL, Costain AH, Nambuya I, Brown SL, Koopman JPR, Langenberg MCC, Janse JJ, Hoogerwerf MA, Ridley AJL, Forde-Thomas JE, Colombo SAP, Winkel BMF, Galdon AA, Hoffmann KF, Cook PC, Roestenberg M, Mpairwe H, MacDonald AS.

03-04-2023

Nat Commun.

<https://pubmed.ncbi.nlm.nih.gov/37012228/>

Schistosomiasis is a parasitic disease affecting over 200 million people in multiple organs, including the lungs. Despite this, there is little understanding of pulmonary immune responses during schistosomiasis. Here, we show type-2 dominated lung immune responses in both patent (egg producing) and pre-patent (larval lung migration) murine *Schistosoma mansoni* (*S. mansoni*) infection. Human pre-patent *S. mansoni* infection pulmonary (sputum) samples revealed a mixed type-1/type-2 inflammatory cytokine profile, whilst a case-control study

showed no significant pulmonary cytokine changes in endemic patent infection. However, schistosomiasis induced expansion of pulmonary type-2 conventional dendritic cells (cDC2s) in human and murine hosts, at both infection stages. Further, cDC2s were required for type-2 pulmonary inflammation in murine pre-patent or patent infection. These data elevate our fundamental understanding of pulmonary immune responses during schistosomiasis, which may be important for future vaccine design, as well as for understanding links between schistosomiasis and other lung diseases.

Life stage-specific glycosylation of extracellular vesicles from *Schistosoma mansoni* schistosomula and adult worms drives differential interaction with C-type lectin receptors DC-SIGN and MGL.

Kuipers ME, Nguyen DL, van Diepen A, Mes L, Bos E, Koning RI, Nolte-'t Hoen ENM, Smits HH, Hokke CH.

15-03-2023

Front Mol Biosci.

<https://pubmed.ncbi.nlm.nih.gov/37006612/>

Molecular dynamics-derived pharmacophores of *Schistosoma* glutathione transferase in complex with bromosulfophthalein: Screening and analysis of potential inhibitors.

Valli A, Achilonu I.

21-03-2023

J Mol Graph Model.

<https://pubmed.ncbi.nlm.nih.gov/37004419/>

Schistosoma glutathione transferases (GSTs) have been identified as attractive drug targets for the design of novel antischistosomal. Here, we used in silico methods to validate the discriminative inhibitory properties of bromosulfophthalein (BSP) against the 26-kDa GST from *S. japonicum* (Sj26GST), and the 28-kDa GST from *S. haematobium* (Sh28GST), versus human GST (hGST) isoforms alpha (hGSTA), mu (hGSTM) and pi (hGSTP). The use of BSP as an archetypal selective inhibitor was harnessed to produce molecular dynamics-derived pharmacophores of the two targets. Pharmacophore-based screening using a large dataset of experimental and approved drug compounds was performed to produce a shortlist of candidates. The top candidate for each target was prioritised via molecular docking, yielding guanosine-3'-monophosphate-5'-diphosphate (G3D) for Sj26GST, and quercetin-3'-O-phosphate (Q3P) for Sh28GST. Comparative molecular dynamics studies of both candidates compared to BSP showed similar characteristics of binding stability and strength, suggesting their potential to emulate the inhibitory effects of BSP.

Detection of cytological abnormalities in urothelial cells from individuals previously exposed or currently infected with *Schistosoma haematobium*.

Smith-Togobo C, Mprah R, Yeboah EA, Anyidoho HK, Asigbe D, Afernorfe JK, Ayrooe F, Duedu KO.

30-03-2023

PLoS One.

<https://pubmed.ncbi.nlm.nih.gov/36996097>

Urinary schistosomiasis has long been associated with bladder cancer, but it is still not clear the mechanisms involved. *Schistosoma haematobium* causes injury and disruptions in the integrity of the urothelium. The cellular and immunologic responses to the infection lead to the formation of granulomata. The ability to use cellular morphological changes to predict the risk of developing bladder cancer following *S. haematobium* infection is thus important. This study assessed the cellular changes in the urine associated with schistosomiasis and the potential of routine urine being used as a risk predictor of the development of bladder cancer. Urine samples (160) were screened for the presence of *S. haematobium* ova. Smears stained with the Papanicolaou method were evaluated using light microscopy to determine the cell populations. A high prevalence (39.9%) of urinary schistosomiasis and haematuria (46.9%) was found among the participants. Polymorphonuclear cells, normal and reactive urothelial cells and lymphocytes were characteristic of *S. haematobium* infection. Squamous metaplastic cells (SMCs) were found in 48% and 47.1% of participants who have had past or current *S. haematobium* infection respectively, but were not found in participants who had no exposure to *S. haematobium*. These squamous metaplastic cells are in transition and are prone to malignant transformation when exposed to a carcinogenic agent. There is still a high burden of schistosomiasis in endemic communities in Ghana. By examining urine, one can find metaplastic cells and dysplastic cells and thus predict cancer in SH-infested patients. Thus, routine urine cytology as a tool to monitor the risk of bladder cancer development is recommended.

A genome sequence for *Biomphalaria pfeifferi*, the major vector snail for the human-infecting parasite *Schistosoma mansoni*.

Bu L, Lu L, Laidemitt MR, Zhang SM, Mutuku M, Mkoji G, Steinauer M, Loker ES.

24-3-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/36961841/>

Identification and characterisation of the tegument-expressed aldehyde dehydrogenase SmALDH₃₁₂ of *Schistosoma mansoni*, a target of disulfiram.

Beutler M, Harnischfeger J, Weber MHW, Hahnel SR, Quack T, Blohm A, Ueberall ME, Timm T, Lochnit G, Rennar GA, Gallinger TL, Houhou H, Rahlfs S, Falcone FH, Becker K, Schlitzer M, Haeblerlein S, Czermak P, Salzig D, Grevelding CG.

05-05-2023

Eur J Med Chem.

<https://pubmed.ncbi.nlm.nih.gov/36948075/>

Differentiation between *Bulinus truncatus* and *Bulinus hexaploides* by morphological characters, chromosomal study and compatibility with *Schistosoma haematobium*.

Mansour SM, Ibrahim AM.

May-2023

Exp Parasitol.

<https://pubmed.ncbi.nlm.nih.gov/36914064/>

Schistosomiasis is a snail-born, neglected tropical disease (NTD) caused by blood flukes (trematode worms) of the genus *Schistosoma*. It is the second most socioeconomically devastating parasitic disease after malaria. Urogenital schistosomiasis is caused by *Schistosoma haematobium* which is transmitted by snail intermediate host of the genus *Bulinus*. This genus is a model system for the study of polyploidy in animals. This study aims to investigate ploidy levels existing among the *Bulinus* species and their compatibility with *S. haematobium*. The specimens were collected from two governorates in Egypt. Chromosomal preparation was made from gonad tissue (ovotestis). This study found two ploidy levels (tetraploid, $n = 36$ and hexaploid, $n = 54$) of *B. truncatus/tropicus* complex in Egypt. Tetraploid *B. truncatus* was found in El-Beheira governorate while-unexpectedly and for the first time in Egypt, the hexaploid population was found in Giza governorate. This identification focused on shell morphology, chromosomal count, and spermatozoa of each species. Afterward, all species were exposed to *S. haematobium* miracidia where *B. hexaploides* snails were the only refractory species. The histopathological study showed early destruction and abnormal development of *S. haematobium* in *B. hexaploides* tissues. In addition, the hematological investigation showed increasing in the total hemocyte count, the formation of vacuoles, several pseudopodia, and more dense granules in the hemocytes of infected *B. hexaploides* snails. In conclusion, there were two types of snails one was refractory and the other was susceptible.

Functional characterization of differentially expressed proteins coming from unisexual and bisexual infected *Schistosoma japonicum* female worms.

Zhong H, Qin F, Ren Y, Li X, Hou L, Gu S, Jin Y.

May-2023

Exp Parasitol.

<https://pubmed.ncbi.nlm.nih.gov/36914063/>

Systematic review of applied mathematical models for the control of *Schistosoma japonicum*.

Lowe C, Ahmadabadi Z, Gray D, Kelly M, McManus DP, Williams G.

May-2023

Acta Trop.

<https://pubmed.ncbi.nlm.nih.gov/36907291/>

Background: *Schistosoma japonicum* remains endemic in China and the Philippines. Substantial progress has been made in the control of *S. japonicum* in both China and the

Philippines. China is reaching elimination thanks to a concerted effort of control strategies. Mathematical modelling has been a key tool in the design of control strategies, in place of expensive randomised-controlled trials. We conducted a systematic review to investigate mathematical models of Japonicum control strategies in China and the Philippines. **Methods:** We conducted a systematic review on July 5, 2020, in four electronic bibliographic databases - PubMed, Web of Science, SCOPUS and Embase. Articles were screened for relevance and for meeting the inclusion criteria. Data extracted included authors, year of publication, year of data collection, setting and ecological context, objectives, control strategies, main findings, the form and content of the model including its background, type, representation of population dynamics, heterogeneity of hosts, simulation period, source of parameters, model validation and sensitivity analysis. Results After screening, 19 eligible papers were included in the systematic review. Seventeen considered control strategies in China and two in the Philippines. Two frameworks were identified; the mean-worm burden framework and the prevalence-based framework, the latter of which increasingly common. Most models considered human and bovine definitive hosts. There were mixed additional elements included in the models, such as alternative definitive hosts and the role of seasonality and weather. Models generally agreed upon the need for an integrated control strategy rather than reliance on mass drug administration alone to sustain reductions in prevalence. **Conclusions:** Mathematical modelling of Japonicum has converged from multiple approaches to modelling using the prevalence-based framework with human and bovine definitive hosts and find integrated control strategies to be most effective. Further research could investigate the role of other definitive hosts and model the effect of seasonal fluctuations in transmission.

Praziquantel promotes protection against *Schistosoma japonicum* infection in mice.

Shao B, Gui X, Lu Z, Lv R, Li H, Lu K, Hong Y, Fu Z, Jin Y, Lin J, Fei C, Liu J.

May-2023

Acta Trop.

<https://pubmed.ncbi.nlm.nih.gov/36863502/>

Praziquantel (PZQ) is the first line drug for the treatment of schistosomiasis. Several studies have confirmed that PZQ regulates host immunity, and we have recently found that pretreatment with PZQ enhances resistance against *Schistosoma japonicum* infection in buffaloes. We speculate that PZQ induces physiological changes in mice that prevent *S. japonicum* infection. To test this hypothesis and provide a practical measure to prevent *S. japonicum* infection, we determined the effective dose (the minimum dose), protection period and onset time of protection by comparing the worm burden, female worm burden and egg burden in PZQ-pretreated mice and blank control mice. Morphological differences between parasites were observed by measuring the total worm length, oral sucker, ventral sucker and ovary. The levels of cytokines, nitrogen monoxide (NO), 5-hydroxytryptamine (5-HT) and specific

antibodies were measured using kits or soluble worm antigens. Hematological indicators on day 0 were analyzed in mice that received PZQ on days -15, -18, -19, -20, -21 and -22. The PZQ concentrations in plasma and blood cells were monitored using high performance liquid chromatography (HPLC). The effective dose was found to be two oral administrations (interval of 24 h) at 300 mg/kg body weight (BW) or one injection at 200 mg/kg BW, and the protection period of PZQ injection was 18 days. The optimal preventive effect was observed at two days post-administration, with a >92% worm reduction rate and significant worm reduction until 21 days after administration. Adult worms from PZQ-pretreated mice were runty showing a shorter length, smaller organs and fewer eggs in the uteri of females. Detection of cytokines, NO, 5-HT and hematological indicators showed that PZQ induced immune-physiological changes, including higher levels of NO, IFN- γ and IL-2, and a lower level of TGF- β . No significant difference in the anti-*S. japonicum* specific antibody levels was observed. The PZQ concentrations in plasma and blood cells 8 and 15 days post-administration were lower than the detection limit. Our results confirmed that pretreatment with PZQ promotes the protection of mice against *S. japonicum* infection within 18 days. Although we observed some immune-physiological changes in the PZQ-pretreated mice, the exact mechanisms involved in the preventive effect require further study.

Addressing the oxamniquine in vitro-in vivo paradox to facilitate a new generation of anti-schistosome treatments.

Toth K, Alwan S, Khan S, McHardy SF, LoVerde PT, Cameron MD.

Apr-2023

Int J Parasitol Drugs Drug Resist.

<https://pubmed.ncbi.nlm.nih.gov/36758271/>

Immunological mechanisms involved in macrophage activation and polarization in schistosomiasis.

Licá ICL, Frazão GCCG, Nogueira RA, Lira MGS, Dos Santos VAF, Rodrigues JGM, Miranda GS, Carvalho RC, Silva LA, Guerra RNM, Nascimento FRF.

Apr-2023

Parasitology.

<https://pubmed.ncbi.nlm.nih.gov/36601859/>

Human schistosomiasis is caused by helminths of the genus *Schistosoma*. Macrophages play a crucial role in the immune regulation of this disease. These cells acquire different phenotypes depending on the type of stimulus they receive. M1 macrophages can be 'classically activated' and can display a proinflammatory phenotype. M2 or 'alternatively activated' macrophages are considered anti-inflammatory cells. Despite the relevance of macrophages in controlling infections, the role of the functional types of these cells in schistosomiasis is unclear. This review highlights different molecules and/or macrophage activation and polarization pathways during *Schistosoma mansoni* and *Schistosoma japonicum*

infection. This review is based on original and review articles obtained through searches in major databases, including Scopus, Google Scholar, ACS, PubMed, Wiley, Scielo, Web of Science, LILACS and ScienceDirect. Our findings emphasize the importance of *S. mansoni* and *S. japonicum* antigens in macrophage polarization, as they exert immunomodulatory effects in different stages of the disease and are therefore important as therapeutic targets for schistosomiasis and in vaccine development. A combination of different antigens can provide greater protection, as it possibly stimulates an adequate immune response for an M1 or M2 profile and leads to host resistance; however, this warrants *in vitro* and *in vivo* studies.

Helminthiases transmises par le sol (ascaridiose, trichuriase, ankylostomiase)

Ascaris lumbricoides a rare cause ileal perforation, a case report.

Molla YD, Beza AD, Tadesse AK, Answar IO.

01-04-2023

Int J Surg Case Rep.

<https://pubmed.ncbi.nlm.nih.gov/37015161/>

Compte rendu The canine hookworm Ancylostoma caninum: A novel threat for anthelmintic resistance in Canada.

Nezami R, Blanchard J, Godoy P.

1apr-2023

Can Vet J.

<https://pubmed.ncbi.nlm.nih.gov/37008647/>

The canine hookworm *Ancylostoma caninum* is one of the most prevalent parasitic nematodes in dogs worldwide and has the potential for zoonotic transmission to humans, including the development of cutaneous larva migrans. Recent confirmation of anthelmintic resistance (AR) in *A. caninum* to several anthelmintic classes, mainly in the USA, indicates the potential for this scenario in Canada. We consider various factors that may lead to resistant isolates in Canada, such as the widespread use of antiparasitic drugs without the assessment of efficacy; increased *A. caninum* prevalence in various Canadian provinces; and the importation of dogs, mostly from the USA, with a history of persistent infection by *A. caninum*. Our objective was to review factors that influence *A. caninum* to develop AR and raise awareness regarding the need for a strategic plan to control this parasitic nematode through the appropriate use of anthelmintics.

Emergence of Ancylostoma caninum parasites with the benzimidazole resistance F167Y polymorphism in the US dog population.

Leutenegger CM, Lozoya CE, Tereski J, Savard C, Ogeer J, Lallier R.

Apr-2023

Int J Parasitol Drugs Drug Resist.

<https://pubmed.ncbi.nlm.nih.gov/36958067/>

Background: Anthelmintic resistance to benzimidazole has been detected in the canine hookworm, *Ancylostoma caninum*. Benzimidazole resistance is believed to have developed originally in greyhounds, but has also been detected in non-greyhound pet dogs. The aim of this study was to validate a probe-based allele-specific real-time PCR tests for the F167Y polymorphism on the β -tubulin isotype-1 gene and to determine the geographic distribution. **Methods:** Allele-specific real-time PCR tests were established and validated to detect the codon 167 polymorphism in the *Ancylostoma caninum* β -tubulin isotype-1 gene. Additionally, real-time PCR tests were validated for *Ancylostoma* spp. and *Uncinaria stenocephala*. Two nucleic acid extraction protocols were validated including mechanical disruption of parasite structures in stool. The frequency of the F167Y single nucleotide polymorphism (SNP) was determined in hookworm confirmed stool samples. Samples with the resistant 167Y genotype were confirmed by β -tubulin gene sequencing and allele frequencies were determined. **Results:** The *Ancylostoma* spp. and *A. caninum* F167Y allele-specific real-time PCR tests were highly sensitive and specific when tested against synthetic DNA, spiked samples, and characterized parasites. Using an optimized total nucleic acid extraction protocol, 54 of 511 (10.6%) were found to contain the benzimidazole resistance allele. All 55 samples containing hookworms with the resistance mutation were confirmed by β -tubulin gene sequencing. The majority of resistant hookworms (44 resistant, 183 tested; 24.4%) originated from Florida, five from California (103 tested, 4.9%), three from Idaho (40 tested, 7.5%), two from Nevada (22 tested, 9.1%), and one sample from Hawaii (13 tested, 7.7%). Resistant genotypes were found in 14 different dog breeds including eight in Greyhounds. Allele-frequency determination revealed resistance allele frequencies between 1 and 100% with 58% above 50%. **Conclusions:** This data strongly supports recent findings of benzimidazole resistant canine hookworms present throughout the general US pet dog population.

Gale

Sarcoptic mange in Felidae: does Sarcoptes scabiei var. felis exist? A first molecular study.

Moroni B, Albanese F, Rita Molinar Min A, Pasquetti M, Guillot J, Pisano SRR, Ryser-Degiorgis MP, Rüfenacht S, Gauthier D, Cano-Terriza D, Scaravelli D, Rossi L, Peano A.

2023

Parasite.

<https://pubmed.ncbi.nlm.nih.gov/37010452/>

Domestic and wild felids are considered suitable hosts for the parasitic mite *Sarcoptes scabiei*, and sarcoptic mange is reported in several felid species in the scientific literature. However, the historic classification of *Sarcoptes* mites into host-specific varieties does not include *S. scabiei* var. *felis*. It is unclear whether sarcoptic mange

transmission in felids involves canids, other sympatric species, or exclusively felids. This study aimed to characterize the genetic structure of *S. scabiei* mites from domestic cats (*Felis catus*) and Eurasian lynx (*Lynx lynx carpathicus*), comparing them with *Sarcoptes* mites from sympatric domestic and wild carnivores. Ten *Sarcoptes* microsatellite markers were used to genotype 81 mites obtained from skin scrapings of 36 carnivores: 4 domestic cats, one dog (*Canis lupus familiaris*), 4 Eurasian lynx, 23 red foxes (*Vulpes vulpes*), and 4 grey wolves (*Canis lupus lupus*) from either Italy, Switzerland or France. Two genetic clusters of *S. scabiei* with a geographical distribution pattern were detected: mites from cats originating from Central Italy clustered with those from sympatric wolves. In contrast, all the other mites from Switzerland, France and Northern Italy clustered together. These results strengthen the previously advanced hypothesis that genetic variants of *S. scabiei* have a predominant geographic-related distribution with cryptic transmission patterns. These patterns may rely on the interactions between different hosts living in the same ecological niche rather than a simple infection among hosts belonging to the same taxon, reinforcing the idea that the *S. scabiei* historic classification into "var" might have little ongoing relevance.

The Role of Eosinophils in the Differential Diagnosis of Inflammatory Skin Diseases.

Caro-Chang LA, Fung MA.

30-03-2023

Hum Pathol.

<https://pubmed.ncbi.nlm.nih.gov/37003367/>

Eosinophils are known to be present in inflammatory skin diseases, but their diagnostic utility is not well established. Upon review of the published status of lesional eosinophils, several categories were identified. 1) Lesional eosinophils highly characteristic such that, in their absence, the pathologist may question the diagnosis. These include arthropod bite reactions and scabies, urticarial dermatitis, and other eosinophilic dermatoses. 2) Lesional eosinophils rare or absent, such that, in their presence, the pathologist may question the diagnosis. These include pityriasis lichenoides, graft versus host disease, and connective tissue disorders. 3) Lesional eosinophils variable and, while in some cases expected, are not required for diagnosis. These include drug reactions, atopic dermatitis and allergic contact dermatitis. Lesional eosinophils variable and not expected but may be seen to a limited extent. These include lichen planus and psoriasis.

Pharmacokinetic and pharmacodynamic considerations for treating sarcoptic mange with cross-relevance to Australian wildlife.

Takano K, de Hayr L, Carver S, Harvey RJ, Mounsey KE.

Apr-2023

Int J Parasitol Drugs Drug Resist.

<https://pubmed.ncbi.nlm.nih.gov/36906936/>

Sarcoptes scabiei is the microscopic burrowing mite responsible for sarcoptic mange, which is reported in approximately 150 mammalian species. In Australia, sarcoptic mange affects a number of native and introduced wildlife species, is particularly severe in bare-nosed wombats (*Vombatus ursinus*) and an emerging issue in koala and quenda. There are a variety of acaricides available for the treatment of sarcoptic mange which are generally effective in eliminating mites from humans and animals in captivity. In wild populations, effective treatment is challenging, and concerns exist regarding safety, efficacy and the potential emergence of acaricide resistance. There are risks where acaricides are used intensively or inadequately, which could adversely affect treatment success rates as well as animal welfare. While reviews on epidemiology, treatment strategies, and pathogenesis of sarcoptic mange in wildlife are available, there is currently no review evaluating the use of specific acaricides in the context of their pharmacokinetic and pharmacodynamic properties, and subsequent likelihood of emerging drug resistance, particularly for Australian wildlife. This review critically evaluates acaricides that have been utilised to treat sarcoptic mange in wildlife, including dosage forms and routes, pharmacokinetics, mode of action and efficacy. We also highlight the reports of resistance of *S. scabiei* to acaricides, including clinical and in vitro observations.

A resistant parasitic flare-up amid children in Italy: Comment on "Diagnosis and management of pediatric scabies: Results from a survey on 317 Italian dermatologists".

Herzum A, Gariazzo L, Viglizzo G, Garibeh E, Pastorino C, Occella C.

Mar-Apr 2023

Travel Med Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/36681292/>

A persistent crusted erythematous plaque on the forearm.

Figuerola-Morales AL, Kubelis-López DE, Pérez-Garza DM, Rodríguez-Tamez G, Vázquez-Martínez OT, Ocampo-Candiani J, Herz-Ruelas ME.

Jan-Mar 2023

Indian J Dermatol Venereol Leprol.

<https://pubmed.ncbi.nlm.nih.gov/35138064/>

Morsures de serpent

Hierarchical cloud architecture for identifying the bite of "Egyptian cobra" based on deep learning and quantum particle swarm optimization.

Hassan A, Elhoseny M, Kayed M.

31-03-2023

Sci Rep.

<https://pubmed.ncbi.nlm.nih.gov/37002322/>

Captive Black Mamba (*Dendroaspis Polylepis*) Bite Leading to Respiratory Failure.

Greene SC, Cue K, Khan R, Gilbert MB, Rahimi J.

Mar-2023

J Emerg Med.

<https://pubmed.ncbi.nlm.nih.gov/36925444/>

Background: Of the 8000-10,000 snake envenomations evaluated in U.S. emergency departments (ED) annually, approximately 1% are due to non-native snakes. We describe a 26-year-old man who was bitten by his captive black mamba (*Dendroaspis polylepis*) as he was packing it up for transport to another snake collector. **Case report:** The patient presented to the ED 1 h after being bitten on the forearm, complaining of left arm pain, oral paresthesias, and dyspnea. His vital signs: heart rate 96 beats/min, blood pressure 167/101 mm Hg, temperature 36.7°C (97.9°F), respiratory rate 20 breaths/min, and room air oxygen saturation 100%. Two mildly tender puncture wounds without swelling or ecchymosis were found on the posterior aspect of the forearm. Over the ensuing 30 min his dyspnea worsened, and he developed objective weakness. He was intubated and placed on mechanical ventilation. He was treated with atropine 2 mg for bronchorrhea. Five vials of South African Vaccine Producers (Johannesburg, South Africa) polyvalent antivenom were administered 2.5 h post-bite and the patient was admitted to the intensive care unit. He was extubated 18 h post-envenomation and discharged the following day. He has remained asymptomatic since leaving the hospital. **WHY SHOULD AN EMERGENCY PHYSICIAN BE AWARE OF THIS?:** The primary manifestations of *D. polylepis* envenomings are neurological. Initial signs may include paresthesias, dysarthria, dysphagia, and ptosis. Progressive descending paralysis leading to respiratory failure develops within 60 min. Muscarinic features are frequently observed. Cardiotoxicity and hematologic laboratory abnormalities may be present. Although pain is common, significant local tissue injury does not occur. In addition to supportive care, several non-native antivenoms are indicated for *D. polylepis* envenomations. Black mamba envenomings differ from the native snakebites with which U.S. physicians are familiar. Rapid, progressive neurological toxicity and muscarinic features are most common. Treatment consists of supportive care and appropriate antivenom administration.

Design and Analysis of Bio-Inspired Micro-Needle for Drug Delivery Applications.

Sravani KG, Desala RK, Chand P, Sathvik K, Rao KS, Lay-Ekuakille A.

Apr-2023

IEEE Trans Nanobioscience.

<https://pubmed.ncbi.nlm.nih.gov/35737616/>

Years of research show that the Trans-dermal drug delivery (TDD) route showed promising results due to good immunogenic responses. In this paper, we have proposed a bio-inspired micro-needle suggested by a snake belonging to the family of Elapids, since they inject

venom with high pressures during the bite. The proposed micro-needle is strong enough to puncture the skin and withstand different kinds of loads during the insertion. The proposed micro-needle is of [Formula: see text] length, and the maximum compressive, buckling, bending, load it can handle are 0.27N, 0.16N, 0.024N respectively. The proposed micro-needle (MN) has an inner channel diameter of 44 [Formula: see text] and it gives a flow rate of [Formula: see text]/s. In our work, we have modeled a substrate of epidermis and dermis as a porous medium with porosity and permeability as 0.74, [Formula: see text] respectively. The porosity and permeability are calculated using an SEM image of the human dermis consisting of only collagen fibers and empty pores. We have applied Darcy's law to the modeled substrate and obtained the velocity field of the drug administrated. The diffusion study of Doxorubicin (87 μ mol/l) is carried out using Darcy velocity field and concentration gradient.

Portable Electrochemical Platform With Carbon Fibre Microelectrodes Integrated on an OHP Sheet for Snake Venom Analysis.

Amreen K, Salve M, Goel S.

Jan-2023

IEEE Trans Nanobioscience.

<https://pubmed.ncbi.nlm.nih.gov/35476572/>