



## **Veille scientifique**

### **Maladies tropicales négligées**

**Semaine 15**  
*10 au 16 avril 2023*

Cysticercose	2
Dengue, chikungunya et maladie à virus Zika	2
Dracunculose	17
Echinococcose	18
Filariose lymphatique	20
Gale	21
Helminthiases transmises par le sol (ascaridiose, trichuriase, ankylostomiase)	22
Leishmaniose	22
Lèpre	27
Morsures de serpent	31
Pian	32
Rage	32
Schistosomiase	34
Trachome	37
Trématodoses d'origine alimentaire (clonorchiose, opisthorchiase, fasciolase et paragonimose)	38
Trypanosomes (trypanosomiase et maladie de Chagas)	39
Ulcère de Buruli	41

---

## Cysticercose

### 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.

---

## Dengue, chikungunya et maladie à virus Zika

**Integrated systems immunology approach identifies impaired effector T cell memory responses as a feature of progression to severe dengue fever.**

Ioannidis LJ, Studniberg SI, Eriksson EM, Suwanto S, Denis D, Liao Y, Shi W, Garnham AL, Sasmono RT, Hansen DS.

13-04-2023

*J Biomed Sci.*

<https://pubmed.ncbi.nlm.nih.gov/37055751/>

**Background:** Typical symptoms of uncomplicated dengue fever (DF) include headache, muscle pains, rash, cough, and vomiting. A proportion of cases progress to severe dengue hemorrhagic fever (DHF), associated with increased vascular permeability, thrombocytopenia, and hemorrhages. Progression to severe dengue is difficult to diagnose at the onset of fever, which complicates patient triage, posing a socio-economic burden on health systems.

**Methods:** To identify parameters associated with protection and susceptibility to DHF, we pursued a systems immunology approach integrating plasma chemokine profiling, high-dimensional mass cytometry and peripheral blood mononuclear cell (PBMC) transcriptomic analysis at the onset of fever in a prospective study conducted in Indonesia. **Results:** After a secondary infection, progression to uncomplicated dengue featured transcriptional profiles associated with increased cell proliferation and metabolism, and an expansion of ICOS<sup>+</sup>CD4<sup>+</sup> and CD8<sup>+</sup> effector memory T cells. These responses were virtually absent in cases progressing to severe DHF, that instead mounted an innate-like response, characterised by inflammatory transcriptional profiles, high circulating levels of inflammatory chemokines and with high frequencies of CD4<sup>low</sup> non-classical monocytes predicting increased odds of severe disease. **Conclusions:** Our results suggests that effector memory T cell activation might play an important role ameliorating severe disease symptoms during a secondary dengue infection, and in the absence of that response, a strong innate inflammatory response is required to control viral replication. Our research also identified discrete cell populations predicting increased odds of severe disease, with potential diagnostic value.

### Impact of prior flavivirus vaccination on immunogenicity and efficacy of an inactivated Zika vaccine in Indian rhesus macaques.

Young G, Zahralban-Steele M, Dean HJ.

11-04-2023

*Vaccine.*

<https://pubmed.ncbi.nlm.nih.gov/37055345/>

### Hydration and clinical warning signs of Dengue fever in primary care: an observational prospective study.

Besnard O, Maillard O, Franco JM, Lebreton N, Reix G, Legrand F, Bertolotti A, Leruste S.

11-04-2023

*Infect Dis Now.*

<https://pubmed.ncbi.nlm.nih.gov/37054972/>

**The relative importance of key meteorological factors affecting**

## numbers of mosquito vectors of dengue fever.

Liu Y, Wang X, Tang S, Cheke RA.

13-04-2023

*PLoS Negl Trop Dis.*

<https://pubmed.ncbi.nlm.nih.gov/37053307/>

Although single factors such as rainfall are known to affect the population dynamics of *Aedes albopictus*, the main vector of dengue fever in Eurasia, the synergistic effects of different meteorological factors are not fully understood. To address this topic, we used meteorological data and mosquito-vector association data including Breteau and ovitrap indices in key areas of dengue outbreaks in Guangdong Province, China, to formulate a five-stage mathematical model for *Aedes albopictus* population dynamics by integrating multiple meteorological factors. Unknown parameters were estimated using a genetic algorithm, and the results were analyzed by k-Shape clustering, random forest and grey correlation analysis. In addition, the population density of mosquitoes in 2022 was predicted and used for evaluating the effectiveness of the model. We found that there is spatiotemporal heterogeneity in the effects of temperature and rainfall and their distribution characteristics on the diapause period, the numbers of peaks in mosquito densities in summer and the annual total numbers of adult mosquitoes. Moreover, we identified the key meteorological indicators of the mosquito quantity at each stage and that rainfall (seasonal rainfall and annual total rainfall) was more important than the temperature distribution (seasonal average temperature and temperature index) and the uniformity of rainfall annual distribution (coefficient of variation) for most of the areas studied. The peak rainfall during the summer is the best indicator of mosquito population development. The results provide important theoretical support for the future design of mosquito vector control strategies and early warnings of mosquito-borne diseases.

## SIR-SI model with a Gaussian transmission rate: Understanding the dynamics of dengue outbreaks in Lima, Peru.

Ramírez-Soto MC, Machuca JVB, Stalder DH, Champin D, Martínez-Fernández MG, Schaerer CE.

13-04-2023

*PLoS One.*

<https://pubmed.ncbi.nlm.nih.gov/37053225/>

## Impact of Social Media Usage on Users' COVID-19 Protective Behavior: Survey Study in Indonesia.

Handayani PW, Zagatti GA, Kefi H, Bressan S.

13-04-2023

*JMIR Form Res.*

<https://pubmed.ncbi.nlm.nih.gov/37052987/>

**Background:** Social media have become the source of choice for many users to search for health information on COVID-19 despite possible detrimental consequences. Several studies have analyzed the association between

health information-searching behavior and mental health. Some of these studies examined users' intentions in searching health information on social media and the impact of social media use on mental health in Indonesia.

**Objective:** This study investigates both active and passive participation in social media, shedding light on confounding effects from these different forms of engagement. In addition, this study analyses the role of trust in social media platforms and its effect on public health outcomes. Thus, the purpose of this study is to analyze the impact of social media usage on COVID-19 protective behavior in Indonesia. The most commonly used social media platforms are Instagram, Facebook, YouTube, TikTok, and Twitter. **Methods:** We used primary data from an online survey. We processed 414 answers to a structured questionnaire to evaluate the relationship between these users' active and passive participation in social media, trust in social media, anxiety, self-efficacy, and protective behavior to COVID-19. We modeled the data using partial least square structural equation modeling. **Results:** This study reveals that social media trust is a crucial antecedent, where trust in social media is positively associated with active contribution and passive consumption of COVID-19 content in social media, users' anxiety, self-efficacy, and protective behavior. This study found that active contribution of content related to COVID-19 on social media is positively correlated with anxiety, while passive participation increases self-efficacy and, in turn, protective behavior. This study also found that active participation is associated with negative health outcomes, while passive participation has the opposite effects. The results of this study can potentially be used for other infectious diseases, for example, dengue fever and diseases that can be transmitted through the air and have handling protocols similar to that of COVID-19. **Conclusions:** Public health campaigns can use social media for health promotion. Public health campaigns should post positive messages and distil the received information parsimoniously to avoid unnecessary and possibly counterproductive increased anxiety of the users.

## Social Media and the Influence of Fake News on Global Health Interventions: Implications for a Study on Dengue in Brazil.

Gagnon-Dufresne MC, Azevedo Dantas M, Abreu Silva K, Souza Dos Anjos J, Pessoa Carneiro Barbosa D, Porto Rosa R, de Luca W, Zahreddine M, Caprara A, Ridde V, Zinszer K.

28-03-2023

*Int J Environ Res Public Health.*

<https://pubmed.ncbi.nlm.nih.gov/37047915/>

## Roles of TGF- $\beta$ 1 in Viral Infection during Pregnancy: Research Update and Perspectives.

Trinh QD, Pham NTK, Takada K, Ushijima H, Komine-Aizawa S, Hayakawa S.

30-03-2023

*Int J Mol Sci.*

<https://pubmed.ncbi.nlm.nih.gov/37047462/>

## Targeting of Tetraspanin CD81 with Monoclonal Antibodies and Small Molecules to Combat Cancers and Viral Diseases.

Bailly C, Thuru X.

06-04-2023

*Cancers (Basel).*

<https://pubmed.ncbi.nlm.nih.gov/37046846/>

Tetraspanin CD81 plays major roles in cell-cell interactions and the regulation of cellular trafficking. This cholesterol-embarking transmembrane protein is a co-receptor for several viruses, including HCV, HIV-1 and Chikungunya virus, which exploits the large extracellular loop EC2 for cell entry. CD81 is also an anticancer target implicated in cancer cell proliferation and mobility, and in tumor metastasis. CD81 signaling contributes to the development of solid tumors (notably colorectal, liver and gastric cancers) and has been implicated in the aggressivity of B-cell lymphomas. A variety of protein partners can interact with CD81, either to regulate attachment and uptake of viruses (HCV E2, claudin-1, IFIM1) or to contribute to tumor growth and dissemination (CD19, CD44, EWI-2). CD81-protein interactions can be modulated with molecules targeting the extracellular domain of CD81, investigated as antiviral and/or anticancer agents. Several monoclonal antibodies anti-CD81 have been developed, notably mAb 5A6 active against invasion and metastasis of triple-negative breast cancer cells. CD81-EC2 can also be targeted with natural products (trachelogenin and harzianoic acids A-B) and synthetic compounds (such as benzothiazole-quinoline derivatives). They are weak CD81 binders but offer templates for the design of new compounds targeting the open EC2 loop. There is no anti-CD81 compound in clinical development at present, but this structurally well-characterized tetraspanin warrants more substantial considerations as a drug target.

## Shared Molecular Signatures Across Zika Virus Infection and Multiple Sclerosis Highlight AP-1 Transcription Factor as a Potential Player in Post-ZIKV MS-Like Phenotypes.

da Silva EV, Fontes-Dantas FL, Dantas TV, Dutra A, Nascimento OJM, Alves-Leon SV.

13-03-2023

*Mol Neurobiol.*

<https://pubmed.ncbi.nlm.nih.gov/37046138/>

Zika virus (ZIKV) is an arbovirus of the Flaviviridae genus that has rapidly disseminated from across the Pacific to the Americas. Robust evidence has indicated a crucial role of ZIKV in congenital virus syndrome, including neonatal microcephaly. Moreover, emerging evidence suggests an association between ZIKV infection and the development of an extensive spectrum of central nervous system inflammatory demyelinating diseases (CNS IDD), such as multiple sclerosis-like clinical phenotypes. However, the underlying mechanisms of host-pathogen neuro-immune interactions remain to be elucidated. This study aimed to identify common transcriptional signatures between multiple sclerosis (MS) and ZIKV infection to generate

molecular interaction networks, thereby leading to the identification of deregulated processes and pathways, which could give an insight of these underlying molecular mechanisms. Our investigation included publicly available transcriptomic data from MS patients in either relapse or remission (RR-MS) and datasets of subjects acutely infected by ZIKV for both immune peripheral cells and central nervous system cells. The protein-protein interaction (PPI) analysis showed upregulated AP-1 transcription factors (JUN and FOS) among the top hub and bottleneck genes in RR-MS and ZIKV data. Gene enrichment analysis retrieved a remarkable presence of ontologies and pathways linked to oxidative stress responses, immune cell function, inflammation, interleukin signaling, cell division, and transcriptional regulation commonly enriched in both scenarios. Considering the recent findings concerning AP-1 function in immunological tolerance breakdown, regulation of inflammation, and its function as an oxidative stress sensor, we postulate that the ZIKV trigger may contribute as a boost for the activation of such AP-1-regulated mechanisms that could favor the development of MS-like phenotypes following ZIKV infection in a genetically susceptible individual.

## Transgene-induced cell death following dengue-2 virus infection in Aedes aegypti.

Carvalho DO, Costa-da-Silva AL, Petersen V, de Souza MS, Ioshino RS, Marques ICS, Franz AWE, Olson KE, James AA, Capurro ML.

12-04-2023

*Sci Rep.*

<https://pubmed.ncbi.nlm.nih.gov/37045866/>

## Dengue and chikungunya virus loads in the mosquito Aedes aegypti are determined by distinct genetic architectures.

Novelo M, Dutra HL, Metz HC, Jones MJ, Sigle LT, Frentiu FD, Allen SL, Chenoweth SF, McGraw EA.

12-04-2023

*PLoS Pathog.*

<https://pubmed.ncbi.nlm.nih.gov/37043515/>

*Aedes aegypti* is the primary vector of the arboviruses dengue (DENV) and chikungunya (CHIKV). These viruses exhibit key differences in their vector interactions, the latter moving more quickly through the mosquito and triggering fewer standard antiviral pathways. As the global footprint of CHIKV continues to expand, we seek to better understand the mosquito's natural response to CHIKV—both to compare it to DENV:vector coevolutionary history and to identify potential targets in the mosquito for genetic modification. We used a modified full-sibling design to estimate the contribution of mosquito genetic variation to viral loads of both DENV and CHIKV. Heritabilities were significant, but higher for DENV (40%) than CHIKV (18%). Interestingly, there was no genetic correlation between DENV and CHIKV loads between siblings. These data suggest *Ae. aegypti* mosquitoes respond to the two viruses using distinct genetic

mechanisms. We also examined genome-wide patterns of gene expression between High and Low CHIKV families representing the phenotypic extremes of viral load. Using RNAseq, we identified only two loci that consistently differentiated High and Low families: a long non-coding RNA that has been identified in mosquito screens post-infection and a distant member of a family of Salivary Gland Specific (SGS) genes. Interestingly, the latter gene is also associated with horizontal gene transfer between mosquitoes and the endosymbiotic bacterium Wolbachia. This work is the first to link the SGS gene to a mosquito phenotype. Understanding the molecular details of how this gene contributes to viral control in mosquitoes may, therefore, also shed light on its role in Wolbachia.

### **Dengue outbreak update in India: 2022.**

**Singh N, Singh AK, Kumar A.**

Jan-Mar 2023

*Indian J Public Health.*

<https://pubmed.ncbi.nlm.nih.gov/37039229/>

Dengue is an emerging illness in India, where it is endemic in some areas and sometimes causes yearly epidemics. Each dengue outbreak starts with high death and morbidity, which has a significant socioeconomic impact. As of September 30, 2022, India had 63,280 dengue cases, according to information provided by the National Centre for Vector Borne Diseases Control. North India is most severely impacted by each outbreak. In Uttar Pradesh, the state with the most population in India, there have been 2060 confirmed cases of dengue and 1 mortality till September 2022 reported. Patients are being reported from semi-urban, rural, and urban areas. It is essential to properly monitor disease cases through disease surveillance in order to ensure prompt case management if dengue outbreak control is to be achieved. An efficient diagnostic approach for early diagnosis is urgently required to reduce the severity of the sickness, the length of the hospital stay, and clinical consequences.

### **Factors associated with malaria and arboviral disease in patients with imported febrile syndrome: a retrospective cohort study.**

**López-Amorós AI, Torrús-Tendero D, Merino de Lucas E, Reus Bañuls S, Boix Martínez V, Llorens Soriano P, Escribano Cañadas I, Ramos-Rincón JM.**

Apr-2023

*Emergencias.*

<https://pubmed.ncbi.nlm.nih.gov/37038942/>

### **Replication and innate immune responses of two chikungunya virus genotypes in human monocyte-derived macrophages.**

**Lau JZH, Chua CL, Chan YF, Nadarajan VS, Lee CLL, Sam IC.**

Apr-2023

*J Gen Virol.*

<https://pubmed.ncbi.nlm.nih.gov/37043371/>

Chikungunya virus (CHIKV) is a re-emerging mosquito-borne virus, which causes epidemics of fever, joint pain and rash. There are three genotypes: West African, East/Central/South/Africa (ECSA) and Asian, with the latter two predominant globally. Genotype-specific differences in clinical presentations, virulence and immunopathology have been described. Macrophages are key cells in immune responses against CHIKV. Circulating blood monocytes enter tissue to differentiate into monocyte-derived macrophages (MDMs) in response to CHIKV infection at key replication sites such as lymphoid organs and joints. This study analyses differences in replication and induced immune mediators following infection of MDMs with Asian and ECSA CHIKV genotypes. Primary human MDMs were derived from residual blood donations. Replication of Asian (MY/06/37348) or ECSA (MY/08/065) genotype strains of CHIKV in MDMs was measured by plaque assay. Nineteen immune mediators were measured in infected cell supernatants using multiplexed immunoassay or ELISA. MY/08/065 showed significantly higher viral replication at 24 h post-infection (h p.i.) but induced significantly lower expression of proinflammatory cytokines (CCL-2, CCL-3, CCL-4, RANTES and CXCL-10) and the anti-inflammatory IL-1Ra compared to MY/06/37348. No differences were seen at later time points up to 72 h p.i. During early infection, MY/08/065 induced lower proinflammatory immune responses in MDMs. *In vivo*, this may lead to poorer initial control of viral infection, facilitating CHIKV replication and dissemination to other sites such as joints. This may explain the consistent past findings that the ECSA genotype is associated with greater viremia and severity of symptoms than the Asian genotype. Knowledge of CHIKV genotype-specific immunopathogenic mechanisms in human MDMs is important in understanding of clinical epidemiology, biomarkers and therapeutics in areas with co-circulation of different genotypes.

### **Health-related quality of life in children with cerebral palsy associated with congenital Zika infection.**

**Marques FJP, Carvalho AL, Borigato EVM, Oliveira LFV, Duarte LMR, Silva AGD, Amarante CLD, Pereira LJM, Tavares EF, Costa LGSD, Alcântara CAR, Salinas AN, Pinto FLDC, Alcântara GC, Utsch F, Silva CRD, Reis DAD, Bessa WM, Dutra RC, Ventura P, Oliveira TS.**

07-04-2023

*Rev Paul Pediatr.*

<https://pubmed.ncbi.nlm.nih.gov/37042942/>

### **Loop-Mediated Isothermal Amplification on Paper Microfluidic Chips for Highly Sensitive and Specific Zika Virus Detection Using Smartphone.**

**Kaarj K, Yoon JY.**

2023

*Methods Mol Biol.*

<https://pubmed.ncbi.nlm.nih.gov/37041453/>

Zika virus (ZIKV) infection may cause serious birth defects and is a critical concern for women of child-bearing age in affected regions. A simple, portable, and easy-to-use ZIKV



detection method would enable point-of-care testing, which may aid in prevention of the spread of the virus. Herein, we describe a reverse transcription isothermal loop-mediated amplification (RT-LAMP) method that detects the presence of ZIKV RNA in complex samples (e.g., blood, urine, and tap water). Phenol red is the colorimetric indicator of successful amplification. Color changes based on the amplified RT-LAMP product from the presence of viral target are monitored using a smartphone camera under ambient light conditions. A single viral RNA molecule per  $\mu\text{L}$  can be detected in as quickly as 15 min using this method with 100% sensitivity and 100% specificity in blood and tap water, while 100% sensitivity and 67% specificity in urine. This platform can also be used to identify other viruses including SARS-CoV-2 and improve the current state of field-based diagnostics.

## A Case Report of Dengue-Associated Maculopathy With Literature Review.

Govinda Raju D, Ramli N, Ramayaj R.

09-03-2023

*Cureus.*

<https://pubmed.ncbi.nlm.nih.gov/37038576/>

## Neglected tropical diseases risk correlates with poverty and early ecosystem destruction.

Magalhães AR, Codeço CT, Svenning JC, Escobar LE, Van de Vuurst P, Gonçalves-Souza T.

10-04-2023

*Infect Dis Poverty.*

<https://pubmed.ncbi.nlm.nih.gov/37038199/>

**Background:** Neglected tropical diseases affect the most vulnerable populations and cause chronic and debilitating disorders. Socioeconomic vulnerability is a well-known and important determinant of neglected tropical diseases. For example, poverty and sanitation could influence parasite transmission. Nevertheless, the quantitative impact of socioeconomic conditions on disease transmission risk remains poorly explored. **Methods:** This study investigated the role of socioeconomic variables in the predictive capacity of risk models of neglected tropical zoonoses using a decade of epidemiological data (2007-2018) from Brazil. Vector-borne diseases investigated in this study included dengue, malaria, Chagas disease, leishmaniasis, and Brazilian spotted fever, while directly-transmitted zoonotic diseases included schistosomiasis, leptospirosis, and hantaviruses. Environmental and socioeconomic predictors were combined with infectious disease data to build environmental and socioenvironmental sets of ecological niche models and their performances were compared. **Results:** Socioeconomic variables were found to be as important as environmental variables in influencing the estimated likelihood of disease transmission across large spatial scales. The combination of socioeconomic and environmental variables improved overall model accuracy (or predictive power) by 10% on average ( $P < 0.01$ ), reaching a maximum of 18% in the case of dengue fever. Gross domestic product was the most important socioeconomic variable (37% relative variable importance,

all individual models exhibited  $P < 0.00$ ), showing a decreasing relationship with disease indicating poverty as a major factor for disease transmission. Loss of natural vegetation cover between 2008 and 2018 was the most important environmental variable (42% relative variable importance,  $P < 0.05$ ) among environmental models, exhibiting a decreasing relationship with disease probability, showing that these diseases are especially prevalent in areas where natural ecosystem destruction is on its initial stages and lower when ecosystem destruction is on more advanced stages. **Conclusions:** Destruction of natural ecosystems coupled with low income explain macro-scale neglected tropical and zoonotic disease probability in Brazil. Addition of socioeconomic variables improves transmission risk forecasts on tandem with environmental variables. Our results highlight that to efficiently address neglected tropical diseases, public health strategies must target both reduction of poverty and cessation of destruction of natural forests and savannas.

## Seroprevalence of viral and bacterial pathogens among malaria patients in an endemic area of southern Venezuela.

Forero-Peña DA, Carrión-Nessi FS, Lopez-Perez M, Sandoval-de Mora M, Amaya ID, Gamardo ÁF, Chavero M, Figuera L, Marciano MV, Camejo-Ávila NA, Hidalgo M, Arenas CJ, Arévalo-Herrera M, Herrera S.

10-04-2023

*Infect Dis Poverty.*

<https://pubmed.ncbi.nlm.nih.gov/37038195/>

**Background:** Malaria remains a leading public health problem worldwide. Co-infections with other pathogens complicate its diagnosis and may modify the disease's clinical course and management. Similarities in malaria clinical presentation with other infections and overlapping endemicity result in underdiagnosis of co-infections and increased mortality. Thus, the aim of this study was to determine the seroprevalence of viral and bacterial pathogens among diagnosed malaria patients in malaria-endemic areas in Venezuela. **Methods:** A cross-sectional study was conducted on malaria patients attending three reference medical centres in Ciudad Bolívar, Venezuela. Clinical evaluation and laboratory tests for dengue virus (DENV), chikungunya virus (CHIKV), viral hepatitis [hepatitis A virus (HAV), hepatitis B virus (HBV), and hepatitis C virus (HCV)], and leptospirosis (LEP) were performed by enzyme-linked immunosorbent assays. Previous exposure to these pathogens was defined by the presence of specific immunoglobulin (Ig) G, and co-infection or recent exposure (CoRE) was determined by the presence of specific IgM alone or IgM + IgG. Data analysis considered descriptive statistics. Parameter distribution was statistically evaluated using Kolmogorov-Smirnov test and the necessary comparison tests. Odds ratio (OR) for complications was determined according to CoRE presence with a 95% confidence interval (CI). **Results:** A total of 161 malaria patients were studied, 66% infected with *Plasmodium vivax*, 27% with *P. falciparum*, and 7.5% harboured *P. vivax/P. falciparum* mixed infection. Previous exposure to DENV (60%) and CHIKV (25%) was frequent. CoRE was confirmed in 55 of the 161

malaria patients (34%) and were more frequent in *P. falciparum* (49%) than in *P. vivax* (29%) and mixed malaria patients (25%) (OR = 2.43, 95% CI: 1.39-4.25, *P* = 0.018). The most frequent CoRE was DENV (15%), followed by HAV (12%), HBV (6.2%), CHIKV (5.5%), and LEP (3.7%); HCV CoRE was absent. Complicated malaria was significantly more frequent in patients with CoRE (56%) than those without CoRE (36%; OR = 2.31, 95% CI: 1.18-4.92, *P* = 0.013). **Conclusions:** We found high CoRE prevalence in malaria patients as determined by serology in the study region; cases were associated with a worse clinical outcome. Further prospective studies with samples from different infection sites and the use of molecular tools are needed to determine the clinical significance of these findings.

### **The Burden of Arboviral Infections in the Military Health System 2012-2019.**

Wellington T, Fraser JA, Kuo HC, Hickey PW, Lindholm DA.

10-04-2023

*Am J Trop Med Hyg.*

<https://pubmed.ncbi.nlm.nih.gov/37037439/>

### **Chimeric flavivirus causes vascular leakage and bone marrow suppression in a mouse model.**

Kurosu T, Hanabara K, Asai A, Pambudi S, Phanthanawiboon S, Omokoko MD, Sakai Y, Suzuki T, Ikuta K.

05-04-2023

*Biochem Biophys Res Commun.*

<https://pubmed.ncbi.nlm.nih.gov/37037066/>

### **Dengue outbreaks in a city with recent transmission in São Paulo state, Brazil.**

Prestes-Carneiro LE, Barbosa Souza A, Belussi GL, Grande GHD, Bertacco EAM, Vieira AG, Flores EF.

10-04-2023

*Int J Environ Health Res.*

<https://pubmed.ncbi.nlm.nih.gov/37036947/>

We investigated the distribution of dengue cases, solid waste deposits (SWDs), forest fragments, water drainage, population income, and the possible association with dengue outbreaks in Presidente Prudente, São Paulo, Brazil. An urban setting with recent transmission. Data were obtained from public agencies. Kernel density maps of the variables were constructed. From 2015 to 2021, 33026 cases of dengue were reported; the incidence and mortality rate were highest in 2016. The number of cases decreased during the COVID-19 pandemic (2020 and 2021) compared with 2019, but alarming rates were registered in 2022. In 2015, 56 points of SWDs were identified, with an increase of 1.6-fold in 2020 and 2021. Multivariate analysis showed a positive correlation between the density of dengue cases and SWDs with the highest correlation (0.70) in 2020. Identifying these areas could guide public health authorities in surveillance measures and improvements in health care infrastructure.

### **Production and Characterization of Two Specific ZIKV Antigens Based on Bioinformatic Analysis and Serological Screening.**

Ribeiro Mota Souza R, Campos GS, Hughes Carvalho R, Brandão Peixoto I, Santos Galante R, Santana Moreira L, Beutinger Marchioro S, José Meyer Nascimento R, Sardi SI.

10-04-2023

*Immunol Invest.*

<https://pubmed.ncbi.nlm.nih.gov/37036441/>

### **DMKPs provide a generalizable strategy for studying genes required for reproduction or viability in non-traditional model organisms.**

Laursen WJ, Busby R, Sarkissian T, Chang EC, Garrity PA.

10-04-2023

*Genetics.*

<https://pubmed.ncbi.nlm.nih.gov/37036394/>

### **Cell-Based Electrical Impedance Platform to Evaluate Zika Virus Inhibitors in Real Time.**

Oeyen M, Meyen E, Schols D.

24-03-2023

*J Vis Exp.*

<https://pubmed.ncbi.nlm.nih.gov/37036247/>

Cell-based electrical impedance (CEI) technology measures changes in impedance caused by a growing or manipulated adherent cell monolayer on culture plate wells embedded with electrodes. The technology can be used to monitor the consequences of Zika virus (ZIKV) infection and adherent cell replication in real time, as this virus is highly cytopathogenic. It is a straightforward assay that does not require the use of labels or invasive methods and has the benefit of providing real-time data. The kinetics of ZIKV infection are highly dependent on the employed cell line, virus strain, and multiplicity of infection (MOI), which cannot be easily studied with conventional endpoint assays. Furthermore, the CEI assay can also be used for the evaluation and characterization of antiviral compounds, which can also have dynamic inhibitory properties over the course of infection. This methods article gives a detailed explanation of the practical execution of the CEI assay and its potential applications in ZIKV research and antiviral research in general.

### **Role of MXRA8 in Ross River Virus Disease Pathogenesis.**

Ng WH, Ling ZL, Kueh AJ, Herold MJ, West NP, King NJC, Mahalingam S, Liu X.

10-04-2023

*mBio.*

<https://pubmed.ncbi.nlm.nih.gov/37036079/>

Arthritogenic alphaviruses such as Ross River virus (RRV) and Chikungunya virus (CHIKV) are responsible for large-scale epidemics that cause debilitating acute and chronic musculoskeletal diseases. MXRA8 was recently discovered as an entry receptor for multiple alphaviruses including

CHIKV, RRV, Mayaro virus (MAYV), and O'nyong-nyong virus (ONNV). However, the role of MXRA8 in the development of alphavirus-induced musculoskeletal inflammation has not yet been fully studied. Here, we attempt to fully characterize the contribution of MXRA8 to RRV disease in an established mouse model. MXRA8 knockout (MXRA8<sup>-/-</sup>) mice generated on a C57BL/6J background, showed abrogated disease signs and reduced viral replication, which correlated with lower viral load, diminished proinflammatory cytokines, and limited cell infiltrates in inflamed tissues. Immunomodulation genes were upregulated to higher levels in RRV-infected wild-type (WT) mice than in MXRA8<sup>-/-</sup> mice. Intriguingly, *Cdkn1a* and *Ifi44* genes in blood and CD127/IL7RA, CD45, BatF3, IFNGR, Ly6G/Ly6C, CD40, CD127, F4/80, and MHC-II genes in quadriceps were found to be upregulated in RRV-infected MXRA8<sup>-/-</sup> mice compared to WT mice. Our results showed an essential role of MXRA8 in the immune response of mice infected with RRV and, more importantly, demonstrated novel changes in immunomodulation genes, which shed light on the immunopathogenesis of alphavirus-induced disease. **IMPORTANCE** Previous studies have shown the importance of the cell surface protein MXRA8 as an entry receptor for several different prominent alphaviruses such as CHIKV, RRV, MAYV, and ONNV. In particular, the role of MXRA8 in the tissue tropism, viral pathogenesis, and immune response of a CHIKV mouse model have already been briefly characterized. However, the role of MXRA8 warrants further characterization in RRV disease background, since there are noticeable differences in the disease profile between CHIKV and RRV. For example, patients infected with CHIKV are usually affected by sudden onset of severe arthritis and fever, whereas RRV-infected patients generally only have minor joint pain and mild fever. Here, we characterized the role of MXRA8 in RRV disease and assessed several key mechanisms of MXRA8 that may contribute to the disease progression.

### Evolution of a Functionally Intact but Antigenically Distinct DENV Fusion Loop.

Meganck RM, Zhu D, Dong S, Snoderly-Foster LJ, Dalben YR, Thiono D, White LJ, DeSilva AM, Baric RS, Tse LV.

27-03-2023

bioRxiv.

<https://pubmed.ncbi.nlm.nih.gov/37034784/>

### Increased interregional virus exchange and nucleotide diversity outline the expansion of the chikungunya virus ECSA lineage in Brazil.

Xavier J, Alcantara L, Fonseca V, Lima M, Castro E, Fritsch H, Oliveira C, Guimarães N, Adelino T, Evaristo M, Rodrigues ES, Santos EV, de La-Roque D, de Moraes L, Tosta S, Neto A, Rosewell A, Mendonça AF, Leite A, Vasconcelos A, Silva de Mello AL, Vasconcelos B, Montalbano CA, Zanluca C, Freitas C, de Albuquerque CFC, Duarte Dos Santos CN, Santos CS, Alves Dos Santos C, Maymone Gonçalves CC, Teixeira D, Neto DFL, Cabral D, de Oliveira EC, Noia Maciel EL, Pereira FM, Iani F, de Carvalho FP, Andrade G, Bezerra G, de Castro Lichs GG,

Pereira GC, Barroso H, Ferreira Franz HC, Ferreira H, Gomes I, Riediger IN, Rodrigues I, de Siqueira IC, Silva J, Rico JM, Lima J, Abrantes J, do Nascimento JPM, Wasserheit JN, Pastor J, de Magalhães JF, Luz KG, Lima Neto LG, Frutuoso LCV, da Silva LB, Sena L, de Sousa LAF, Pereira LA, Demarchi L, Câmara MCB, Astete MG, Almiron M, Lima M, Umaki Zardin MCS, Presibella MM, Falcão MB, Gale M, Freire N, Marques N, de Moura NFO, Almeida Da Silva PE, Rabinowitz P, da Cunha RV, Trinta KS, do Carmo Said RF, Kato R, Stabeli R, de Jesus R, Santos RH, Haddad SK, Slavov SN, Andrade T, Rocha T, Carneiro T, Nardy V, da Silva V, Carvalho WG, Van Voorhis WC, Araujo WN, de Filippis AMB, Giovanetti M.

03-04-2023

medRxiv.

<https://pubmed.ncbi.nlm.nih.gov/37034611/>

The emergence and reemergence of mosquito-borne diseases in Brazil such as Yellow Fever, Zika, Chikungunya, and Dengue have had serious impacts on public health. Concerns have been raised due to the rapid dissemination of the chikungunya virus (CHIKV) across the country since its first detection in 2014 in Northeast Brazil. Faced with this scenario, on-site training activities in genomic surveillance carried out in partnership with the National Network of Public Health Laboratories have led to the generation of 422 CHIKV genomes from 12 Brazilian states over the past two years (2021-2022), a period that has seen more than 312 thousand chikungunya fever cases reported in the country. These new genomes increased the amount of available data and allowed a more comprehensive characterization of the dispersion dynamics of the CHIKV East-Central-South-African (ECSA) lineage in Brazil. Tree branching patterns revealed the emergence and expansion of two distinct subclades. Phylogeographic analysis indicated that the northeast region has been the leading hub of virus spread towards other regions. Increased frequency of C>T transitions among the new genomes suggested that host restriction factors from the immune system such as ADAR and AID/APOBEC deaminases might be driving CHIKV ECSA lineage genetic diversity in Brazil.

### Development of insecticide-impregnated polyester/cotton blend fabric and assessment of their repellent characteristics against Cimex lectularius and dengue vectors Aedes albopictus and Aedes aegypti.

Kakati A, Banerjee A, Das P, Saha B, Goyary D, Karmakar S, Kishor S, Bhutia YD, Chattopadhyay P.

09-04-2023

Parasit Vectors.

<https://pubmed.ncbi.nlm.nih.gov/37032336/>

### Spatiotemporal dynamics and recurrence of chikungunya virus in Brazil: an epidemiological study.

de Souza WM, de Lima STS, Simões Mello LM, Candido DS, Buss L, Whittaker C, Claro IM, Chandradeva N, Granja F, de Jesus R, Lemos PS, Toledo-Teixeira DA, Barbosa PP, Firmino ACL, Amorim MR, Duarte LMF, Pessoa IB Jr,



Forato J, Vasconcelos IL, Maximo ACBM, Araújo ELL, Perdigão Mello L, Sabino EC, Proença-Módena JL, Faria NR, Weaver SC.

06-04-2023

*Lancet Microbe.*

<https://pubmed.ncbi.nlm.nih.gov/37031687/>

**Background:** Chikungunya virus (CHIKV) is an Aedes mosquito-borne virus that has caused large epidemics linked to acute, chronic, and severe clinical outcomes. Currently, Brazil has the highest number of chikungunya cases in the Americas. We aimed to investigate the spatiotemporal dynamics and recurrence pattern of chikungunya in Brazil since its introduction in 2013.

**Methods:** In this epidemiological study, we used CHIKV genomic sequencing data, CHIKV vector information, and aggregate clinical data on chikungunya cases from Brazil. The genomic data comprised 241 Brazilian CHIKV genome sequences from GenBank (n=180) and the 2022 CHIKV outbreak in Ceará state (n=61). The vector data (Breteau index and House index) were obtained from the Brazilian Ministry of Health for all 184 municipalities in Ceará state and 116 municipalities in Tocantins state in 2022. Epidemiological data on laboratory-confirmed cases of chikungunya between 2013 and 2022 were obtained from the Brazilian Ministry of Health and Laboratory of Public Health of Ceará. We assessed the spatiotemporal dynamics of chikungunya in Brazil via time series, mapping, age-sex distribution, cumulative case-fatality, linear correlation, logistic regression, and phylogenetic analyses. **Findings:** Between March 3, 2013, and June 4, 2022, 253 545 laboratory-confirmed chikungunya cases were reported in 3316 (59.5%) of 5570 municipalities, mainly distributed in seven epidemic waves from 2016 to 2022. To date, Ceará in the northeast has been the most affected state, with 77 418 cases during the two largest epidemic waves in 2016 and 2017 and the third wave in 2022. From 2016 to 2022 in Ceará, the odds of being CHIKV-positive were higher in females than in males (odds ratio 0.87, 95% CI 0.85-0.89, p<0.0001), and the cumulative case-fatality ratio was 1.3 deaths per 1000 cases. Chikungunya recurrences in the states of Ceará, Tocantins (recurrence in 2022), and Pernambuco (recurrence in 2021) were limited to municipalities with few or no previously reported cases in the previous epidemic waves. The recurrence of chikungunya in Ceará in 2022 was associated with a new East-Central-South-African lineage. Population density metrics of the main CHIKV vector in Brazil, *Aedes aegypti*, were not correlated spatially with locations of chikungunya recurrence in Ceará and Tocantins. **Interpretation:** Spatial heterogeneity of CHIKV spread and population immunity might explain the recurrence pattern of chikungunya in Brazil. These results can be used to inform public health interventions to prevent future chikungunya epidemic waves in urban settings. **Funding:** Global Virus Network, Burroughs Wellcome Fund, Wellcome Trust, US National Institutes of Health, São Paulo Research Foundation, Brazil Ministry of Education, UK Medical Research Council, Brazilian National Council for Scientific and Technological Development, and UK Royal Society.

## Coinfection and circulation of chikungunya virus and dengue virus in pediatric patients in Myanmar, 2019.

Ngwe Tun MM, Kyaw AK, Nabeshima T, Dumre SP, Soe AM, Nwe KM, Myaing SS, Lwin EP, Win YT, Inoue S, Takamatsu Y, Urano T, Thu HM, Thant KZ, Htun ZT, Morita K.

06-04-2023

*Microbes Infect.*

<https://pubmed.ncbi.nlm.nih.gov/37030472/>

Myanmar is an endemic country for arboviruses, and outbreaks occur frequently. A cross-sectional analytical study was conducted during the peak season of the chikungunya virus (CHIKV) outbreak in 2019. A total of 201 patients with acute febrile illness who were admitted to the 550-bedded Mandalay Children Hospital in Myanmar were enrolled in the study, and virus isolation, serological tests, and molecular tests for the dengue virus (DENV) and CHIKV were performed for all samples. Out of 201 patients, 71 (35.3%) were only DENV-infected, 30 (14.9%) were only CHIKV-infected and 59 (29.4%) were coinfecting with DENV and CHIKV. The viremia levels of the DENV- and CHIKV- mono-infected groups were significantly higher than those of the group coinfecting with DENV and CHIKV. Genotype I of DENV-1, genotypes I and III of DENV-3, genotype I of DENV-4 and the East/Central/South African genotype of CHIKV were co-circulating during the study period. Two novel epistatic mutations of CHIKV (E1:K211E and E2:V264A) were noted. This study highlighted that there were many coinfection cases during the outbreak and that the co-circulation of both viruses in DENV-endemic regions warrants effective monitoring of these emerging pathogens via comprehensive surveillance to facilitate the implementation of effective control measures.

## Tropical infections as occupational diseases among young volunteers in social projects.

Kölsch Y, Phiri BSJ, Küpper T.

06-04-2023

*Int J Hyg Environ Health.*

<https://pubmed.ncbi.nlm.nih.gov/37030087/>

## The First Genomic Characterization of the Chikungunya Virus in Saudi Arabia.

Alguridi HI, Alzahrani F, Altayb HN, Almalki S, Zaki E, Algarni S, Assiri A, Memish ZA.

08-04-2023

*J Epidemiol Glob Health.*

<https://pubmed.ncbi.nlm.nih.gov/37029884/>

**Background:** Chikungunya is an arboviral infection caused by the Chikungunya virus (CHIKV) transmitted to humans by mosquitoes of *Aedes* spp. CHIKV has been confined to African countries and South-East Asia up to 2004, but since then, the pathogen has become more global, and its high morbidity rate has become more visible. Saudi Arabia is not an endemic region of CHIKV, and the virus's origin is not yet fully understood. This study aimed to characterize the genome of CHIKV from samples detected in Jeddah in

2018. **Method:** Twenty-two sets of primers were designed to amplify near-full length genome of CHIKV. RT-PCR was conducted from clinical samples. Two samples were used for studying near complete genome sequence while the remaining samples were used to study the E1 gene. Different bioinformatics tools were utilized. **Results:** Phylogenetic analysis showed that the CHIKV strains clustered with strains isolated from Kenya during 2017-2018 and belonged to ECSA genotype. E1: L136F, K211E and I317V mutations were identified in our strains. Also, E2: M74I, A76T, and V264A mutations were documented. Additionally, the capsid N79S substitution was also detected. **Conclusion:** The genome of CHIKV was analyzed for the first time in Saudi Arabia to better understand the origin of the CHIKV and its genetic diversity, which showed high similarity with IE-a subclade of CHIKV strains detected in Mombasa (Kenya) indicating its possible origin.

### Chikungunya vaccines: An update in 2023.

Roongaraya P, Boonyasuppayakorn S.  
Mar-2023

*Asian Pac J Allergy Immunol.*

<https://pubmed.ncbi.nlm.nih.gov/37029782/>

A recent chikungunya outbreak affected 1.5 million cases in more than 60 countries. The virus causes low mortality but moderate to severe morbidities such as high fever, myalgia, and polyarthrititis. The chikungunya virus is transmitted by *Aedes* spp. mosquitoes, of which the population has increased due to urbanization and global warming. Currently, no commercial vaccine is available, but several candidates are being tested in clinical trials. This review aimed to summarize the recent updates of candidates on each platform, ranging from traditional inactivation, live attenuation with reverse genetics, virus-like particles, viral vectors, and mRNA, mainly focusing on the candidates in clinical trials or recently developed.

### Detection of DENV-2 and ZIKV coinfection in southeastern Brazil by serum and urine testing.

da Conceição PJP, de Carvalho LR, de Godoy BLV, Nogueira ML, Terzian ACB, de Godoy MF, Calmon MF, Bittar C, Rahal P.

07-04-2023

*Med Microbiol Immunol.*

<https://pubmed.ncbi.nlm.nih.gov/37029306/>

**Purpose:** *Aedes aegypti* mosquito-borne diseases have a significant impact on public health in Brazil. In this study, we investigated the presence of the Zika virus (ZIKV) and dengue virus (DENV) in serum and urine samples from symptomatic participants who attended an Emergency Care Unit located in a city in the northwestern region of São Paulo between February 2018 and April 2019.

**Methods:** Serum and urine samples were collected from participants suspected of having arbovirus infection. After the extraction of viral RNA, viral detection was performed by real-time quantitative reverse transcription polymerase chain reaction (RT-qPCR) (One-Step RT-qPCR). **Results:** A total of 305 participants participated in this study. A total of 283 blood and 270 urine samples were collected. Of 305

patients, 36.4% (111/305) were positive for ZIKV, 43.3% (132/305) for DENV2, and 0.3% (1/305) for DENV1. Coinfection with ZIKV/DENV2 was observed in 13.1% of participants. If only serum samples were used, ZIKV detection would have decreased to 23.3% (71/305). Of all the participants included in the study, only one was suspected of having ZIKV infection based on clinical diagnosis, and the remaining participants were suspected of having DENV. **Conclusion:** By testing serum and urine samples, we increased the detection of both viruses and detected considerable levels of ZIKV and DENV-2 coinfection when compared to other studies. Additionally, we detected an unnoticed ZIKV outbreak in the city. These findings highlight the importance of the molecular diagnosis of arboviruses to aid public health surveillance and management strategies.

### Insecticide susceptibility and detection of kdr-gene mutations in *Aedes aegypti* of Peshawar, Pakistan.

Tanzila G, Rasheed SB, Khan NH, Kausar A, Jahan F, Wahid S.

05-04-2023

*Acta Trop.*

<https://pubmed.ncbi.nlm.nih.gov/37028585/>

### Mechanisms of Zika astrocyte infection and neuronal toxicity.

Veilleux C, Eugenin EA.

25-03-2023

*NeuroImmune Pharm Ther.*

<https://pubmed.ncbi.nlm.nih.gov/37027343/>

### Tracing the future of epidemics: Coincident niche distribution of host animals and disease incidence revealed climate-correlated risk shifts of main zoonotic diseases in China.

Cao B, Bai C, Wu K, La T, Su Y, Che L, Zhang M, Lu Y, Gao P, Yang J, Xue Y, Li G.

07-04-2023

*Glob Chang Biol.*

<https://pubmed.ncbi.nlm.nih.gov/37026556/>

Climate has critical roles on the origin, pathogenesis and transmission of infectious zoonotic diseases. However, large-scale epidemiologic trend and specific response pattern of zoonotic diseases under future climate scenarios are poorly understood. Here, we projected the distribution shifts of transmission risks of main zoonotic diseases under climate change in China. First, we shaped the global habitat distribution of main host animals for three representative zoonotic diseases (2, 6, and 12 hosts for dengue, hemorrhagic fever and plague, respectively) with 253,049 occurrence records using maximum entropy (Maxent) modeling. Meanwhile, we predicted the risk distribution of the above three diseases with 197,098 disease incidence records from 2004 to 2017 in China using an integrated Maxent modeling approach. The comparative analysis showed that there exist highly coincident niche distributions between habitat distribution of hosts and risk distribution of diseases,

indicating that the integrated Maxent modeling is accurate and effective for predicting the potential risk of zoonotic diseases. On this basis, we further projected the current and future transmission risks of 11 main zoonotic diseases under four representative concentration pathways (RCPs) (RCP2.6, RCP4.5, RCP6.0, RCP8.5) in 2050 and 2070 in China using the above integrated Maxent modeling with 1,001,416 disease incidence records. We found that Central China, Southeast China and South China are concentrated regions with high transmission risks for main zoonotic diseases. More specifically, zoonotic diseases had diverse shift patterns of transmission risks including increase, decrease and unstable. Further correlation analysis indicated that these patterns of shifts were highly correlated with global warming and precipitation increase. Our results revealed how specific zoonotic diseases respond in a changing climate, thereby calling for effective administration and prevention strategies. Furthermore, these results will shed light on guiding future epidemiologic prediction of emerging infectious diseases under global climate change.

### Epidemiological and clinical features of the 2016-2018 Zika virus outbreak in northern Argentina.

Byrne AB, Bonnin FA, Bruno A, Bono MM, Contrini MM, López EL, Quipildor MO, Talarico LB.

07-04-2023

*Trans R Soc Trop Med Hyg.*

<https://pubmed.ncbi.nlm.nih.gov/37026534/>

**Background:** During the American epidemic, Zika virus (ZIKV) expanded rapidly through dengue virus (DENV)-endemic regions. We analyzed the presentation of ZIKV infection in patients from the City of Orán, Argentina, and compared some of its features with dengue presentation in the same region. **Methods:** A retrospective study was conducted at San Vicente de Paul Hospital during 2016-2018. Clinical and demographic characteristics, pre-existing immunity to DENV, viral load and type I interferon (IFN) responses were studied in 63 patients with ZIKV infection. **Results:** Clinical manifestations of ZIKV infection were generally mild compared with dengue, although rash ( $p<0.001$ ) and itching ( $p<0.001$ ) were significantly more prevalent in ZIKV patients. ZIKV patients aged  $<15$  y manifested relatively mild disease compared with older ZIKV patients, showing a decreased prevalence of headache ( $p=0.008$ ), retro-orbital pain ( $p=0.001$ ) and arthralgia ( $p=0.001$ ). Increased Zika incidence was observed in female patients (60.3%). Serum viral load was low to undetectable in ZIKV patients and was not associated with serum anti-DENV IgG titers. Interferon- $\alpha$  and IFN- $\beta$  serum levels did not correlate with serum viral load in ZIKV patients. **Conclusions:** Clinical presentation of ZIKV and DENV infections is largely overlapping, presenting a challenge for diagnosis and risk assessment for uniquely at-risk populations.

### Investigation of Chikungunya virus genotype at tertiary care center in Western Maharashtra, India.

Suryavanshi KT, Chakraborty A.

Jan-Mar 2023

*J Vector Borne Dis.*

<https://pubmed.ncbi.nlm.nih.gov/37026227/>

### Use Of dry blots for serotyping and genotyping of dengue viruses: A pilot study.

Bishwal S, Kumar R, Minj P, Godbole S, Sahare L, Ukey M, Barde P.

Jan-Mar 2023

*J Vector Borne Dis.*

<https://pubmed.ncbi.nlm.nih.gov/37026222/>

**Background & objectives:** Dengue (DEN) is a result of infection by one or multiple types of four dengue viruses known as Dengue virus (DENV) 1-4. Identifying circulating serotype and genotype is epidemiologically important, however, it is challenging in resource limited areas. Moreover, transporting samples from the collection site to the laboratory in appropriate condition is an exigent task. To overcome this, we evaluated the usefulness of dry blots of serum for DENV diagnosis, serotyping and genotyping. **Methods:** Serum samples received for diagnosis were divided into parts; one was used for providing the diagnosis. Remaining sample was distributed in three parts (100  $\mu$ l each), one part was used for molecular testing and two parts were mixed with RNAlater reagent® in equal volumes and was blotted on Whatman filter paper no 3. The blots were dried and stored at 4°C and 28°C and tested for presence of dengue RNA, serotypes and genotypes after 7 days of incubation. **Results:** The diagnosis and serotyping results of serum sample and dry serum blots were in concordance. Out of 20 positive samples, 13 (65%) gave satisfactory sequencing results. Genotype III of DENV-1, Genotype IV of DENV 2 and Genotype I of DENV-4 were detected. **Interpretation & conclusion:** The results demonstrate that serum mixed with RNA protective solution and blotted on Whatman filter paper no 3 can be effectively used for diagnosis, serotyping and genotyping of DENVs. This will help in easy transportation, diagnosis and effective data generation in resource limited settings.

### Current status of insecticide resistance and its underlying mechanisms in Aedes aegypti (L.) in Punjab, Pakistan.

Ramzan H, Manzoor F, Oneeb M.

Jan-Mar 2023

*J Vector Borne Dis.*

<https://pubmed.ncbi.nlm.nih.gov/37026220/>

### Chemical constituents and strong larvicidal activity of Solanum xanthocarpum among selected plants extracts against the malaria, filaria, and dengue vectors.

Kumar P, Shakya R, Kumar V, Kumar D, Chauhan R, Singh H.

Jan-Mar 2023

*J Vector Borne Dis.*

<https://pubmed.ncbi.nlm.nih.gov/37026216/>

## 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- $\alpha$  were also found in DF patients. However, we failed to

detect IL-1 $\beta$ , IL-17A and TNF- $\alpha$  in plasma, because of off-target. In our study, there was no relation between IL-6, IL-10, and IFN- $\alpha$  expressions and IL-37b in serum ( $P > 0.05$ ). The IL-37b-producing monocytes were negatively correlated with the level of IFN- $\alpha$  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/>

## The NK cell receptor NKp46 recognizes ecto-calreticulin on ER-stressed cells.

Sen Santara S, Lee DJ, Crespo Â, Hu JJ, Walker C, Ma X, Zhang Y, Chowdhury S, Meza-Sosa KF, Lewandrowski M, Zhang H, Rowe M, McClelland A, Wu H, Junqueira C, Lieberman J.

Apr-2023

*Nature.*

<https://pubmed.ncbi.nlm.nih.gov/37020026/>

Natural killer (NK) cell kill infected, transformed and stressed cells when an activating NK cell receptor is triggered<sup>1</sup>. Most NK cells and some innate lymphoid cells express the activating receptor NKp46, encoded by NCR1, the most evolutionarily ancient NK cell receptor<sup>2,3</sup>. Blockage of NKp46 inhibits NK killing of many cancer targets<sup>4</sup>. Although a few infectious NKp46 ligands have been identified, the endogenous NKp46 cell surface ligand is unknown. Here we show that NKp46 recognizes externalized calreticulin (ecto-CRT), which translocates from the endoplasmic reticulum (ER) to the cell membrane during ER stress. ER stress and ecto-CRT are hallmarks of chemotherapy-induced immunogenic cell death<sup>5,6</sup>, flavivirus infection and senescence. NKp46 recognition of the P domain of ecto-CRT triggers NK cell signalling and NKp46 caps with ecto-CRT in NK immune synapses. NKp46-mediated killing is inhibited by knockout or knockdown of CALR, the gene encoding CRT, or CRT antibodies, and is enhanced by ectopic expression of glycosylphosphatidylinositol-anchored CRT. NCR1-deficient human (and Nrc1-deficient mouse) NK cells are impaired in the killing of ZIKV-infected, ER-stressed and senescent cells and ecto-CRT-expressing cancer cells. Importantly, NKp46 recognition of ecto-CRT controls mouse B16 melanoma and RAS-driven lung cancers and enhances tumour-infiltrating NK cell degranulation and cytokine secretion. Thus, NKp46 recognition of ecto-CRT as a danger-associated molecular pattern eliminates ER-stressed cells.

## Early diagnosis of dengue: Diagnostic utility of the SD BIOLINE Dengue Duo rapid test in Reunion Island.



**Maillard O, Belot J, Adenis T, Rollot O, Adenis A, Guihard B, Gérardin P, Bertolotti A.**

30-03-2023

*PLoS Negl Trop Dis.*

<https://pubmed.ncbi.nlm.nih.gov/36996260/>

**Background:** In Reunion Island, dengue outbreaks have been occurring since 2018. The healthcare facilities are facing the problem of managing a massive influx of patients and a growing care burden. The aim of this study was to evaluate the performance of the SD Bioline Dengue Duo rapid diagnostic test in adults consulting at an emergency department during the 2019 epidemic.

**Methodology/principal findings:** This retrospective study of diagnostic accuracy included patients over 18 years old, suspected of dengue, who were admitted to emergency units of the University Hospital of Reunion between the 1st of January and 30th of June, 2019, and were tested for dengue fever with the SD Bioline Dengue Duo rapid diagnostic test and reverse transcriptase polymerase chain reaction. Over the study period, 2099 patients were screened retrospectively. Of them, 671 patients matched the inclusion criteria. The overall rapid diagnostic test performance was 42% for sensitivity and 15% for specificity. The non-structural 1 antigen component had a good specificity of 82% but a low sensitivity of 12%. The immunoglobulin M component had a sensitivity of 28% and a specificity of 33%. Sensitivities were slightly improved beyond the 5th day of illness compared to the early stage for all components, but only the non-structural 1 antigen component had a better specificity of 91%. Furthermore, predictive values were low and post-test probabilities never improved pre-test probabilities in our setting. **Conclusions/significance:** These results suggest that the SD Bioline Dengue Duo RDT did not achieve sufficient performance levels to rule in, or discard, an early point of care dengue diagnosis in the emergency department during the 2019 epidemic in Reunion.

### **Differences in gene expression in field populations of Wolbachia-infected Aedes aegypti mosquitoes with varying release histories in northern Australia.**

**Wimalasiri-Yapa BMCR, Huang B, Ross PA, Hoffmann AA, Ritchie SA, Frentiu FD, Warrilow D, van den Hurk AF.**

29-03-2023

*PLoS Negl Trop Dis.*

<https://pubmed.ncbi.nlm.nih.gov/36989319/>

### **Frequent first-trimester pregnancy loss in rhesus macaques infected with African-lineage Zika virus.**

**Rosinski JR, Raasch LE, Barros Tiburcio P, Breitbach ME, Shepherd PM, Yamamoto K, Razo E, Krabbe NP, Bliss MI, Richardson AD, Einwalter MA, Weiler AM, Sneed EL, Fuchs KB, Zeng X, Noguchi KK, Morgan TK, Alberts AJ, Antony KM, Kabakov S, Ausderau KK, Bohm EK, Pritchard JC, Spanton RV, Ver Hoove JN, Kim CBY, Nork TM, Katz AW, Rasmussen CA, Hartman A, Mejia A, Basu P, Simmons HA, Eickhoff JC, Friedrich TC, Aliota MT, Mohr EL, Dudley DM, O'Connor DH, Newman CM.**

28-03-2023

*PLoS Pathog.*

<https://pubmed.ncbi.nlm.nih.gov/36976812/>

In the 2016 Zika virus (ZIKV) pandemic, a previously unrecognized risk of birth defects surfaced in babies whose mothers were infected with Asian-lineage ZIKV during pregnancy. Less is known about the impacts of gestational African-lineage ZIKV infections. Given high human immunodeficiency virus (HIV) burdens in regions where African-lineage ZIKV circulates, we evaluated whether pregnant rhesus macaques infected with simian immunodeficiency virus (SIV) have a higher risk of African-lineage ZIKV-associated birth defects. Remarkably, in both SIV+ and SIV- animals, ZIKV infection early in the first trimester caused a high incidence (78%) of spontaneous pregnancy loss within 20 days. These findings suggest a significant risk for early pregnancy loss associated with African-lineage ZIKV infection and provide the first consistent ZIKV-associated phenotype in macaques for testing medical countermeasures.

### **Evaluation of repRNA vaccine for induction and in utero transfer of maternal antibodies in a pregnant rabbit model.**

**Khandhar AP, Landon CD, Archer J, Krieger K, Warner NL, Randall S, Berube BJ, Erasmus JH, Sather DN, Staats HF.**

05-04-2023

*Mol Ther.*

<https://pubmed.ncbi.nlm.nih.gov/36965482/>

### **Functionalized sulfonyl anthranilic acid derivatives inhibit replication of all the four dengue serotypes.**

**Felicetti T, Gwee CP, Burali MS, Chan KWK, Alonso S, Pismataro MC, Sabatini S, Barreca ML, Cecchetti V, Vasudevan SG, Manfroni G.**

05-04-2023

*Eur J Med Chem.*

<https://pubmed.ncbi.nlm.nih.gov/36965228/>

Dengue virus (DENV), a mosquito-borne flavivirus, continues to be a major public health threat in many countries and no approved antiviral therapeutics are available yet. In this work, we designed and synthesized a series of sulfonyl anthranilic acid (SAA) derivatives using a ligand-based scaffold morphing approach of the 2,1-benzothiazine 2,2-dioxide core, previously used by us to develop DENV polymerase inhibitors resulting devoid of any cell-based antiviral activity. Several derivatives based on the new SAA chemotype exhibited potent inhibition against DENV infection in the cell-based assay but did not inhibit DENV NS5 polymerase activity in the in vitro de novo initiation and elongation assays. Notably, best compounds 26 and 39 showed EC<sub>50</sub> values in the range of 0.54-1.36 µM against cells infected with the four dengue serotypes (DENV-1-4). Time-of-drug-addition assay revealed that analogue 26 is a post-entry replication inhibitor that appears to be specific for cells of primate origin, implicating a host target with a high barrier to resistance. In conclusion, SAA derivatives offer a valuable starting point for developing effective Dengue antiviral therapeutics.



### **Recent advances in the development of methyltransferase (MTase) inhibitors against (re)emerging arboviruses diseases dengue and Zika.**

**Delgado-Maldonado T, Moreno-Herrera A, Pujadas G, Vázquez-Jiménez LK, González-González A, Rivera G.**

05-04-2023

*Eur J Med Chem.*

<https://pubmed.ncbi.nlm.nih.gov/36958266/>

### **Secondary metabolites as potential drug candidates against Zika virus, an emerging looming human threat: Current landscape, molecular mechanism and challenges ahead.**

**Sadeer NB, El Kalamouni C, Khalid A, Abdalla AN, Zengin G, Khoa Bao LV, Mahomoodally MF.**

May-2023

*J Infect Public Health.*

<https://pubmed.ncbi.nlm.nih.gov/36958171/>

Nature has given us yet another wild card in the form of Zika virus (ZIKV). It was found in 1947, but has only recently become an important public health risk, predominantly to pregnant women and their unborn offspring. Currently, no specific therapeutic agent exists for ZIKV and treatment is mainly supportive. Natural products (NPs) can serve as a major source of potent antiviral drugs. To create this review, a comprehensive search was conducted from different databases (PubMed, ScienceDirect, Google scholar). A statistical analysis on the number of publications related to NPs and ZIKV was conducted to analyse the trend in research covering the period 1980-2020. From the data collated in this review, a number of NPs have been found to be inhibitive towards different stages of the ZIKV lifecycle in vitro studies. For instance, baicalin, (-)-epigallocatechin gallate, curcumin, nanchangmycin, gossypol, cephaeline, emetine, resveratrol, berberine, amongst others, can prevent viral entry by attacking ZIKV E protein. Compounds luteolin, myricetin, astragalin, rutin, (-)-epigallocatechin gallate, carnosine, pedalitin, amongst others, inhibited NS2B-NS3 protease activity which consequently hamper replication. Interestingly, a few NPs had the ability to arrest both viral entry and replication, namely baicalin, (-)-epigallocatechin gallate, curcumin, cephaeline, emetine, and resveratrol. To the best of our knowledge, we obtained only one in vivo study conducted on emetine and results showed that it decreased the levels of circulating ZIKV by approximately 10-fold. Our understanding on NPs exhibiting anti-ZIKV effects in vivo testing as well as clinical trials is limited. Our trend analysis showed that interest in searching for a cure or prevention against Zika in NPs is negligible and there are no publications yet covering the clinical evaluation. NPs with anti-ZIKV property can be a winning strategy in controlling the bio-burden of an epidemic or pandemic. We therefore opine that in the future, more research should be devoted to ZIKV. This review attempts to provide baseline data and roadmap to pursue detailed investigations for developing potent and novel therapeutic agents to prevent and cure ZIKV infection.

### **Zika virus NS1 suppresses VE-cadherin via hsa-miR-29b-3p/DNMT3b/MMP-9 pathway in human brain microvascular endothelial cells.**

**Bhardwaj U, Singh SK.**

Jun-2023

*Cell Signal.*

<https://pubmed.ncbi.nlm.nih.gov/36948479/>

Zika virus infection has been reported to cause microcephaly in newborns. ZIKV exploits various strategies to cross the blood-brain barrier. ZIKV NS1 may compromise the barrier integrity of endothelial cells by regulating expression of junctional proteins. MicroRNAs play an important role in post-transcriptional gene regulations. We demonstrated that ZIKV-NS1 affected the adherence junction protein in human brain microvascular endothelial cells via hsa-miR-29b-3p/DNMT3b/MMP-9 pathway. The hCMEC/D3 cells were exposed to ZIKV-NS1 with different doses (500 ng/mL and 1000 ng/mL) for 24 h. The expression pattern of DNMT3b, MMP-9, and VE-cadherin were studied using immunoblotting and the distribution of DNMT3b and MMP-9 were studied using immunofluorescence. The quantification of hsa-miR-29b-3p was done through qRT-PCR. Direct regulation of DNMT3b by hsa-miR-29b-3p was demonstrated by overexpression of hsa-miR-29b-3p using hsa-miR-29b-3p mimic, and knockdown of hsa-miR-29b-3p by using hsa-miR-29b-3p inhibitors. The ZIKV-NS1 affected the barrier function of endothelial cells through the increased expression of hsa-miR-29b-3p, which suppressed the DNMT3b, thus enhanced expression of MMP-9, which finally suppressed the expression of VE-cadherin. These findings suggested that ZIKV-NS1 alters the expression of Adherens Junction protein in human brain microvascular endothelial cells through hsa-miR-29b-3p/DNMT3b/MMP-9 pathway, which compromised the barrier function of human brain microvascular endothelial cells.

### **Loop Dynamics and Conformational Flexibility in Dengue Serine Protease Activity: Noninvasive Perturbation by Solvent Exchange.**

**Misra R, Maity A, Kundu S, Bhunia M, Nanda B, Maiti NC, Pal U.**

10-04-2023

*J Chem Inf Model.*

<https://pubmed.ncbi.nlm.nih.gov/36943246/>

### **Synthesis and virucide activity on zika virus of 1,2,3-triazole-containing vanillin derivatives.**

**da Silva Rodrigues JV, Rodrigues Gazolla PA, da Cruz Pereira I, Dias RS, Poly da Silva IE, Oliveira Prates JW, de Souza Gomes I, de Azevedo Silveira S, Costa AV, de Oliveira FM, de Aguiar AR, Canedo da Silva C, Teixeira RR, de Paula SO.**

Apr-2023

*Antiviral Res.*

<https://pubmed.ncbi.nlm.nih.gov/36934985/>

The Zika virus (ZIKV) is an arbovirus and belongs to the Flaviviridae family and Flavivirus genus, with dissemination in the Americas. In Brazil, the predominant strain is the Asian, promoting outbreaks that started in 2015 and are directly related to microcephaly in newborns and Guillain-Barré syndrome in adults. Recently, researchers identified a new African strain circulating in Brazil at the mid-end of 2018 and the beginning of 2019, with the potential to originate a new epidemic. To date, there is no approved vaccine or drug for the treatment of Zika syndrome, and the development of therapeutic alternatives to treat it is of relevance. A critical approach is to use natural products when searching for new chemical agents to treat Zika syndrome. The present investigation describes the preparation of a series of 1,2,3-triazoles derived from the natural product vanillin and the evaluation of their virucide activity. A series of fourteen derivatives were prepared via alkylation of vanillin followed by CuAAC (the copper(I)-catalyzed azide-alkyne cycloaddition) reaction. The compounds were fully characterized by infrared (I.R.), nuclear magnetic resonance (NMR), and high-resolution mass spectrometry (HRMS) techniques. The cytotoxicity of Vero cells and the effect on the Zika Virus of the vanillin derivatives were evaluated. It was found that the most effective compound corresponded to 4-((1-(4-isopropylbenzyl)-1H-1,2,3-triazol-4-yl)methoxy)-3-methoxybenzaldehyde (8) ( $EC_{50}$  = 27.14  $\mu$ M,  $IC_{50}$  = 334.9  $\mu$ M). Subsequent assessments, namely pre and post-treatment assays, internalization and adsorption inhibition assays, kinetic, electronic microscopy analyses, and zeta potential determination, revealed that compound 8 blocks the Zika virus infection in vitro by acting on the viral particle. A molecular docking study was performed, and the results are also discussed.

### **AT-752 targets multiple sites and activities on the Dengue virus replication enzyme NS5.**

**Feracci M, Eydoux C, Fattorini V, Lo Bello L, Gauffre P, Selisko B, Sutto-Ortiz P, Shannon A, Xia H, Shi PY, Noel M, Debart F, Vasseur JJ, Good S, Lin K, Moussa A, Sommadossi JP, Chazot A, Alvarez K, Guillemot JC, Decroly E, Ferron F, Canard B.**

Apr-2023

*Antiviral Res.*

<https://pubmed.ncbi.nlm.nih.gov/36905944/>

### **Venezuelan equine encephalitis virus E1 protein interacts with PDIA6 and PDI inhibition reduces alphavirus production.**

**Panny L, Akrhymuk I, Bracci N, Woodson C, Flor R, Elliott I, Zhou W, Narayanan A, Campbell C, Kehn-Hall K.**

Apr-2023

*Antiviral Res.*

<https://pubmed.ncbi.nlm.nih.gov/36822370/>

Venezuelan equine encephalitis virus (VEEV) is an alphavirus transmitted by mosquitos that can cause a febrile illness and induce severe neurological complications in humans and equine populations. Currently there are no FDA approved vaccines or antiviral

treatments to combat VEEV. Proteomic techniques were utilized to create an interactome of the E1 fusion glycoprotein of VEEV. VEEV E1 interacted with a number of cellular chaperone proteins including protein disulfide isomerase family A member 6 (PDIA6). PDI inhibition through LOC14 and/or nitazoxanide treatment effectively decreased production of VEEV and other alphaviruses in vitro, including eastern equine encephalitis virus, Sindbis virus, and chikungunya virus. Decreased oxidoreductive capabilities of PDIs through LOC14 or nitazoxanide treatment impacted both early and late events in viral replication, including the production of non-infectious virions and decreased VEEV E1 disulfide bond formation. Results from this study identified PDIs as critical regulators of alphavirus replication and potential therapeutic targets.

### **Congenital Zika Virus Syndrome and Autoimmunity: Two Case Reports of Type 1 Diabetes Mellitus.**

**Arrais NMR, Arrais RF, Coelho MC, Deghaide NHS, Donadi EA, Maia CRS, de Moraes-Pinto MI.**

01-05-2023

*Pediatr Infect Dis J.*

<https://pubmed.ncbi.nlm.nih.gov/36795588/>

### **Breastfeeding by chikungunya virus-infected dams confers resistance to challenge in the offspring.**

**de Paula Souza J, de Jesus BLS, Giusti AL, Viana RMM, de Souza Cardoso R, Almeida GM, Pontelli MC, Kümmerer BM, Espósito DLA, de Melo DM, de Lima TM, Salustiano SG, Martins RB Jr, Ferraz IS, Arruda E.**

May-2023

*Transl Res.*

<https://pubmed.ncbi.nlm.nih.gov/36526155/>

Vertical transmission of Chikungunya virus (CHIKV) has been reported in humans, but the transmission routes have not been completely understood, and experimental animal models are needed to enable detailed investigation of the transmission and pathogenesis of congenital infections. The intertwining of immune response and virus components at the gestation/breastfeeding interfaces between mother and fetus/newborn may have effects during the offspring development. An experimental model of CHIKV was established by infecting pregnant BALB/c female mice that enabled confirmation that dams inoculated up to the 10<sup>th</sup> gestational day transmit CHIKV transplacentally to approximately 8.4% of the fetuses, resulting in severe teratogenic effects. CHIKV neutralizing antibodies were detected in sera from adult mice born to healthy females and breastfed by CHIKV-infected dams, while no neutralization was detected in sera from animals born to CHIKV-infected dams. Moreover, adult mice born to healthy dams and cross-fostered for breastfeeding by CHIKV-infected dams were resistant to challenge with CHIKV on the 90<sup>th</sup> day after birth. The animals also had reduced viral loads in brain and spleen as compared to controls. There was expression of fluorescent CHIKV non-structural protein, and detection of viral RNA by RT-PCR in breast tissue from infected dams. CHIKV RNA and proteins were also detected in breast milk retrieved from the

stomachs of recently fed newborns. The experimental results were also complemented by the finding of CHIKV RNA in 6% of colostrum samples from healthy lactating women in a CHIKV-endemic area. Breastfeeding induces immune protection to challenge with CHIKV in mice.

### Educational interventions for the prevention and control of dengue in adults: An integrative review.

**Llorente-Pérez YJ, Rodríguez-Acelas AL, Cañon-Montañez W.**

Mar-Apr 2023

*Enferm Clin (Engl Ed).*

<https://pubmed.ncbi.nlm.nih.gov/36375729/>

**Objective:** To review and synthesize the scientific production of educational interventions for the prevention and control of dengue in adults. **Method:** Integrative literature review, protocol registered in INPLASY (202170038). The search was performed in MEDLINE, LILACS, Web of Science and EMBASE, with no start date until March 31, 2021. Intervention studies were included: randomized clinical trials, cluster and quasi-experimental studies. The outcome evaluated was dengue prevention and control. The evaluation of the methodological quality and the level of evidence of the included studies was carried out. **Results:** 10 studies were included with levels of evidence between 1c and 2dm, corresponding to low- and middle-income countries in Asia and America. The use of didactic aids was evidenced against educational processes, digital tools, and a field of action by nursing was observed, from health education.

**Conclusions:** Health education in scenarios other than clinical ones can favor empowerment by the population to improve health behaviors. On the other hand, the use of electronic tools is of great help in evaluating the effect of an intervention.

### Wolbachia-Virus interactions and arbovirus control through population replacement in mosquitoes.

**Ant TH, Mancini MV, McNamara CJ, Rainey SM, Sinkins SP.**

May 2023

*Pathog Glob Health.*

<https://pubmed.ncbi.nlm.nih.gov/36205550/>

### 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/>

This century has introduced very deadly, dangerous, and infectious diseases to humankind such as the influenza virus, Ebola virus, Zika virus, and the most infectious SARS-CoV-2 commonly known as COVID-19 and have caused epidemics and pandemics across the globe. For some of these diseases, proper medications, and vaccinations are

missing and the early detection of these viruses will be critical to saving the patients. And even the vaccines are available for COVID-19, the new variants of COVID-19 such as Delta, and Omicron are spreading at large. The available virus detection techniques take a long time, are costly, and complex and some of them generates false negative or false positive that might cost patients their lives. The biosensor technique is one of the best qualified to address this difficult challenge. In this systematic review, we have summarized recent advancements in biosensor-based detection of these pandemic viruses including COVID-19. Biosensors are emerging as efficient and economical analytical diagnostic instruments for early-stage illness detection. They are highly suitable for applications related to healthcare, wearable electronics, safety, environment, military, and agriculture. We strongly believe that these insights will aid in the study and development of a new generation of adaptable virus biosensors for fellow researchers.

### Comprehensive Molecular Interaction Studies to Construe the Repellent/Kill Activity of Geraniol During Binding Event Against Aedes aegypti Proteins.

**Setlur AS, K C, Pandey S, Sarkar M, Niranjana V.**

May-2023

*Mol Biotechnol.*

<https://pubmed.ncbi.nlm.nih.gov/36169809/>

*Aedes aegypti* is an etiological agent for dengue, chikungunya, Zika, and yellow fever viruses. With the advent of the use of natural alternatives as repellents, their precise mode of action during the event of binding is still unclear. Geraniol is one such bioactive natural that has been previously shown to have some insecticide properties. Thus, the present study aimed to understand the mechanism of the binding event of geraniol with the whole proteome of *A. aegypti*. Twenty protein target categories were shortlisted for the mosquito, wherein the proteins were downloaded with respect to the reference proteome. Conserved domain analysis was performed for the same using the CDD search tool to find the proteins that have common domains. 309 proteins were modeled using RaptorX standalone tool, and validated using Ramachandran plots from SAVES v6.0 from ProCheck. These modeled and validated proteins were then docked against geraniol, using POAP software, for understanding the binding energies. The top 3 best-docked complexes were then analyzed for their stabilities and event of binding via 100 ns simulation studies using DESMOND's Maestro environment. The docking results showed that the geraniol-voltage-gated sodium channel had the best energy of - 7.1 kcal/mol, followed by geraniol-glutathione-S-transferase (- 6.8 kcal/mol) and geraniol-alpha esterase (- 6.8 kcal/mol). The simulations for these 3 complexes revealed that several residues of the proteins interacted well with geraniol at a molecular level, and all three docked complexes were found to be stable when simulated (RMSD: 16-18 Å, 3.6-4.8 Å, 4.8-5.6 Å, respectively). Thus, the present study provides insights into the mechanism of the binding event of geraniol with the major *A. aegypti* targets, thereby, assisting the use of geraniol as a natural repellent.

## Structures and dynamics of peptide and peptidomimetic inhibitors bound to the NS2B-NS3 protease of the ZIKA virus.

Pant S, Bhattacharya G, Jena NR.

Apt-2023

*J Biomol Struct Dyn.*

<https://pubmed.ncbi.nlm.nih.gov/35238272/>

## Virtual screening of small natural compounds against NS1 protein of DENV, YFV and ZIKV.

de Lima Menezes G, Vogel Saivish M, Lacerda Nogueira M, Alves da Silva R.

Apt-2023

*J Biomol Struct Dyn.*

<https://pubmed.ncbi.nlm.nih.gov/35188085/>

Diseases caused by viruses of the genus *Flavivirus* are among the main diseases that affect the world and they are a serious public health problem. Three of them stand out: Dengue, Yellow fever and Zika viruses. The non-structural protein 1 (NS1), encoded by this viral genus, in its dimeric form, plays important roles in the pathogenesis and RNA replication of these viruses. Therefore, the identification of chemicals with the potential to inhibit the formation of the NS1 protein dimer of DENV, YFV and ZIKV would enable them to act as a multi-target drug. For this, we selected conformations of the NS1 protein monomer with similar  $\beta$ -roll domain structure among the three virus species from conformations obtained from molecular dynamics simulations performed in GROMACS in 5 replicates of 150 ns for each species. After selecting the protein structures, a virtual screening of compounds from the natural products catalog of the ZINC database was performed using AutoDock Vina. The 100 best compounds were classified according efficiency criteria. Two compounds were observed in common to the species, with energy scores ranging from -9.2 kcal/mol to -10.1 kcal/mol. The results obtained here demonstrate the high similarity of NS1 proteins in the *Flavivirus* genus and high affinity for the same compounds; thus justifying the potential of these small molecules act in multitarget therapy. Communicated by Ramaswamy H. Sarma.

## The Public Health Importance of Flaviviruses as an Etiological Environmental Factor in Nonsyndromic Cleft Lip and/or Palate: In silico Study.

Silva KCP, Messias TS, Soares S.

May-2023

*Cleft Palate Craniofac J.*

<https://pubmed.ncbi.nlm.nih.gov/35164580/>

This *in silico* study aims to investigate flaviviruses as an environmental factor in the etiology of nonsyndromic cleft lip and/or palate (CL/P). A scoring method with 7 topics-disease, transplacental passage, tropism, cellular damage, reported case, analysis of genome similarity, and transcriptome between virus and host, was created based on literature and *in silico* experimentation. Viral genomes of NCBI virus were obtained and BLAST 2.12.0 was applied for the similarity analysis, adjusted to search for only

human sequences related to CL/P with the statistical threshold defined for E-value  $\leq 1$ . Flaviviruses with high potential to cause CL/P were: serotypes 2, 3, and 4 of the *Dengue virus* and lineage 2 of the *West Nile virus*, while the *Yellow Fever virus*, *Japanese encephalitis virus*, *Tick-borne encephalitis virus*, and *Saint Louis encephalitis virus* presented with medium potential to cause CL/P. As for the *Zika virus*, even strains associated with microcephaly showed only medium potential. *Dengue virus* and *West Nile virus* presented with high potential to act as environmental factors in the etiology of CL/P.

## Dracunculose

### Histological and molecular insights in to in vitro regeneration pattern of Xanthosoma sagittifolium.

Bansal S, Sharma MK, Singh S, Joshi P, Pathania P, Malhotra EV, Rajkumar S, Misra P.

10-04-2023

*Sci Rep.*

<https://pubmed.ncbi.nlm.nih.gov/37037867/>

A study on the effect of various phytohormonal combinations on in vitro propagation of Cocoyam [*Xanthosoma sagittifolium* (L.) Schott] was conducted to develop an improved and efficient in vitro regeneration protocol for its mass multiplication. Histological analysis to understand the in vitro regeneration pattern and genetic fidelity assessment of regenerated plants were also carried out. Single shoots excised from in vitro established cultures of *X. sagittifolium* were used as explants. Among the 32 different phytohormonal combinations tested, indirect organogenesis with intervening callus phase was observed on majority of the media combinations. Meristematic clump formation was optimally achieved on all the tested media combinations with maximum  $43.54 \pm 0.51$  shoot primordia on MS medium containing 0.2 mg/L BAP + 0.1 mg/L NAA followed by  $36.44 \pm 0.76$  shoot primordia on MS medium having 2.5 mg/L TDZ. Micro-morphological analysis of different morphogenetic structures revealed that the regeneration of cocoyam is well executed via meristematic nodules, shoot primordia formation that may evolve in to proper shoots. Adventitious shoots ( $> 2$  cm) were successfully ( $100.00 \pm 0.00\%$ ) rooted on the half-strength MS medium containing IBA (0.05-1.0 mg/L) and IAA (0.05-0.5 mg/L). The number of roots ranged from  $0.78 \pm 0.31$  on the control half-strength MS medium to  $13.94 \pm 0.46$  on half-strength MS supplemented with 1.0 mg/L IBA. Considering somaclonal variations as a potential restriction to in vitro multiplication of plants, genetic stability was assessed using 40 ISSR primers. The PCR amplification profiles obtained from all the tested propagules (calli, meristematic clumps, regenerated plantlets) were similar to the mother plants indicating the homogeneity of the individuals raised through the regeneration protocol reported here.

### Effects of Abelmoschus manihot gum content, heating temperature and salt ions on the texture and rheology



## properties of konjac gum/*Abelmoschus manihot* gum composite gel.

Li Y, He D, Zheng C, Zhou A, Yi D, Wu Y.

01-05-2023

*Int J Biol Macromol.*

<https://pubmed.ncbi.nlm.nih.gov/36906206/>

## Metabolic flexibility during a trophic transition reveals the phenotypic plasticity of greater duckweed (*Spirodela polyrhiza* 7498).

Sun Z, Zhao X, Li G, Yang J, Chen Y, Xia M, Hwang I, Hou H.

May-2023

*New Phytol.*

<https://pubmed.ncbi.nlm.nih.gov/36856336/>

The greater duckweed (*Spirodela polyrhiza* 7498) exhibits trophic diversity (photoautotrophic, heterotrophic, photoheterotrophic, and mixotrophic growth) depending on the availability of exogenous organic carbon sources and light. Here, we show that the ability to transition between various trophic growth conditions is an advantageous trait, providing great phenotypic plasticity and metabolic flexibility in *S. polyrhiza* 7498. By comparing *S. polyrhiza* 7498 growth characteristics, metabolic acclimation, and cellular ultrastructure across these trophic modes, we show that mixotrophy decreases photosynthetic performance and relieves the CO<sub>2</sub> limitation of photosynthesis by enhancing the CO<sub>2</sub> supply through the active respiration pathway. Proteomic and metabolomic analyses corroborated that *S. polyrhiza* 7498 increases its intracellular CO<sub>2</sub> and decreases reactive oxygen species under mixotrophic and heterotrophic conditions, which substantially suppressed the wasteful photorespiration and oxidative-damage pathways. As a consequence, mixotrophy resulted in a higher biomass yield than the sum of photoautotrophy and heterotrophy. Our work provides a basis for using trophic transitions in *S. polyrhiza* 7498 for the enhanced accumulation of value-added products.

## Echinococcosis

### Pediatric Echinococcosis of the Liver in Austria: Clinical and Therapeutical Considerations.

Hager J, Sergi CM.

04-04-2023

*Diagnostics (Basel).*

<https://pubmed.ncbi.nlm.nih.gov/37046561/>

Echinococcosis is considered a neglected disease in most European countries. However, migratory flows of populations, long-term stays in endemic areas, uninterrupted tourism (travel to *Echinococcus*-endemic countries), traveling dogs and dog translocations from endemic areas, and inappropriate hygiene practices are potential factors that alarm public health officials. Identifying a cyst-like mass in the liver or lung of an individual with a travel history of likely exposure to

sheepdogs in an area where the parasite *Echinococcus* (*E.*) *granulosus* (sive *cysticus*) is endemic advocates for a prompt preliminary diagnosis of cystic echinococcosis (CE), no matter the age of the affected individuals. Routine imaging techniques, including ultrasonography, computed tomography (CT) scans, and magnetic resonance imaging (MRI) scans, are used to detect cysts. After a cyst has been discovered, serologic investigations are used to confirm the diagnosis. Typically, alveolar echinococcosis (AE) is found in older individuals. Yet young people are also affected because frequent oral exploration of the environment is a regular behavior for infants and toddlers. In this review, therapeutic considerations for pediatric echinococcosis-drug-based benzimidazole therapy; AE: atypical liver resection, the resection of individual or multiple segments, a right or left hemi-hepatectomy, or an extended hemi-hepatectomy; CE: PAIR-technique, cyst excision, liver segment(s) resection (laparoscopically or conventionally)-are revised following experience in one of the most affected regions of Europe. In addition, we performed a systematic review using three databases (i.e., PubMed, EMBASE, and Scopus) to evaluate the quality of evidence in published studies on pediatric echinococcosis.

### Cystic Echinococcosis in Northern New Hampshire, USA.

AlSalman A, Mathewson A, Martin IW, Mahatanan R, Talbot EA.

12-04-2023

*Emerg Infect Dis.*

<https://pubmed.ncbi.nlm.nih.gov/37044131/>

### Antigen discovery by bioinformatics analysis and peptide microarray for the diagnosis of cystic echinococcosis.

Batisti Biffignandi G, Vola A, Sassera D, Najafi-Fard S, Gomez Morales MA, Brunetti E, Teggi A, Goletti D, Petrone L, Tamarozzi F.

12-04-2023

*PLoS Negl Trop Dis.*

<https://pubmed.ncbi.nlm.nih.gov/37043489/N>

### A Diverse Virome Is Identified in Parasitic Flatworms of Domestic Animals in Xinjiang, China.

Zhang P, Zhang Y, Cao L, Li J, Wu C, Tian M, Zhang Z, Zhang C, Zhang W, Li Y.

12-04-2023

*Microbiol Spectr.*

<https://pubmed.ncbi.nlm.nih.gov/37042768/>

Parasitic flatworms infect diverse vertebrates and are major threats to animal and even human health; however, little is known about the virome of these lower life forms. Using viral metagenomic sequencing, we characterized the virome of the parasitic flatworms collected from major domestic animals, including *Dicrocoelium lanceatum* and *Taenia hydatigena*, *Echinococcus granulosus sensu stricto* and *Echinococcus multilocularis*. Seven and three different viruses were discovered from *D. lanceatum* and *T. hydatigena*, respectively, and no viral sequences were found in adult tapeworms and protoscoleces of *E.*



*granulosus sensu stricto* and *E. multilocularis*. Two out of the five parasitic flatworm species carry viruses, showing a host specificity of these viruses. These viruses belong to the *Parvoviridae*, *Circoviridae*, unclassified circular, Rep-encoding single-stranded (CRESS) DNA virus, *Rhabdoviridae*, *Endornaviridae*, and unclassified RNA viruses. The presence of multiple highly divergent RNA viruses, especially those that cluster with viruses found in marine animals, implies a deep evolutionary history of parasite-associated viruses. In addition, we found viruses with high identity to common pathogens in dogs, including canine circovirus and canine parvovirus 2. The presence of these viruses in the parasites implies that they may infect parasitic flatworms but does not completely exclude the possibility of contamination from host intestinal contents. Furthermore, we demonstrated that certain viruses, such as CRESS DNA virus may integrate into the genome of their host. Our results expand the knowledge of viral diversity in parasites of important domestic animals, highlighting the need for further investigations of their prevalence among other parasites of key animals. **IMPORTANCE** Characterizing the virome of parasites is important for unveiling the viral diversity, evolution, and ecology and will help to understand the "Russian doll" pattern among viruses, parasites, and host animals. Our data indicate that diverse viruses are present in specific parasitic flatworms, including viruses that may have an ancient evolutionary history and viruses currently circulating in parasite-infected host animals. These data also raise the question of whether parasitic flatworms acquire and/or carry some viruses that may have transmission potential to animals. In addition, through the study of virus-parasite-host interactions, including the influence of viral infection on the life cycle of the parasite, as well as its fitness and pathogenicity to the host, we could find new strategies to prevent and control parasitic diseases.

### Single-Cell RNA Sequencing Reveals Unique Alterations in the Immune Panorama and Treg Subpopulations in Mice during the Late Stages of *Echinococcus granulosus* Infection.

Wu J, Xiao J, Bai M, Shi C, Xin Y, Zhao W, Gao X, Yin M, Zhao J.

11-04-2023

*Infect Immun.*

<https://pubmed.ncbi.nlm.nih.gov/37039643/>

### *Echinococcus* Species Infections among Wild Canids in Pennsylvania, USA.

Garrett K, Brown J, Grunert RKA, Hunte J, Ruder MG, Van Why K, Yabsley MJ, Cleveland CA.

06-04-2023

*J Wildl Dis.*

<https://pubmed.ncbi.nlm.nih.gov/37036486/>

*Echinococcus* species are zoonotic tapeworms that can impact the health of wildlife, domestic animals, livestock, and humans. Two species of interest in North America are *Echinococcus multilocularis* and *Echinococcus canadensis* (*Echinococcus granulosus sensu lato*). The primary wildlife definitive hosts for *E. multilocularis* and *E. canadensis* are

similar, including red foxes (*Vulpes vulpes*), gray foxes (*Urocyon cinereoargenteus*), coyotes (*Canis latrans*), and wolves (*Canis lupus*). These two *Echinococcus* spp. use different intermediate hosts, including small mammals for *E. multilocularis* and artiodactylids for *E. canadensis*. Although historically absent from much of the eastern US, recent reports in new US states (e.g., Virginia, Vermont, Maine, Missouri) highlight the need for *Echinococcus* spp. surveillance in this region. During 2019-2020, 308 gastrointestinal tracts were collected from wild canids in Pennsylvania and microscopically screened for adult *Echinococcus* species. Two coyotes (2/155) were co-infected with both *E. multilocularis* and *E. canadensis* as determined by molecular confirmation. No red foxes (n=137) or gray foxes (n=16) were positive. These data indicate both *Echinococcus* species are present in Pennsylvanian coyotes, highlighting the need to understand the ecological and epidemiological consequences for human and animal health better.

### Transforming growth factor- $\beta$ signalling regulates protoscolex formation in the *Echinococcus multilocularis* metacestode.

Kaethner M, Epping K, Bernthaler P, Rudolf K, Thomann I, Leitschuh N, Bergmann M, Spiliotis M, Koziol U, Brehm K.

22-03-2023

*Front Cell Infect Microbiol.*

<https://pubmed.ncbi.nlm.nih.gov/37033489/>

### Percutaneous management in hepatic alveolar echinococcosis: A sum of single center experiences and a brief overview of the literature.

Eren S, Aydın S, Kantarci M, Kızılgöz V, Levent A, Şenbil DC, Akhan O.

27-03-2023

*World J Gastrointest Surg.*

<https://pubmed.ncbi.nlm.nih.gov/37032805/>

**Background:** Hepatic alveolar echinococcosis (HAE) is a serious zoonotic infection that affects humans. It may have a tumor-like appearance at times. Percutaneous treatment of HAE patients is extremely relaxing for them. HAE is a significant human zoonotic infection caused by the fox tapeworm *Echinococcus Multilocularis* larvae. It possesses the characteristics of an invasive tumor-like lesion due to its infiltrative growth pattern and protracted incubation period. The disease is endemic over central Europe, Asia, and North America. **Aim:** To characterize HAE patients who were treated percutaneously, their outcomes, and the major technical features of percutaneous treatment in HAE. **Methods:** Patients who were treated with percutaneous cyst drainage and/or percutaneous biliary drainage were included in the study. Uncorrected abnormal coagulation values and solid or non-infected HAE with minor necrotic change were excluded. **Results:** Thirty-two patients underwent percutaneous cyst drainage, two patients underwent percutaneous biliary drainage, and four patients underwent percutaneous biliary drainage alone.

Interventional radiology is utilized to drain echinococcal necrosis and abscesses within/without the liver, as well as diseased and clogged bile ducts. **Conclusion:** Percutaneous drainage of cyst contents and/or biliary channels using a minimally invasive technique is a very beneficial. Percutaneous cyst drainage with albendazole therapy improves quality of life in patients who are unable to undergo surgery, even when the mass resolves with long-term treatment.

### Tapeworms detected in wolf populations in Central Italy (Umbria and Marche regions): A long-term study.

**Crotti S, Spina S, Cruciani D, Bonelli P, Felici A, Gavaudan S, Gobbi M, Morandi F, Piseddu T, Torricelli M, Morandi B.**

27-03-2023

*Int J Parasitol Parasites Wildl.*

<https://pubmed.ncbi.nlm.nih.gov/37025622/>

Tapeworms are trophically-transmitted and multi-host parasites with a complex indirect life cycle, strictly depending on predator-prey interactions. Their presence in a free-living population, mainly definitive hosts, is arduous to study due to the complexity of collecting fecal samples. However, epidemiological studies on their frequency are crucial from a public health perspective, providing information on food habits and prey selection of predators. The present study aims to update the frequency of tapeworms detected in stool samples by molecular analysis in Italian wolf populations of Umbria and Marche regions collected from 2014 to 2022. Tapeworm's total frequency was 43.2%. In detail, *Taenia serialis* was detected in 27 samples (21.6%), *T. hydatigena* in 22 (17.6%), and *Mesocestoides corti* (syn. *M. vogae*) in 2 (1.6%). Three samples were identified as *M. litteratus* and *E. granulosus* s.s. (G3) and *T. pisiformis*, with a proportion of 0.8%, respectively. The low frequency of *E. granulosus* in a hyperendemic area is discussed. The results show for the first time a high frequency of *Taenia serialis* not comparable to other Italian studies conducted on wild Carnivora; thus, a new ecological niche is conceivable. These findings suggest a plausible wolf-roe deer cycle for *T. serialis* in the investigated area.

### Update on the genetic diversity and population structure of *Echinococcus granulosus* in Gansu Province, Tibet Autonomous Region, and Xinjiang Uygur Autonomous Region, Western China, inferred from mitochondrial *cox1*, *nad1*, and *nad5* sequences.

**Shumuye NA, Li L, Ohiolei JA, Qurishi SA, Li WH, Zhang NZ, Wu YT, Wu YD, Gao SZ, Zhang FH, Tian XQ, Tian WJ, Fu Y, Wang XZ, Pan YH, Zhan F, Zhang LS, Guo MK, Li WD, Fu BQ, Yan HB, Jia WZ.**

May-2023

*Parasitol Res.*

<https://pubmed.ncbi.nlm.nih.gov/36933066/>

### Increased prevalence of canine echinococcosis a decade after the discontinuation of a governmental deworming program in Tierra del Fuego, Southern Chile.

**Eisenman EJJ, Uhart MM, Kusch A, Vila AR, Vanstreels RET, Mazet JAK, Briceño C.**

May-2023

*Zoonoses Public Health.*

<https://pubmed.ncbi.nlm.nih.gov/36514826/>

Hydatid disease is a neglected zoonotic parasitic disease caused by cysts of the tapeworm *Echinococcus granulosus*. Canids, especially domestic dogs, are definitive hosts of the parasite and are the most pragmatic targets for control programs. A governmental dog deworming campaign was established in 1979 to control hydatidosis in southern Chile, which succeeded in reducing the prevalence of canine echinococcosis in Tierra del Fuego province from 68.4% (in 1978) to 1.2% (in 2002). In 2004, however, the program was dismantled to reduce costs, and since then, no follow-up echinococcosis monitoring has been conducted. We surveyed 356 domestic dogs and interviewed owners or workers at 45 ranches in Chilean Tierra del Fuego during the summer of 2015-2016. Faecal flotation was employed to detect Taeniidae eggs, and PCR was used to test faecal samples for *Echinococcus granulosus*. Taeniidae eggs and *Echinococcus* sp. DNA were detected in the faeces of 45.4% (147/324) and 6.9% (23/331) of dogs, respectively. Infrequent dog deworming and the presence of culpeo foxes (*Lycalopex culpaeus*) were significant predictors of the prevalence of *Echinococcus* sp. DNA and Taeniidae eggs. Furthermore, the presence of introduced chilla foxes (*Lycalopex griseus*), the municipality, and several operational characteristics of ranches (number of sheep, frequency of sheep slaughter, number of dogs, frequency of removal of dog faeces, feeding of dogs with sheep viscera) were also predictive of the prevalence of Taeniidae eggs. Our findings reveal an ongoing risk of echinococcosis with pathogen maintenance in ranch dogs in Chilean Tierra del Fuego, and in the absence of adequate control programmes, there is a tangible risk of re-emergence of hydatid disease as a public health concern.

### Filariose lymphatique

### Immunophenotypic and Functional Characterization of Eosinophil and Migratory Dendritic Cell Subsets during Filarial Manifestation of Tropical Pulmonary Eosinophilia.

**Ganga L, Sharma P, Tiwari S, Satoeya N, Jha R, Srivastava M.**

11-04-2023

*ACS Infect Dis.*

<https://pubmed.ncbi.nlm.nih.gov/37040430/>

### Chemical constituents and strong larvicidal activity of *Solanum*

## xanthocarpum among selected plants extracts against the malaria, filaria, and dengue vectors.

Kumar P, Shakya R, Kumar V, Kumar D, Chauhan R, Singh H.

Jan-Mar 2023

*J Vector Borne Dis.*

<https://pubmed.ncbi.nlm.nih.gov/37026216/>

**Background & objectives:** The role of mosquitoes is instrumental in the transmission of various diseases. Mosquito-borne diseases account for a significant share of the global burden of total infectious diseases. Vector control is the principal method for the control of these mosquito-borne diseases. Plant-derived insecticides serve as an effective alternative to chemical insecticides. The present study has been undertaken to assess the larvicidal potential of methanol and petroleum ether extracts of leaves of *Solanum xanthocarpum*, *Parthenium hysterophorus*, *Manihot esculenta*, and *Chamaecyparis obtusa*. **Methods:** Larvicidal activity was tested against the early four-stage instar larvae of laboratory-reared susceptible strains of the malaria vector, *Anopheles stephensi*, dengue fever vector, *Aedes aegypti*, and the lymphatic filariasis vector, *Culex quinquefasciatus* at 20 to 120 ppm concentrations. Further, liquid chromatography-mass spectrometry (LC-MS) and gas chromatography-mass spectroscopy (GC-MS) analyses were carried out to identify the bioactive compounds present in the methanolic leaf extracts of *Solanum xanthocarpum* for designing a larvicidal product in future. **Results:** After 72 h of exposure high larvicidal activities were observed in methanolic and petroleum ether leaves extract of *S. xanthocarpum* against *An. stephensi*, *Ae. aegypti* and *Cx. quinquefasciatus*. The larvicidal activities for methanol and petroleum ether leaf extract of *S. xanthocarpum* with  $LC_{50}$  = 09.201 and 12.435 ppm and  $LC_{90}$  = 21.578 and 27.418 ppm for *An. stephensi*;  $LC_{50}$  = 11.450 and 10.026 ppm and  $LC_{90}$  = 26.328 and 22.632 ppm for *Ae. aegypti* and  $LC_{50}$  = 12.962 and 13.325 ppm and  $LC_{90}$  = 26.731 and 30.409 ppm for *Cx. quinquefasciatus*, respectively, were found to be most effective. GC-MS analysis revealed 43 compounds, amongst these phytol (13.09%), 3-allyl-2-methoxy phenol (9.55%), (9Z, 12Z)-9, 12-octadecadienoyl chloride (7.93%), linoleic acid (5.45%), alpha-tocospiro B (5.08%) and hexadecanoic acid (4.35%) were identified as major compounds. **Interpretation & conclusion:** Present work showed that leaf extracts of *S. xanthocarpum* are a source of potential natural candidate that possess several phytochemicals which can be explored further for the development of ecologically safer mosquito control products.

## Coverage of mass drug administration (MDA) and operational issues in elimination of lymphatic filariasis in selected districts of Jharkhand, India.

Kumar D, Kumar A, Vikas K, Kumar C, Sircar S.

Jan-2023

*J Family Med Prim Care.*

<https://pubmed.ncbi.nlm.nih.gov/37025230/>

**Background:** Despite annual rounds of mass drug administration (MDA) being carried out every year since 2004 to break the transmission of lymphatic filariasis, India has not achieved elimination status in many areas of country. This study was conducted to determine the operational issues in the implementation of MDA for elimination of lymphatic filariasis in selected districts of Jharkhand. **Methods:** Two districts of Jharkhand state were selected for present cross-sectional study. Multi-staged cluster sampling was adopted to select study participants. Data were collected with use of prescribed questionnaire of National Vector Borne Disease Control Programme (NVBDCP) from the study participants. Data related to socio-demographic details, coverage and compliance of MDA and operational issues were collected. **Results:** Findings of independent assessment show that percentage of MDA coverage and compliance for Hazaribag district was 96.02% and 88.90%, respectively. On the other hand, percentage of MDA coverage and compliance was found to be only 67.06% and 48.44% in Chatra district. Overall drug consumption was significantly associated with age group (p-value = 0.045), educational status (p-value = <0.0001) and socio-economic status (p-value <0.0001) of eligible population. Most common reason for not swallowing the drugs was found to be absence of family members at the time of MDA rounds followed by no visit of house by drug distributors. **Conclusions:** Coverage and compliance of MDA was better in Hazaribag district as compared to Chatra district. In order to increase compliance, socio-demographic factors must also be addressed apart from other operational issues.

---

## Gale

### Current status of mites and mite-borne diseases in India.

Govindarajan R, Rajamannar V, Kumar A, Samuel PP.

Jan-Mar 2023

*J Vector Borne Dis.*

<https://pubmed.ncbi.nlm.nih.gov/37026214/>

Mites act as the vectors of zoonotic vector-borne disease scrub typhus caused by the rickettsial pathogen *Orientia tsutsugamushi*. In India, scrub typhus is transmitted by the mite *Leptotrombidium deliense*. Rodents are the reservoirs and support the spread of this disease. *Sarcoptes scabiei* or the itch mite is causing scabies which is a common skin infection in India. Dermatitis, trombiculosis, and mite dust allergy are common mite-borne diseases transmitted by Pyemotidae family. *D. brevis* folliculorum and *Demodex brevis* are two major mite species found on humans also causing a disease; "Demodicosis", common in India. *Dermanyssus gallinae*, fowl mite causes pruritis in poultry birds, transmits infections to poultry workers when they come into contact with birds. There is a re-emergence of mite-borne diseases, especially scrub typhus, in many parts of India requiring urgent attention for its control. This review is aimed to update the available information on mites and mite transmitted diseases prevalent in India to highlight

the importance of rodent and chigger mite vector control to prevent forthcoming mite-borne diseases in India.

## Helminthiasis transmits par le sol (ascaridiose, trichuriase, ankylostomiase)

**The first study on the prevalence of gastrointestinal parasites in owned and sheltered cats in Yangon, Myanmar.**

Soe BK, Hlaing KS, Naing TW, Thaw ZH, Myint AW.

Feb-2023

*Vet World.*

<https://pubmed.ncbi.nlm.nih.gov/37041997/>

**Background and aim:** People who used to rear companion animals are healthier than others who do not. Gastrointestinal (GI) helminths are common in cats and serve as reservoirs for zoonotic diseases. However, the prevalence of GI parasites in cats in Myanmar has never been reported. This study aimed to estimate the prevalence of GI parasites in cats in Myanmar and to identify the potential risk factors associated with GI parasites. **Materials and methods:** A total of 230 fecal samples were collected from seven veterinary clinics and two shelters within the Yangon region from January to May 2022. Sampled cats were classified according to age, gender, and the deworming and rearing practices. Fecal samples were analyzed by fecal wet mount, ethyl acetate centrifugal sedimentation, and zinc sulfate centrifugal flotation techniques. Descriptive data were described, and Pearson's  $\chi^2$  test was used to identify associated risk factors, such as age, gender, and the deworming and rearing practices. **Results:** The overall prevalence of GI parasites was 79.56%, and 57.82% of cats were infected with a diagnostic stage of more than one parasite species. Seven GI parasites were detected, including *Ancylostoma* spp. (55.65%), *Toxocara* spp. (46.08%), *Trichuris* spp. (20.86%), *Platynosomum* spp. (11.73%), *Dipylidium caninum* (7.39%), *Taenia* spp. (4.34%), and *Cystoisospora* spp. (32.17%). Based on statistical analysis, the deworming and rearing practices were significantly associated ( $p < 0.05$ ) with GI parasitic infections. **Conclusion:** This study is the first to reveal the prevalence of GI parasites that could assist the need for effective control measures for zoonotic hookworm and roundworm infections in cats. Even with simple microscopic examination, the remarkably high prevalence of GI parasitic infections warrants regular deworming practice. Further molecular studies should also be performed to understand their genetic diversity.

## Leishmaniose

**Comprehensive proteomic analysis of autophagosomes derived from Leishmania-infected macrophages.**

Nandan D, Chen E, Chang F, Moon KM, Foster LJ, Reiner N.

07-04-2023

*PLoS One.*

<https://pubmed.ncbi.nlm.nih.gov/37027358/>

**Expression profile in Leishmania major exposed to Staphylococcus aureus and group A beta-hemolytic Streptococcus.**

Bafghi AF, Eslami G, Ajamein V, Barzegar K, Vakili M.

Jan-Mar 2023

*J Vector Borne Dis.*

<https://pubmed.ncbi.nlm.nih.gov/37026217/>

**Background & objectives:** The interaction of *Leishmania* spp. with microbiota inside the midgut vector has significant output in pathogenesis. This study aimed to identify the profile of *Leishmania* major gene expression of LACK, gp63, and hsp70 after exposure to *Staphylococcus aureus* and group A beta-hemolytic *Streptococcus* (GABHS). **Methods:** *Leishmania* major (MRHO/IR/75/ER) promastigotes were exposed with *S. aureus*, with GABHS, and with both GABHS and *S. aureus* at 25°C for 72 h. The gene expression analysis of Lmpgp63, Lmhsp70, and LmLACK was assessed using SYBR Green real-time PCR by  $\Delta\Delta Ct$ . All experiments were repeated in triplicate. Statistical analysis was done using two-way ANOVA. A P-value less than 0.05 was considered significant. **Results:** Lmpgp63 was expressed in the group exposed to GABHS with 1.75-fold lower than the control group ( $p=0.000$ ). The LmLACK had expression in both groups exposed with GABHS and GABHS with *S. aureus* with 2.8 and 1.33-fold more than the control group, respectively ( $p=0.000$ ). The Lmhsp70 gene expression was reported in the group exposed with GABHS with relative quantification of 5.7-fold more than the control group. **Interpretation & conclusion:** This study showed that the important genes encoding LACK, gp63, and hsp70 changed their expression after exposure to the *S. aureus* and GABHS.

**Leishmania donovani 6-phosphogluconolactonase: Crucial for growth and host infection?**

Paul A, Roy PK, Babu NK, Dhumal TT, Singh S.

May-2023

*Microb Pathog.*

<https://pubmed.ncbi.nlm.nih.gov/36958644/>

The hexose monophosphate shunt is a crucial pathway in a variety of microorganisms owing to its vital metabolic products and intermediates such as NADPH, ribose 5-phosphate etc. The enzyme 6-phosphogluconolactonase catalyzes the second step of this pathway, converting 6-phosphogluconolactone to 6-phosphogluconic acid. This enzyme has been known to have a significant involvement in growth, pathogenesis and sensitivity to oxidative stress in bacterial and protozoal pathogens. However, the functional role of kinetoplastid *Leishmania donovani* 6-phosphogluconolactonase (Ld6PGL) remains unexplored. *L. donovani* is the second largest parasitic killer and causative organism of life threatening visceral leishmaniasis. To understand its possible functional role in the parasite, the alleles of Ld6PGL were sequentially knocked-out followed by gene complementation. The Ld6PGL mutant cell lines showed decrease in



transcriptional and translational expression as well as in the enzyme activity. In case of Ld6PGL null mutants, approximately 2-fold reduction was observed in growth. The null mutants also showed ~38% decrease in infectivity, which recovered to ~15% on complementation. Scanning electron microscopy showed a marked decrease in flagellar length in the knockout parasites. When treated with the standard drug miltefosine, the mutant strains had no significant change in the drug sensitivity. However, the Ld6PGL mutants were more susceptible to oxidative stress. Our findings suggest that 6PGL is required for parasite growth and infection, but it is not essential.

### **ITS1 and cpb genetic polymorphisms in Algerian and Tunisian Leishmania infantum isolates from humans and dogs.**

**Benikhlef R, Chaouch M, Abid MB, Aoun K, Harrat Z, Bouratbine A, BenAbderrazak S.**

May-2023

*Zoonoses Public Health.*

<https://pubmed.ncbi.nlm.nih.gov/36443904/>

### **Detection of Leishmania (Mundinia) macropodum (Kinetoplastida: Trypanosomatidae) and heterologous Leishmania species antibodies among blood donors in a region of Australia with marsupial Leishmania endemicity.**

**Panahi E, Stanicic DI, Skinner EB, Faddy HM, Young MK, Herrero LJ.**

May-2023

*Int J Infect Dis.*

<https://pubmed.ncbi.nlm.nih.gov/36241162/>

**Objectives:** The Australian Leishmania (Mundinia) macropodum parasite causes cutaneous leishmaniasis among marsupial species. Although cutaneous leishmaniasis is a major public health burden worldwide, it is not clear if humans are naturally exposed to the unique L. macropodum. To assess whether humans have an immunoglobulin (Ig) G response to L. macropodum, we examined anti-Leishmania antibodies among humans residing in a region of marsupial Leishmania endemicity in Australia. **Methods:** Using a serological enzyme-linked immunosorbent assay, we characterized Leishmania-specific IgG and IgG subclass responses to soluble Leishmania antigen from L. macropodum, and other Leishmania species (L. donovani, L. major, and L. mexicana) in 282 blood donor samples. **Results:** We found that 20.57% of individuals demonstrated a positive total IgG response to L. macropodum. For individuals with antibodies to soluble Leishmania antigen from one Leishmania species, there was no increased likelihood of recognition to other Leishmania species. For samples with detectable L. macropodum IgG, IgG1 and IgG2 were the prevalent subclasses detected. **Conclusion:** It is not yet clear whether the IgG antibody detection in this study reflects exposure to Leishmania parasites or a cross-reactive immune response that was induced against an unrelated immunogen. Future studies should investigate

whether L. macropodum can result in a viable infection in humans.

### **Biodiversity and vector-borne diseases: Host dilution and vector amplification occur simultaneously for Amazonian leishmaniases.**

**Kocher A, Cornuault J, Gantier JC, Manzi S, Chavy A, Girod R, Dusfour I, Forget PM, Ginouves M, Prévot G, Guégan JF, Bañuls AL, de Thoisy B, Murienne J.**

Apr-2023

*Mol Ecol.*

<https://pubmed.ncbi.nlm.nih.gov/35000240/>

### **Experimental feeding of Sergentomyia minuta on reptiles and mammals: comparison with Phlebotomus papatasi.**

**Ticha L, Volfova V, Mendoza-Roldan JA, Bezerra-Santos MA, Maia C, Sadlova J, Otranto D, Volf P.**

13-04-2023

*Parasit Vectors.*

<https://pubmed.ncbi.nlm.nih.gov/37055860/>

**Background:** *Sergentomyia minuta* (Diptera: Phlebotominae) is an abundant sand fly species in the Mediterranean basin and a proven vector of reptile parasite *Leishmania* (*Sauroleishmania*) *tarentolae*. Although it feeds preferentially on reptiles, blood meal analyses and detection of *Leishmania* (*Leishmania*) *infantum* DNA in wild-caught *S. minuta* suggest that occasional feeding may occur on mammals, including humans. Therefore, it is currently suspected as a potential vector of human pathogens. **Methods:** A recently established *S. minuta* colony was allowed to feed on three reptile species (i.e. lizard *Podarcis siculus* and geckos *Tarentola mauritanica* and *Hemidactylus turcicus*) and three mammal species (i.e. mouse, rabbit and human). Sand fly mortality and fecundity were studied in blood-fed females, and the results were compared with *Phlebotomus papatasi*, vector of *Leishmania* (*L.*) *major*. Blood meal volumes were measured by haemoglobinometry. **Results:** *Sergentomyia minuta* fed readily on three reptile species tested, neglected the mouse and the rabbit but took a blood meal on human. However, the percentage of females engorged on human volunteer was low in cage (3%) and feeding on human blood resulted in extended defecation times, higher post-feeding mortality and lower fecundity. The average volumes of blood ingested by females fed on human and gecko were 0.97 µl and 1.02 µl, respectively. *Phlebotomus papatasi* females readily fed on mouse, rabbit and human volunteer; a lower percentage of females (23%) took blood meal on the *T. mauritanica* gecko; reptilian blood increased mortality post-feeding but did not affect *P. papatasi* fecundity. **Conclusions:** Anthropophilic behaviour of *S. minuta* was experimentally demonstrated; although sand fly females prefer reptiles as hosts, they were attracted to the human volunteer and took a relatively high volume of blood. Their feeding times were longer than in sand fly species regularly feeding on mammals and their physiological parameters suggest that *S. minuta* is not adapted well for digestion of mammalian blood.



Nevertheless, the ability to bite humans highlights the necessity of further studies on *S. minuta* vector competence to elucidate its potential role in circulation of Leishmania and phleboviruses pathogenic to humans.

### **Molecular detection of Wolbachia and Bartonella as part of the microbiome of phlebotomine sand flies from Chiapas, Mexico.**

**Lozano-Sardaneta YN, Marina CF, Torres-Monzón JA, Sánchez-Cordero V, Becker I.**

14-04-2023

*Parasitol Res.*

<https://pubmed.ncbi.nlm.nih.gov/37055642/>

### **Elucidation of conserved multi-epitope vaccine against Leishmania donovani using reverse vaccinology.**

**Dikhit MR, Sen A.**

13-04-2023

*J Biomol Struct Dyn.*

<https://pubmed.ncbi.nlm.nih.gov/37054523/>

### **Evaluation of expression variations in virulence-related genes of Leishmania major after several culture passages compared with Phlebotomus papatasi isolated promastigotes.**

**Nemati Haravani T, Parvizi P, Hejazi SH, Sedaghat MM, Eskandarian A, Nateghi Rostami M.**

13-04-2023

*PLoS One.*

<https://pubmed.ncbi.nlm.nih.gov/37053214/>

Cutaneous leishmaniasis (CL) is a prevalent infectious disease with considerable morbidity annually. Here, we aimed to investigate the likely variations in gene expression of glycoprotein63 (gp63), heat shock protein 70 (HSP70), histone, arginase, cysteine protease B (CPB), Leishmania homologue of receptors for activated C kinase (LACK), small hydrophilic endoplasmic reticulum-associated protein (SHERP) in metacyclic promastigotes of *L. major* isolated from *Phlebotomus papatasi* sand flies and promastigotes excessively cultured in culture medium. The parasites were collected from suspected CL cases in Pasteur Institute of Iran, cultured and inoculated into the female BALB/c mice (2×10<sup>6</sup> promastigotes). Sand flies were trapped in Qom province, fed with the blood of euthanized infected mice and subsequently dissected in order to isolate the midgut including stomodeal valve. The metacyclic promastigotes were isolated from *Ph. papatasi* (Pro-Ppap) using peanut agglutinin test (PNA), then continuously cultured in RPMI-1640 medium enriched with fetal bovine serum, penicillin (100 U/ml) and streptomycin (100 mg/ml) to reach stationary phase (Pro-Stat). The gene expression was evaluated in both parasitic stages (Pro-Ppap and Pro-Stat) using qRT-PCR. Out results showed a significant increased gene expression at Pro-Ppap stage for gp63 ( $P = 0.002$ ), SHERP ( $P = 0.001$ ) and histone ( $P = 0.026$ ) genes, in comparison with Pro-Stat stage. Noticeably, significant changes were, also, demonstrated in 10th to 15th passages [gp63 ( $P = 0.041$ ),

arginase ( $P = 0.016$ ), LACK ( $P = 0.025$ )] and in 5th to 20th passage (SHERP) ( $P = 0.029$ ). In conclusion, the findings of the present study seem to be essential in designing Leishmania studies, in particular regarding host-parasite interaction, immunization and infectivity studies.

### **A review of nemorosone: Chemistry and biological properties.**

**Cuesta-Rubio O, Monzote L, Fernández-Acosta R, Pardo-Andreu GL, Rastrelli L.**

10-04-2023

*Phytochemistry.*

<https://pubmed.ncbi.nlm.nih.gov/37044362/>

Nemorosone is a bicyclic polyprenylated acylphloroglucinol derivative originally isolated from *Clusia* spp. and it can be obtained through chemical synthesis employing different synthetic strategies. Since its discovery, it has attracted great attention both from a biological and chemical viewpoint. In the present article, we attempted to review various chemical and biological topics around nemorosone, with an emphasis on its antiproliferative activities. For this purpose, relevant data was collected from different scientific databases including Google Scholar, PubMed, Scopus and ISI Web of Knowledge. This natural compound has shown activity against several types of malignancies such as leukemia, human colorectal, pancreatic, and breast cancer because it modulates multiple molecular pathways. Nemorosone has both cytostatic and cytotoxic activity and it also seems to induce apoptosis and ferroptosis. Additionally, it has antimicrobial capabilities against Gram-positive bacteria and parasites belonging to genus *Leishmania*. Its promising antiproliferative pre-clinical effects deserve further attention for anticancer and anti-parasitic drug development and translation to the clinic.

### **Cloning, expression and in vitro validation of chimeric multi epitope vaccine candidate against visceral leishmaniasis infection.**

**Ojha R, Chand K, Vellingiri B, Prajapati VK.**

10-04-2023

*Life Sci.*

<https://pubmed.ncbi.nlm.nih.gov/37044174/>

### **Diversity and temporal distribution of sand flies in an endemic area of cutaneous leishmaniasis in Centre-West Colombia.**

**Posada-López L, Galvis-Ovallos F, Vélez-Mira A, Vélez ID, Galati EAB.**

12-04-2023

*J Med Entomol.*

<https://pubmed.ncbi.nlm.nih.gov/37043628/>

The community structure of sand flies indicates the level of adaptation of vector species in a region, and in the context of vector management and control, this information allows for identifying the potential risks of pathogen transmission. This study aimed to analyze sand fly diversity and spatial-temporal distribution in an

endemic area of cutaneous leishmaniasis. The study was carried out in the Carrizales hamlet (Caldas), between September 2019 and October 2021. The monthly distribution of sand fly species was evaluated through collections with CDC traps. Shannon and evenness indices were calculated and used to compare species frequencies at each house. The association between climatic variables and the frequency of sand flies was evaluated using Spearman's correlation. A total of 6,265 females and 1,958 males belonging to 23 species were found. Low diversity and evenness were observed, with the dominance of *Nyssomyia yuilli yuilli* (Young & Porter). Ecological and diversity indices did not reveal differences between the houses. The sand fly community was composed of 3 dominant species, *Ny. yuilli yuilli*, *Psychodopygus ayrozai* (Barretto & Coutinho), and *Ps. panamensis* (Shannon), representing 75.8% of the total catches. No statistical association was found between the absolute frequency of sand flies, rainfall, and temperature. The results show one dominant species, this fact has epidemiological relevance since density influences parasite-vector contact. The high densities of sand flies recorded in peri- and intradomiciliary areas highlight the necessity of periodic monitoring of vector populations and control activities to reduce the risk of *Leishmania* transmission in this endemic area.

### Genomic analysis of two phlebotomine sand fly vectors of leishmania from the new and old World.

Labbé F, Abdeladhim M, Abrudan J, Araki AS, Araujo RN, Arensburger P, Benoit JB, Brazil RP, Bruno RV, Bueno da Silva Rivas G, Carvalho de Abreu V, Charamis J, Coutinho-Abreu IV, da Costa-Latgé SG, Darby A, Dillon VM, Emrich SJ, Fernandez-Medina D, Figueiredo Gontijo N, Flanley CM, Gatherer D, Genta FA, Gesing S, Giraldo-Calderón GI, Gomes B, Aguiar ERGR, Hamilton JGC, Hamarsheh O, Hawksworth M, Hendershot JM, Hickner PV, Imler JL, Ioannidis P, Jennings EC, Kamhawi S, Karageorgiou C, Kennedy RC, Krueger A, Latorre-Estivalis JM, Ligoxygakis P, Meireles-Filho ACA, Minx P, Miranda JC, Montague MJ, Nowling RJ, Oliveira F, Ortigão-Farias J, Pavan MG, Horacio Pereira M, Nobrega Pitaluga A, Proveti Olmo R, Ramalho-Ortigao M, Ribeiro JMC, Rosendale AJ, Sant'Anna MRV, Scherer SE, Secundino NFC, Shoue DA, da Silva Moraes C, Gesto JSM, Souza NA, Syed Z, Tadros S, Teles-de-Freitas R, Telleria EL, Tomlinson C, Traub-Csekö YM, Marques JT, Tu Z, Unger MF, Valenzuela J, Ferreira FV, de Oliveira KPV, Vigoder FM, Vontas J, Wang L, Weedall GD, Zhioua E, Richards S, Warren WC, Waterhouse RM, Dillon RJ, McDowell MA.

12-04-2023

*PLoS Negl Trop Dis.*

<https://pubmed.ncbi.nlm.nih.gov/37043542/>

### A pediatric case of disseminated American cutaneous leishmaniasis in Rio de Janeiro, Brazil.

Barbosa SM, De Alencar AG, Braga RM, Destefani CA, Vilar EG.

15-02-2023

*Dermatol Online J.*

<https://pubmed.ncbi.nlm.nih.gov/37040907/>

### Drugs and nanoformulations for the management of Leishmania infection: a patent and literature review (2015-2022).

Verdan M, Taveira I, Lima F, Abreu F, Nico D.

12-04-2023

*Expert Opin Ther Pat.*

<https://pubmed.ncbi.nlm.nih.gov/37038719/>

### Bioecological Study on the Sand Flies (Diptera: Psychodidae, Phlebotominae) in Sari County, North of Iran.

Hosseini-Vasoukolaei N, Ghavibazou L, Akhavan AA, Enayati AA, Jahanifard E, Fazeli-Dinan M, Yazdani-Charati J, Nikookar SH, Saeidi Z, Shemshadian A.

30-06-2023

*J Arthropod Borne Dis.*

<https://pubmed.ncbi.nlm.nih.gov/37038510/>

### PCR Positivity of Gerbils and Their Ectoparasites for Leishmania Spp. in a Hyperendemic Focus of Zoonotic Cutaneous Leishmaniasis in Central Iran.

Azarmi S, Zahraei-Ramazani A, Mohebbali M, Rassi Y, Akhavan AA, Azarm A, Dehghan O, Elikaee S, Abdoli R, Mahmoudi M.

30-06-2023

*J Arthropod Borne Dis.*

<https://pubmed.ncbi.nlm.nih.gov/37038507/>

**Background:** Various arthropods, including *Rhipicephalus sanguineus* and *Ctenocephalides felis felis* have been suggested as secondary vectors of *Leishmania* spp. many years ago. This study was conducted to determine zoonotic cutaneous leishmaniasis (ZCL) PCR positivity of reservoir hosts and their ectoparasites for *Leishmania* spp. in Segzi plain in Esfahan Province from October 2016 to October 2017. **Methods:** Microscopic examination and nested PCR were used to detect and identify *Leishmania* spp. isolated from rodents' ears and ectoparasites, and then, the results were confirmed by two methods, PCR-restriction fragment length polymorphism and sequencing. **Results:** Totally, 93 rodents (92 *Rhombomys opimus* and one *Nesokia indica*) and nine different species of ectoparasites (n=527) including fleas, mites, and ticks were collected during different seasons in the study area. Fourteen *R. opimus* were positive for *Leishmania* spp. by microscopic examination while one *N. indica* and 77 *R. opimus* were positive by nested PCR. The infection rate of rodents with *Leishmania major* and *Leishmania turanica* was 39.79% (n=37) and 15.05% (n=14), respectively. Mixed natural infections with *L. major* and *L. turanica* were seen in rodents. Moreover, 72.22% of fleas (39/54), 75.0% of mites (5/8), and 100% of tick nymph (1/1) were PCR positive for *Leishmania* parasites. **Conclusions:** The highest rate of infection with *L. major* and *L. turanica* in *R. opimus* populations was observed in summer and spring, respectively. It is suggested that the role of *L. turanica* and the probable role of ectoparasites in the epidemiology of

disease should be investigated. A Xenodiagnostic test is recommended for future study.

### Genetic diversity and haplotype analysis of *Leishmania tropica* identified in sand fly vectors of the genera *Phlebotomus* and *Sergentomyia* using next-generation sequencing technology.

Al-Jawabreh A, Ereqat S, Al-Jawabreh H, Dumaidi K, Nasereddin A.

10-04-2023

*Parasitol Res.*

<https://pubmed.ncbi.nlm.nih.gov/37036520/>

Next-generation sequencing (NGS) was used to investigate the genetic diversity of *Leishmania tropica* in the sand fly vector, targeting the internal transcribed spacer 1 (ITS1) of the genus *Leishmania*. Bioinformatics analyses were conducted using Galaxy, MEGA version X, DnaSP ver. 6.12.03, and PopART 1.7 software for NGS analysis, phylogenetic tree, genetic diversity, and haplotype networking, respectively. A total of 307 engorged sand flies were trapped, with an overall *Leishmania* infection rate of 9.4 (29/307) and 6.8% by NGS and ITS1-PCR, respectively. Two *Leishmania*-infected sand fly genera were identified: *Phlebotomus* (10.2%, 26/254) and *Sergentomyia* (5.7% (3/53)). The phylogenetic tree showed two clusters, cluster I included the four study sequences along with 25 GenBank-retrieved DNA sequences. Cluster II consisted of three sequences from Iran and Pakistan. The genetic diversity analysis for the 29 *L. tropica* sequences showed high haplotype (gene) diversity index (Hd) ( $0.62 \pm 0.07$ ) but low nucleotide diversity index ( $\pi$ ) ( $0.04 \pm 0.01$ ). Tajima's D, a neutrality test, is more negative in cluster I ( $D = -2.0$ ) than in total population ( $D = -1.83$ ), but both are equally significant ( $P < 0.001$ ), indicating that observed variation in cluster I and whole population is less frequent than expected. The median-joining haplotype network produced a total of 11 active haplotypes. In conclusion, *L. tropica* from sand flies in Palestine is monophyletic that assembled in one main phylogroup and one haplotype.

### A single-set functional training program increases muscle power, improves functional fitness, and reduces pro-inflammatory cytokines in postmenopausal women: A randomized clinical trial.

Rocha JNS, Vasconcelos ABS, Aragão-Santos JC, de Resende-Neto AG, Monteiro MRP, Nogueira AC, Cardoso AP, Corrêa CB, de Moura TR, Da Silva-Grigoletto ME.

22-03-2023

*Front Physiol.*

<https://pubmed.ncbi.nlm.nih.gov/37035659/>

### Unwinding the mechanism of macrophage repolarization potential of *Oceanimonas* sp. BPMS22-derived protein protease inhibitor through Toll-like receptor 4 against experimental visceral leishmaniasis.

Jayaraman A, Srinivasan S, Uppuluri KB, Kar Mahapatra S.

22-03-2023

*Front Cell Infect Microbiol.*

<https://pubmed.ncbi.nlm.nih.gov/37033485/>

The *Oceanimonas* sp. BPMS22-derived protein protease inhibitor (PPI) has been proven to shift macrophages towards an inflammatory state and reduce *Leishmania donovani* infection *in vitro* and *in vivo*. The current study explored and validated the mechanistic aspects of the PPI and Toll-like receptor (TLR) interaction. The PPI exhibited the upregulation of TLR2, TLR4, and TLR6 during treatment which was proven to orchestrate parasite clearance effectively. An *in silico* study confirmed the high interaction with TLR4 and PPI. Immune blotting confirmed the significant upregulation of TLR4 in macrophages irrespective of *L. donovani* infection. Pharmacological inhibition and immune blot study confirmed the involvement of the PPI in TLR4-mediated phosphorylation of p38 MAPK and dephosphorylation of ERK1/2, repolarizing to pro-inflammatory macrophage state against experimental visceral leishmaniasis. In addition, in TLR4 knockdown condition, PPI treatment failed to diminish M2 phenotypical markers (CD68, Fizz1, Ym1, CD206, and MSR-2) and anti-inflammatory cytokines (IL-4, IL-10, and TGF- $\beta$ ). Simultaneously, the PPI failed to upregulate the M1 phenotypical markers and pro-inflammatory cytokines (IL-1 $\beta$ , IL-6, IL-12, and IFN- $\gamma$ ) ( $p < 0.001$ ) during the TLR4 knockdown condition. In the absence of TLR4, the PPI also failed to reduce the parasite load and T-cell proliferation and impaired the delayed-type hypersensitivity response. The absence of pro-inflammatory cytokines was observed during a co-culture study with PPI-treated macrophages (in the TLR4 knockdown condition) with day 10 T-cell obtained from *L. donovani*-infected mice. This study supports the immunotherapeutic potential of the PPI as it interacted with TLR4 and promoted macrophage repolarization (M2-M1) to restrict the *L. donovani* parasite burden and helps in the mounting immune response against experimental visceral leishmaniasis.

### Modulating leishmanial pteridine metabolism machinery via some new coumarin-1,2,3-triazoles: Design, synthesis and computational studies.

Hassan NW, Sabt A, El-Attar MAZ, Ora M, Bekhit AEA, Amagase K, Bekhit AA, Belal ASF, Elzahhar PA.

05-04-2023

*Eur J Med Chem.*

<https://pubmed.ncbi.nlm.nih.gov/37031526/>

In accordance with WHO statistics, leishmaniasis is one of the top neglected tropical diseases, affecting around 700 000 to one million people per year. To that end, a new series of coumarin-1,2,3-triazole hybrid compounds was designed and synthesized. All new compounds exerted higher activity than miltefosine against *L. major* promastigotes and amastigotes. Seven compounds showed single digit micromolar  $IC_{50}$  values whereas three compounds (13c, 14b and 14c) displayed submicromolar potencies. A mechanistic study to elucidate the antifolate-dependent activity of these compounds revealed that folic

and folinic acids abrogated their antileishmanial effects. These compounds exhibited high safety margins in normal VERO cells, expressed as high selectivity indices. Docking simulation studies on the folate pathway enzymes pteridine reductase and DHFR-TS imparted strong theoretical support to the observed biological activities. Besides, docking experiments on human DHFR revealed minimal binding interactions thereby highlighting the selectivity of these compounds. Predicted in silico physicochemical and pharmacokinetic parameters were adequate. In view of this, the structural characteristics of these compounds demonstrated their suitability as antileishmanial lead compounds.

### TLR9 agonist CpG ODN 2395 promotes the immune response against *Leishmania donovani* in obesity and undernutrition mice.

He J, Huang F, Liao X, Zhang J, Wei S, Xiao Y, Zheng X, Zhu Z, Chen D, Chen J.

06-04-2023

*Acta Trop.*

<https://pubmed.ncbi.nlm.nih.gov/37030488/>

### Urinary cystatin C and N-acetyl-beta-D-glucosaminidase (NAG) as early biomarkers for renal disease in dogs with leishmaniosis.

Ruiz P, Durán Á, Duque FJ, González MA, Cristóbal JI, Nicolás P, Pérez-Merino EM, Macías-García B, Barrera R.

06-04-2023

*Vet Parasitol.*

<https://pubmed.ncbi.nlm.nih.gov/37030024/>

Canine leishmaniasis (CanL) is a disease caused by *Leishmania infantum* that can vary from a subclinical infection to a severe disease. Dogs affected with CanL present varying degrees of renal dysfunction. Unfortunately, traditional biomarkers such as urea and creatinine detect renal damage in advanced stages of the disease, so more accurate biomarkers are needed. Hence, we aimed to study how urinary cystatin C (CysC) and N-acetyl-beta-D-glucosaminidase (NAG), behave in dogs with CanL at different stages of the disease. Eighty-six CanL infected dogs were classified according to LeishVet stages: LI (16 dogs), LIIa (12 dogs), LIIb (12 dogs), LIII (16 dogs) and LIV (30 dogs); as a control, 17 healthy dogs were studied. Blood samples were collected for complete haematological and biochemistry analysis including plasma cystatin C. Urine analysis included urine specific gravity (USG), urine protein to creatinine ratio (UPC), CysC and NAG expressed as a ratio with creatinine uCysCc ( $\mu\text{g/g}$ ) and uNAGc (IU/g). The haematological, biochemical and urinary analysis coincided with the LeishVet guidelines. The statistical study of the uCysCc ratio and the uNAGc, showed significant increase when compared against control starting from group LI ( $p < 0.05$ ). Interestingly, when the cut-off values were calculated using the ROC curve, uCysCc ( $258.85 \mu\text{g/g}$ ) and uNAGc ( $2.25 \text{ IU/g}$ ) 75 % of the dogs included in LI groups surpassed the threshold. Hence our study indicates that uCysCc and uNAGc, could help to detect early renal damage in CanL affected dogs.

## Lèpre

### Little Doctors: Agents of change in Indian rural communities.

Premkumar K, Ramasamy R, Ramasamy M, Aiyer H.

13-04-2023

*Med Teach.*

<https://pubmed.ncbi.nlm.nih.gov/37053445/>.

### Oral *Candida* colonization and antifungal susceptibility pattern in patients with hematological malignancy.

Talebshoushtari Zadeh M, Lotfali E, Fattahi M, Abolgasemi S.

Sep-2022

*Curr Med Mycol.*

<https://pubmed.ncbi.nlm.nih.gov/37051553/>

**Background and purpose:** Candidiasis is regarded as one of the most important fungal infections and a cause of disease and mortality in patients with hematological malignancy. Accordingly, antifungal prophylaxis is of significant importance in this regard. This study aimed to identify the epidemiology of *Candida* colonization and evaluate its antifungal susceptibility pattern in patients with hematological malignancy. **Materials and methods:** In this study, the samples were collected from the oral cavity of 100 patients, and *Candida* colonization was confirmed by fungal culture. *Candida* strains were also identified by ITS-PCR. *In vitro* antifungal susceptibility tests against fluconazole, amphotericin B, and caspofungin were performed according to CLSI M60. **Results:** Demographic characteristics, comorbidities, distribution of *Candida* species (spp.), and antifungal susceptibility were analyzed in this study. The study participants included 100 patients with a mean age of  $15.48 \pm 48.74$  years (age range: 17-84 years). Regarding gender distribution, the majority (64%) of the patients were male. In terms of the distribution of underlying hematologic malignancy, 27% of the cases had lymphoma. The most commonly isolated species among patients were *C. albicans* complex (49%;  $n=49$ ), *C. glabrata* (39%;  $n=39$ ), and co-colonization of *C. albicans* complex and *C. glabrata* (10%;  $n=10$ ). The overall resistance of *C. albicans* complex was 5% to fluconazole ( $n=5$ ) and 2% to amphotericin B ( $n=2$ ). Furthermore, *C. glabrata* showed 11% ( $n=11$ ) resistance to fluconazole and was susceptible to amphotericin B. All *Candida* spp. isolated from patients who were susceptible to caspofungin. **Conclusion:** The high rate of colonization of *Candida* spp., especially the significant increase in the frequency of *C. glabrata* in patients with blood malignancies and the gradual increase in resistance to fluconazole, necessitate a change in the use of antifungal drugs for the prevention and experimental treatment of hematological malignancy.

### *Mycobacterium leprae* and host immune transcriptomic signatures for reactional states in leprosy.

Das M, David D, Horo I, Van Hooij A, Tió-Coma M, Geluk A, Vedithi SC.



27-03-2023

*Front Microbiol.*

<https://pubmed.ncbi.nlm.nih.gov/37051521/>

**Background:** *Mycobacterium leprae* transcriptomic and human host immune gene expression signatures that demonstrate a plausible association with type I (T1R) and type II reactions (T2R) aid in early diagnosis, prevention of nerve damage and consequent demyelinating neuropathy in leprosy. The aim of the study is to identify *M. leprae* and host-associated gene-expression signatures that are associated with reactional states in leprosy. **Methods:** The differentially expressed genes from the whole transcriptome of *M. leprae* were determined using genome-wide hybridization arrays with RNA extracted from skin biopsies of 20 T1R, 20 T2R and 20 non reactional controls (NR). Additionally, human immune gene-expressions were profiled using RT2-PCR profiler arrays and real-time qPCRs. **Results:** The RNA quality was optimal in 16 NR, 18 T1R and 19 T2R samples. Whole transcriptome expression array of these samples revealed significant upregulation of the genes that encode integral and intrinsic membrane proteins, hydrolases and oxidoreductases. In T1R lesional skin biopsy specimens, the top 10 significantly upregulated genes are ML2064, ML1271, ML1960, ML1220, ML2498, ML1996, ML2388, ML0429, ML2030 and ML0224 in comparison to NR. In T2R, genes ML2498, ML1526, ML0394, ML1960, ML2388, ML0429, ML0281, ML1847, ML1618 and ML1271 were significantly upregulated. We noted ML2664 was significantly upregulated in T1R and repressed in T2R. Conversely, we have not noted any genes upregulated in T2R and repressed in T1R. In both T1R and T2R, ML2388 was significantly upregulated. This gene encodes a probable membrane protein and epitope prediction using Bepipred-2.0 revealed a distinct B-cell epitope. Overexpression of ML2388 was noted consistently across the reaction samples. From the host immune gene expression profiles, genes for CXCL9, CXCL10, CXCL2, CD40LG, IL17A and CXCL11 were upregulated in T1R when compared to the NR. In T2R, CXCL10, CXCL11, CXCL9, CXCL2 and CD40LG were upregulated when compared to the NR group. **Conclusion:** A gene set signature involving bacterial genes ML2388, ML2664, and host immune genes CXCL10 and IL-17A can be transcriptomic markers for reactional states in leprosy.

### **Histopathological analysis revealed that *Mycobacterium abscessus* proliferates in the fat bodies of silkworms.**

**Matsumoto Y, Fukano H, Katano H, Hoshino Y, Sugita T.**

12-04-2023

*Drug Discov Ther.*

<https://pubmed.ncbi.nlm.nih.gov/37045782/>

### **Capecitabine-induced palmo-plantar erythrodysesthesia (toxic erythema of chemotherapy).**

**Pugalia N, Singh R, Madke B, Rusia K, Jaiswal S.**

15-02-2023

*Dermatol Online J.*

<https://pubmed.ncbi.nlm.nih.gov/37040922/>

### **Qua vadis leprosy?**

**Daniel E, Ebenezer GJ.**

Jan-2023

*Indian J Med Res.*

<https://pubmed.ncbi.nlm.nih.gov/37040221/>

### **Global leprosy scenario: Eradication, elimination or control?**

**Gupte M.**

Jan-2023

*Indian J Med Res.*

<https://pubmed.ncbi.nlm.nih.gov/37040220/>

### **Clinico-Epidemiological profile of new leprosy cases detected in leprosy case detection campaign in North Maharashtra during 2018-2020.**

**Surywanshi SP, Lokhande GS.**

Jan-Mar 2022

*Indian J Public Health.*

<https://pubmed.ncbi.nlm.nih.gov/37039221/>

Leprosy is a leading cause of disability in India. The percentage of disability and deformity can be reduced by diagnosing leprosy at an early stage. In order to detect the hidden leprosy cases, leprosy case detection campaigns, on line with Pulse Polio Campaign have been introduced specifically for high endemic districts, by the Central Leprosy Division. Records of cases from 2018 to 2020 were evaluated retrospectively to study the trend of new cases. The present study denotes the presence of hidden undiagnosed cases in the community and will require an intensification of leprosy control activities through contact tracing and active case detection. Continued quality surveillance is required for early detection, timely management, and prevention of the spread of the disease.

### **Spatial Modeling of leprosy disease in east java province with spatially varying regression coefficients models.**

**Chotimah H, N Mindra Jaya IG.**

Oct-Dec 2022

*Indian J Public Health.*

<https://pubmed.ncbi.nlm.nih.gov/37039182/>

Indonesia ranks third with the most leprosy cases globally. East Java is the province that has the highest leprosy cases. The Provincial Government socialized the East Java Leprosy Eradication Program, which targets a maximum of one leprosy case per 10,000 residents. We propose spatially varying regression coefficients models to evaluate the effects of risk factors on of leprosy cases in East Java, use Geographically Weighted Generalized Poisson Regression and Geographically Weighted Negative Binomial Regression (GWNBR) models. The best models GWNBR categorize municipalities into six groups based on variables that have a significant impact on leprosy cases. The percentage of households with access to adequate sanitation is a significant factor in determining leprosy cases in all municipalities in East Java. We can conclude that clean and healthy living behavior, health



facilities, and health workers significantly affect the number of leprosy cases in East Java.

### Looking back to move forward: A travel rule underlined by the current pandemic.

Panda S.

Oct-Dec 2022

*Indian J Public Health.*

<https://pubmed.ncbi.nlm.nih.gov/37039163/>

### Efficacy of Fractional CO<sub>2</sub> Laser for Improvement of Limited Mouth Opening in Systemic Sclerosis.

Bhat YJ, Bashir Y, Latif I, Daing A, Devi R, Shah IH, Akhtar S, Rather S, Nabi N, Saqib NU.

Oct-Dec 2022

*J Cutan Aesthet Surg.*

<https://pubmed.ncbi.nlm.nih.gov/37035592/>

### Ichthyosis Follicularis with Alopecia and Photophobia Syndrome with Coexisting Palmoplantar Keratoderma Treated with Acitretin.

Rajesh S, Loganathan E, Shanmukhappa AG.

Nov-Dec 2022

*Int J Trichology.*

<https://pubmed.ncbi.nlm.nih.gov/37034548/>

Ichthyosis follicularis with alopecia and photophobia (IFAP) syndrome is a rare congenital genetic disorder characterized clinically by a triad of follicular ichthyosis, alopecia and photophobia. The genetic inheritance pattern in IFAP syndrome is said to be X-linked with mutations of the membrane-bound transcription factor peptidase, site 2 gene. Histopathology of the skin shows dilated hair follicles with keratin plugs extending above the surface of the skin. In this case report, we describe a 6-year-old girl with clinical features of IFAP along with palmoplantar keratoderma. Skin biopsy was done to confirm the diagnosis after which she was started on acitretin (10 mg per day). Good improvement in cutaneous features was observed after 1 month.

### Psoriasiform Drug Eruption to Finasteride: Uncommon Side Effect of a Commonly Used Drug.

Muddebihal A, Khurana A, Kulhari A, Ahuja A.

Nov-Dec 2022

*Int J Trichology.*

<https://pubmed.ncbi.nlm.nih.gov/37034544/>

### Targeting dormant phenotype acquired mycobacteria using natural products by exploring its important targets: In vitro and in silico studies.

Sharma S, Chikhale R, Shinde N, Khan AM, Gupta VK.

24-03-2023

*Front Cell Infect Microbiol.*

<https://pubmed.ncbi.nlm.nih.gov/37033483/>

The dormant phenotype of *Mycobacterium tuberculosis* that develops during infection poses a major challenge in disease treatment, since these bacilli show tolerance to front-line drugs. An *in vitro* hypoxia dormancy model was established, which produced phenotypically dormant *Mycobacterium smegmatis* after prolonged incubation under conditions of low oxygen, low pH, and nutrient limitation. Bacilli in this model displayed the classical dormancy characters, including loss of acid fastness, altered morphology, and, most importantly, tolerance to front-line drugs. The dormant form of *M. smegmatis* was treated with drugs and phytochemicals. Three phytochemicals exhibited activity against dormant bacilli, as shown by lack of regrowth in solid and liquid media. Further investigation of dormancy-active hits was carried out using *in silico* approaches to understand the druggable targets of these phytochemicals in dormant bacilli. For this study, molecular docking, molecular dynamics simulations (MDS), and molecular mechanics-generalized born solvent accessibility (MM-GBSA)-based binding energy ( $\Delta G_{\text{bind}}$ ) calculations were performed. Five different targets, namely, isocitrate lyase (ICL), GMP synthase, LuxR, DosR, and serine/threonine protein kinase (STPK), from *M. smegmatis* and *M. tuberculosis* were studied in details. DosR and STPK were found to be the common targets in both the species that were more prone to the phytochemicals. The standard DosR inhibitor, HC104A, showed a lower dock score and binding energy of -4.27 and -34.50 kcal/mol, respectively, compared to the natural products under study. The phytochemical, icariin, showed better docking score (dock score = -5.92 kcal/mol with and binding energy  $\Delta G_{\text{bind}}$  = -52.96 kcal/mol) with DosR compared to known DosR inhibitor, HC104A (dock score = -4.27 kcal/mol and binding energy  $\Delta G_{\text{bind}}$  = -34.50 kcal/mol). Similarly, the known STPK inhibitor MRCT67127 showed a lower dock score and binding energy of -4.25 and -29.43 kcal/mol, respectively, compared to the phytochemical, icariin (dock score = -5.74 kcal/mol and  $\Delta G_{\text{bind}}$  = -43.41 kcal/mol). These compounds might ultimately lead to new therapeutics or may be useful as adjuvants to the first-line drugs to reduce the lengthy anti-TB therapy in the future.

### Severity grading of dermatological emergencies based on comorbidities and systemic involvement: An observational study.

Kedia A, Ranugha PSS, Chethana GS, Kanthraj GR.

08-04-2023

*Arch Dermatol Res.*

<https://pubmed.ncbi.nlm.nih.gov/37031345/>

Dermatological emergency is defined as any urgent/immediate care. Dermatological conditions compromise about 5-8% of all cases presenting to the emergency department. A grading system can help dermatologist's and allied medical personnel to triage a patient accordingly. Currently no severity grading for dermatological emergencies is available. All patients seen in OPD for dermatological consultations requiring urgent interventions were included. Detailed history and clinical examination were done. Patients were assessed according to the onset, symptoms, distribution, examination, body

surface area percentage and mucosal involvement. The severity was graded separately based on comorbidities and systemic involvement. Grade I was no comorbidity or systemic involvement. Grade II was 1 comorbidity or systemic involvement. Grade III was 2 comorbidities or systemic involvement. Grade IV was > 2 comorbidities or multiorgan involvement. Interesting emergency cases observed in Covid period were noted. There were 202 cases, the most common age group was 19-64 (69.8%). Male (49%) and females (51%) had equal preponderance. Most common emergency was acute urticaria with or without angioedema (25.24%). There were 113 (55.94%) inpatients and 89 (44.05%) were outpatients. Acute on chronic onset (34.5%), pain (41.6%), vesicles (30.1%), erosion (23.9%), ulcers (9.7%) and more than 50% body surface area involvement (64.6%) were seen more in admitted cases. Grade I was most common for both comorbidities and systemic involvement. However, grades II, III and IV were higher in admitted cases for both grading systems. The presence of comorbidities and systemic involvement increases the severity of dermatological emergency. Six patients had relapse. Seven patients had methotrexate toxicity. The proposed grading system based on comorbidities and systemic involvement helps to assess the severity of dermatological emergencies.

### **Concurrent acute generalized exanthematous pustulosis in siblings.**

**Pareek S, Mohta A, Ghiya BC, Kumar Y.**

07-04-2023

*Pediatr Dermatol.*

<https://pubmed.ncbi.nlm.nih.gov/37029098/>

### **Actinic Lichen Planus: Significance of Dermoscopic Assessment.**

**Singh R, Jawade S, Madke B.**

03-03-2023

*Cureus.*

<https://pubmed.ncbi.nlm.nih.gov/37025742/>

Actinic lichen planus (LP) is a rare variant of the already infrequent LP. LP is a chronic inflammatory skin disorder seen in 1-2% population of the world. The classical presentation is in the form of the four P's namely pruritic, purplish, polygonal, papules and plaques. On the contrary in this variant of actinic LP, although the lesions look similar in appearance they are characteristically distributed over the photo-exposed areas of the body like the face, extensors of the upper limbs, and dorsum of hands. Koebner's phenomenon which is characteristic of LP is absent. The commonest differentials that leave the clinician in a fix are usually discoid lupus erythematosus, granuloma annulare, and polymorphous light eruptions. A detailed clinical history followed by histopathological examination aids in the final diagnosis in such cases. In scenarios where the patient is not willing for a minor interventional procedure such as a punch biopsy, dermoscopic assessment comes to the rescue. Dermoscopy being an inexpensive, non-invasive, and minimal time-consuming procedure helps in the early diagnosis of a wide range of cutaneous disorders. Fine, reticulate white streaks over the surface of papules or

plaques of LP known as "Wickham's striae" act as the diagnosis clincher for most cases of LP. The numerous variants of LP have consistent biopsy findings and the mainstay for treatment remains topical or systemic corticosteroids. We report this case of a 50-year-old female farmer that presented with multiple violaceous plaques on photo-exposed areas of the body owing to its rarity and use of dermoscopy in enabling a prompt diagnosis that helped improve the patient's quality of life.

### **Availability of Laboratory Diagnosis of Gonorrhoea and Its Meaning in Case Reporting in Shandong Province, China.**

**Chen X, Gan Y, Liu D.**

31-03-2023

*Clin Cosmet Investig Dermatol.*

<https://pubmed.ncbi.nlm.nih.gov/37025397/>

### **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/>

### **Allele-dependent interaction of LRRK2 and NOD2 in leprosy.**

**Dallmann-Sauer M, Xu YZ, da Costa ALF, Tao S, Gomes TA, Prata RBDS, Correa-Macedo W, Manry J, Alcais A, Abel L, Cobat A, Fava VM, Pinheiro RO, Lara FA, Probst CM, Mira MT, Schurr E.**

27-03-2023

*PLoS Pathog.*

<https://pubmed.ncbi.nlm.nih.gov/36972292/>

Leprosy, caused by *Mycobacterium leprae*, rarely affects children younger than 5 years. Here, we studied a multiplex leprosy family that included monozygotic twins aged 22 months suffering from paucibacillary leprosy. Whole genome sequencing identified three amino acid mutations previously associated with Crohn's disease and Parkinson's disease as candidate variants for early onset leprosy: LRRK2 N551K, R1398H and NOD2 R702W. In genome-edited macrophages, we demonstrated that cells expressing the LRRK2 mutations displayed reduced apoptosis activity following mycobacterial challenge independently of NOD2. However, employing co-immunoprecipitation and confocal microscopy we showed that LRRK2 and NOD2 proteins interacted in RAW cells and monocyte-derived macrophages, and that this interaction was substantially reduced for the NOD2 R702W mutation. Moreover, we observed a joint effect of LRRK2 and NOD2 variants on *Bacillus Calmette-Guérin* (BCG)-induced respiratory burst, NF- $\kappa$ B activation and cytokine/chemokine secretion with a strong impact for the genotypes found in the twins consistent with a role of the identified mutations in the development of early onset leprosy.

### Not all black fungus is mucormycosis: A challenging case of *Medicopsis romeroi*.

Bhardwaj N, Parvathy N, Kaur H, Handa S, Srinivasan R.  
May-2023

*Cytopathology*.

<https://pubmed.ncbi.nlm.nih.gov/36648323/>

---

## Morsures de serpent

### Point-of-care ultrasound assessment of a swollen limb following snakebite envenomation - an adjunct to avoid fasciotomy.

Smit A, Laloo V, Engelbrecht A, Mashego LD, Monzon BI.  
Mar-2023

*S Afr J Surg*.

<https://pubmed.ncbi.nlm.nih.gov/37052284/>

Acute limb compartment syndrome can occur with cytotoxic snake envenomation. Ultrasound (US) assessment of the affected limb has been suggested as an adjunct to the administration of snakebite polyvalent antivenom to ameliorate the systemic and local effects. US may also aid in the diagnosis of compartment syndrome and the need for fasciotomy to prevent limb loss. This report presents an adult male who had severe soft tissue swelling from a puff adder bite to the wrist and highlights the use of US in assessing and monitoring the degree of swelling in subcutaneous and fascial compartments of the arm. This US monitoring in conjunction with frequent physical examination avoided the need for a fasciotomy and its attendant morbidity, resulting in complete resolution of the swelling and full recovery of limb function.

### Stomach content analysis of young Russell's oarfish (*Regalecus russelii*) from Taiwan, and a report on an unusual case of predation.

Huang SP, Shao KT.

23-09-2022

*Zootaxa*.

<https://pubmed.ncbi.nlm.nih.gov/37045185/>

### Snakebite Induced Cerebral Venous Sinus Thrombosis: A Case Report.

Yousaf M, Khan QA, Anthony MR, Badshah A, Abdi P, Farkouh C, Hadi FA, Jan R, Khan A, Iram S.

03-04-2023

*Clin Med Insights Case Rep*.

<https://pubmed.ncbi.nlm.nih.gov/37033678/>

**Introduction:** Cerebral venous sinus thrombosis (CVST) is a rare but highly fatal neurological condition mostly caused by prothrombotic conditions like antiphospholipid syndrome, factor V Leiden, and G20210A prothrombin polymorphism. Snake bites are a rare cause of cerebral venous sinus thrombosis that must be recognized and treated promptly to improve survival. **Case presentation:** We present a case of a 25-year-old male who developed headaches and seizures following a Viper snake bite. The

diagnosis was made based on a magnetic resonance venogram (MRV) showing transverse sinus thrombosis with sigmoid sinus stenosis. Initially, the patient was treated with antivenom and supportive treatment for disseminated intravascular coagulation (DIC). After the diagnosis of CVST, the patient was treated with rivaroxaban and levetiracetam. The patient improved within 1 week of treatment and was advised to follow up in 3 months. **Conclusion:** A high index of suspicion for cerebral venous sinus thrombosis is required if the patient presents with headaches, seizures, or abnormal vision following a snake bite. Early diagnosis and management can prevent further neurological damage.

### Development of sandwich ELISA and lateral flow assay for the detection of *Bungarus multicinctus* venom.

Nong JF, Huang Z, Huang ZZ, Yang J, Li JC, Yang F, Huang DL, Wang F, Wang W.

30-03-2023

*PLoS Negl Trop Dis*.

<https://pubmed.ncbi.nlm.nih.gov/36996245/>

Snakebite envenoming adversely affects human health and life worldwide. Presently, no suitable diagnostic tools for snakebite envenoming are available in China. Therefore, we sought to develop reliable diagnostic tests for snakebite management. We conducted affinity purification experiments to prepare species-specific antivenom antibody (SSAb). In brief, affinity chromatography with an antibody purification column (Protein A) was conducted to purify immunoglobulin G from *Bungarus multicinctus* (BM) venom hyperimmunized rabbit serum. The cross-reactive antibodies were removed from commercial BM antivenin by immune adsorption on the affinity chromatography columns of the other three venoms, *Bungarus fasciatus* (FS), *Naja atra* (NA), and *O. hannah* (OH), generating SSAb. The results of western blot analysis and enzyme-linked immunosorbent assay (ELISA) showed the high specificity of the prepared SSAb. The obtained antibodies were then applied to ELISA and lateral flow assay (LFA) to detect BM venom. The resulting ELISA and LFA could specifically and rapidly detect BM venom in various samples with the limits of quantification as 0.1 and 1 ng/ml, respectively. This method could effectively detect snake venom in experimentally envenomed rats (simulating human envenomation), which could distinguish positive and negative samples within 10-15 min. This method also showed promise in serving as a highly useful tool for a rapid clinical distinguishing of BM bites and rational use of antivenom in emergency centers. The study also revealed cross-reactivity between BM and heterogenous venoms, suggesting that they shared common epitopes, which is of great significance for developing detection methods for venoms of the snakes belonging to the same family.

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

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

Mar-2023

### Characterizing and applying immunoglobulins in snakebite diagnostics: A simple and rapid venom detection assay for four medically important snake species in Southeast Asia.

Lee LP, Tan CH, Khomvilai S, Sitprija V, Chaiyabutr N, Tan KY.

01-05-2023

Int J Biol Macromol.

<https://pubmed.ncbi.nlm.nih.gov/36863668/>

Snakebite envenoming is a medical emergency requiring urgent and specific treatment. Unfortunately, snakebite diagnostics are scarce, time-consuming and lacking specificity. Hence, this study aimed to develop a simple, quick and specific snakebite diagnostic assay using animal antibodies. Anti-venom horse immunoglobulin G (IgG) and chicken immunoglobulin Y (IgY) were produced against the venoms of four major medically important snake species in Southeast Asia, i.e., the Monocled Cobra (*Naja kaouthia*), Malayan Krait (*Bungarus candidus*), Malayan Pit Viper (*Calloselasma rhodostoma*), and White-lipped Green Pit Viper (*Trimeresurus albolabris*). Different capture:detection configurations of double-antibody sandwich enzyme-linked immunosorbent assay (ELISA) were constructed using both immunoglobulins, and the horse IgG:IgG-HRP configuration was found to be most selective and sensitive in detecting the corresponding venoms. The method was further streamlined to develop a rapid immunodetection assay, which is able to produce a visual color change within 30 min for discrimination between different snake species. The study shows it is feasible to develop a simple, quick and specific immunodiagnostic assay using horse IgG, which can be derived directly from antisera prepared for antivenom production. The proof-of-concept indicates it is a sustainable and affordable approach in keeping with ongoing antivenom manufacturing activities for specific species in the region.

---

## Pian

### Treponemal Antibody Seroprevalence Using a Multiplex Bead Assay from Samples Collected during the 2018 Nigeria HIV/AIDS Indicator and Impact Survey: Searching for Yaws in Nigeria.

Guagliardo SAJ, Parameswaran N, Agala N, Abubakar A, Cooley G, Ye T, Kamb M, Mba N, William N, Greby S, Iriemenam N, Alagi M, Okoye M, Martin D.

10-04-2023

Am J Trop Med Hyg.

<https://pubmed.ncbi.nlm.nih.gov/37037444/>

Yaws is a chronic, relapsing disease of skin, bone, and cartilage caused by *Treponema pallidum* subsp. *pertenue*. Yaws was last reported in Nigeria in 1996, although neighboring countries have recently reported cases. We

investigated serological evidence for yaws among children aged 0-14 years in Nigeria by measuring antibodies to the treponemal antigens rp17 and TmpA in blood specimens from a 2018 nationally representative HIV survey using a multiplex bead assay. The presence of antibodies to both antigens ("double positive") likely reflects current or recent treponemal infection. Overall, 1.9% (610/31,549) of children had anti-TmpA antibodies, 1.5% (476/31,549) had anti-rp17 antibodies, and 0.1% (39/31,549) were double positive. Among households, 0.5% (84/18,021) had a double-positive child, with a clustering of double-positive children. Although numbers are low, identification of antibodies to both TmpA and rp17 may warrant investigation, including more granular epidemiologic and clinical data, to assess the potential for continuing yaws transmission in Nigerian children.

---

## Rage

### "Self-inactivating" rabies viruses are susceptible to loss of their intended attenuating modification.

Jin L, Matsuyama M, Sullivan HA, Zhu M, Lavin TK, Hou Y, Lea NE, Pruner MT, Dam Ferdínez ML, Wickersham IR.

14-02-2023

Proc Natl Acad Sci U S A.

<https://pubmed.ncbi.nlm.nih.gov/37053554/>

### Seroprevalence of and Risk Factors for *Toxoplasma gondii* Infection in Cats from Greece.

Kokkinaki KCG, Saridomichelakis MN, Mylonakis ME, Leontides L, Xenoulis PG.

26-03-2023

Animals (Basel).

<https://pubmed.ncbi.nlm.nih.gov/37048429/>

Toxoplasmosis is one of the most important protozoan diseases with a global impact on the health of domestic cats and with zoonotic significance. The aims of this study were to determine the prevalence of seropositivity for *Toxoplasma gondii* in different populations of cats in Greece and to assess risk factors for seropositivity. A total of 457 cats were prospectively enrolled, and a commercially available indirect immunofluorescence antibody testing (IFAT) kit was used for the detection of anti-*T. gondii* immunoglobulin G (IgG) in serum. Overall, 95 (20.8%) of the 457 cats were seropositive for *T. gondii*. Based on multivariate analysis, factors associated with seropositivity included older age [Odds ratio (OR), 1.33;  $p < 0.001$ ]; a history of cat-fight trauma (OR, 3.88;  $p = 0.004$ ); and lack of vaccination against calicivirus, herpesvirus-1, panleukopenia, and rabies (OR, 10;  $p = 0.002$ ). This study shows a high prevalence of seropositivity for *T. gondii* in cats in Greece. This implies that toxoplasmosis is still a major public health concern and that optimal strategies for the prevention of infection with *T. gondii* in cats should be established.



## Evaluation of Dynamics, Demography and Estimation of Free-Roaming Dog Population in Herat City, Afghanistan.

Nasiry Z, Mazlan M, Noordin MM, Mohd Lila MA.

23-03-2023

*Animals (Basel).*

<https://pubmed.ncbi.nlm.nih.gov/37048382/>

FRDs pose a serious challenge in countries where dog-bite-related rabies is endemic. Understanding the size and core demographic characteristics of FRD populations is essential for the planning and implementation of effective dog-population and canine-rabies-control programmes. The photographic sight-resight method was used to estimate the FRD population and evaluate its demographic characteristics in Herat city. A total of 928 free-roaming dogs (FRD) were identified through 3172 sightings, and the total free-roaming population was estimated to amount to 1821 (95% CI: 1565-2077), which led to the estimation of 10 dogs/km<sup>2</sup> and the human-to-FRD ratio of 315:1. The male-to-female ratio was 2.85:1. The majority of them were healthy, with an ideal body score. Although the FRD density is considered low, it is still a concern and significant, since the majority of the people are unaware of the importance of canine populations in the transmission of zoonotic diseases such as rabies, and there were no specific measures for managing and controlling FRD populations. The information gained can be useful in animal health planning to design effective dog-population-control programmes, and for the planning of national rabies-prevention programmes.

## Households' Practices towards Rabies Prevention and Control in Rural Nepal.

Dhakal A, Ghimire RP, Regmi S, Kaple K.

06-04-2023

*Int J Environ Res Public Health.*

<https://pubmed.ncbi.nlm.nih.gov/37048041/>

## Morphogenesis of Bullet-Shaped Rabies Virus Particles Regulated by TSG101.

Itakura Y, Tabata K, Saito T, Intaruck K, Kawaguchi N, Kishimoto M, Torii S, Kobayashi S, Ito N, Harada M, Inoue S, Maeda K, Takada A, Hall WW, Orba Y, Sawa H, Sasaki M.

12-04-2023

*J Virol.*

<https://pubmed.ncbi.nlm.nih.gov/37042780/>

Viral protein assembly and virion budding are tightly regulated to enable the proper formation of progeny virions. At this late stage in the virus life cycle, some enveloped viruses take advantage of the host endosomal sorting complex required for transport (ESCRT) machinery, which contributes to the physiological functions of membrane modulation and abscission. Bullet-shaped viral particles are unique morphological characteristics of rhabdoviruses; however, the involvement of host factors in rhabdovirus infection and, specifically, the molecular mechanisms underlying virion formation are not fully understood. In the present study, we used a small interfering RNA (siRNA) screening approach and found

that the ESCRT-I component TSG101 contributes to the propagation of rabies virus (RABV). We demonstrated that the matrix protein (M) of RABV interacts with TSG101 via the late domain containing the PY and YL motifs, which are conserved in various viral proteins. Loss of the YL motif in the RABV M or the downregulation of host TSG101 expression resulted in the intracellular aggregation of viral proteins and abnormal virus particle formation, indicating a defect in the RABV assembly and budding processes. These results indicate that the interaction of the RABV M and TSG101 is pivotal for not only the efficient budding of progeny RABV from infected cells but also for the bullet-shaped virion morphology. **IMPORTANCE** Enveloped viruses bud from cells with the host lipid bilayer. Generally, the membrane modulation and abscission are mediated by host ESCRT complexes. Some enveloped viruses utilize their late (L-) domain to interact with ESCRTs, which promotes viral budding. Rhabdoviruses form characteristic bullet-shaped enveloped virions, but the underlying molecular mechanisms involved remain elusive. Here, we showed that TSG101, one of the ESCRT components, supports rabies virus (RABV) budding and proliferation. TSG101 interacted with RABV matrix protein via the L-domain, and the absence of this interaction resulted in intracellular virion accumulation and distortion of the morphology of progeny virions. Our study reveals that virion formation of RABV is highly regulated by TSG101 and the virus matrix protein.

## United Against Rabies Forum: The first 2 years.

Tidman R, Fahrion AS, Thumbi SM, Wallace RM, De Balogh K, Iwar V, Yale G, Dieuzy-Labaye I.

23-03-2023

*Front Public Health.*

<https://pubmed.ncbi.nlm.nih.gov/37033019/>

Rabies continues to kill an estimated 59,000 people annually, with up to 99% of human cases transmitted by domestic dogs. The elimination of human deaths from dog-mediated rabies is achievable by applying a One Health approach, and the framework to do this is outlined in Zero by 30: the Global Strategic Plan to end human deaths from dog-mediated rabies by 2030. To build on this global goal, and implement the approaches set out in Zero by 30, the United Against Rabies Forum was launched in 2020. This paper gives a review of the objectives, governance, activities and achievements of the United Against Rabies Forum to date. It also outlines ongoing work, and next steps as the United Against Rabies Forum reviews its first 2 years of activities and identifies priority areas for the coming 12 months.

## Mapping rabies in China: a geospatial analysis of national surveillance data.

Li H, Li Y, Chen Y, Chen B, Su Q, Hu Y, Xiong C.

06-04-2023

*Int J Infect Dis.*

<https://pubmed.ncbi.nlm.nih.gov/37030651/>

**Viral vectored vaccines: design, development, preventive and**



## therapeutic applications in human diseases.

Wang S, Liang B, Wang W, Li L, Feng N, Zhao Y, Wang T, Yan F, Yang S, Xia X.

07-04-2023

*Signal Transduct Target Ther.*

<https://pubmed.ncbi.nlm.nih.gov/37029123/>

Human diseases, particularly infectious diseases and cancers, pose unprecedented challenges to public health security and the global economy. The development and distribution of novel prophylactic and therapeutic vaccines are the prioritized countermeasures of human disease. Among all vaccine platforms, viral vector vaccines offer distinguished advantages and represent prominent choices for pathogens that have hampered control efforts based on conventional vaccine approaches. Currently, viral vector vaccines remain one of the best strategies for induction of robust humoral and cellular immunity against human diseases. Numerous viruses of different families and origins, including vesicular stomatitis virus, rabies virus, parainfluenza virus, measles virus, Newcastle disease virus, influenza virus, adenovirus and poxvirus, are deemed to be prominent viral vectors that differ in structural characteristics, design strategy, antigen presentation capability, immunogenicity and protective efficacy. This review summarized the overall profile of the design strategies, progress in advance and steps taken to address barriers to the deployment of these viral vector vaccines, simultaneously highlighting their potential for mucosal delivery, therapeutic application in cancer as well as other key aspects concerning the rational application of these viral vector vaccines. Appropriate and accurate technological advances in viral vector vaccines would consolidate their position as a leading approach to accelerate breakthroughs in novel vaccines and facilitate a rapid response to public health emergencies.

## Defining County-Level Terrestrial Rabies Freedom Using the US National Rabies Surveillance System: Surveillance Data Analysis.

Kunkel A, Veytsel G, Bonaparte S, Meek H, Ma X, Davis AJ, Bonwitt J, Wallace RM.

07-04-2023

*JMIR Public Health Surveill.*

<https://pubmed.ncbi.nlm.nih.gov/37027194/>

**Background:** Rabies is a deadly zoonotic disease with nearly 100% fatality rate. In the United States, rabies virus persists in wildlife reservoirs, with occasional spillover into humans and domestic animals. The distribution of reservoir hosts in US counties plays an important role in public health decision-making, including the recommendation of lifesaving postexposure prophylaxis upon suspected rabies exposures. Furthermore, in surveillance data, it is difficult to discern whether counties have no cases reported because rabies was not present or because counties have an unreported rabies presence. These epizootics are monitored by the National Rabies Surveillance System (NRSS), to which approximately 130 state public health, agriculture, and academic laboratories report animal rabies testing statistics. Historically, the

NRSS classifies US counties as free from terrestrial rabies if, over the previous 5 years, they and any adjacent counties did not report any rabies cases and they tested  $\geq 15$  reservoir animals or 30 domestic animals. **Objective:** This study aimed to describe and evaluate the historical NRSS rabies-free county definition, review possibilities for improving this definition, and develop a model to achieve more precise estimates of the probability of terrestrial rabies freedom and the number of reported county-level terrestrial rabies cases. **Methods:** Data submitted to the NRSS by state and territorial public health departments and the US Department of Agriculture Wildlife Services were analyzed to evaluate the historical rabies-free definition. A zero-inflated negative binomial model created county-level predictions of the probability of rabies freedom and the expected number of rabies cases reported. Data analyzed were from all animals submitted for laboratory diagnosis of rabies in the United States from 1995 to 2020 in skunk and raccoon reservoir territories, excluding bats and bat variants. **Results:** We analyzed data from 14,642 and 30,120 county-years in the raccoon and skunk reservoir territories, respectively. Only 0.85% (9/1065) raccoon county-years and 0.79% (27/3411) skunk county-years that met the historical rabies-free criteria reported a case in the following year (99.2% negative predictive value for each), of which 2 were attributed to unreported bat variants. County-level model predictions displayed excellent discrimination for detecting zero cases and good estimates of reported cases in the following year. Counties classified as rabies free rarely (36/4476, 0.8%) detected cases in the following year. **Conclusions:** This study concludes that the historical rabies freedom definition is a reasonable approach for identifying counties that are truly free from terrestrial raccoon and skunk rabies virus transmission. Gradations of risk can be measured using the rabies prediction model presented in this study. However, even counties with a high probability of rabies freedom should maintain rabies testing capacity, as there are numerous examples of translocations of rabies-infected animals that can cause major changes in the epidemiology of rabies.

---

## Schistosomiasis

### To Target or Not to Target *Schistosoma mansoni* Cyclic Nucleotide Phosphodiesterase 4A?

Zheng Y, Schroeder S, Kanev GK, Botros SS, William S, Sabra AA, Maes L, Caljon G, Gil C, Martinez A, Salado IG, Augustyns K, Edink E, Sijm M, de Heuvel E, de Esch IJP, van der Meer T, Siderius M, Sterk GJ, Brown D, Leurs R.

06-04-2023

*Int J Mol Sci.*

<https://pubmed.ncbi.nlm.nih.gov/37047792/>

Schistosomiasis is a neglected tropical disease with high morbidity. Recently, the *Schistosoma mansoni* phosphodiesterase SmPDE4A was suggested as a putative new drug target. To support SmPDE4A targeted drug discovery, we cloned, isolated, and biochemically characterized the full-length and catalytic domains of SmPDE4A. The enzymatically active catalytic domain was

crystallized in the apo-form (PDB code: 6FG5) and in the cAMP- and AMP-bound states (PDB code: 6EZU). The SmpPDE4A catalytic domain resembles human PDE4 more than parasite PDEs because it lacks the parasite PDE-specific P-pocket. Purified SmpPDE4A proteins (full-length and catalytic domain) were used to profile an in-house library of PDE inhibitors (PDE4NPD toolbox). This screening identified tetrahydrophthalazinones and benzamides as potential hits. The PDE inhibitor NPD-0001 was the most active tetrahydrophthalazinone, whereas the approved human PDE4 inhibitors roflumilast and piclamilast were the most potent benzamides. As a follow-up, 83 benzamide analogs were prepared, but the inhibitory potency of the initial hits was not improved. Finally, NPD-0001 and roflumilast were evaluated in an in vitro anti-*S. mansoni* assay. Unfortunately, both SmpPDE4A inhibitors were not effective in worm killing and only weakly affected the egg-laying at high micromolar concentrations. Consequently, the results with these SmpPDE4A inhibitors strongly suggest that SmpPDE4A is not a suitable target for anti-schistosomiasis therapy.

### Ethnobotanical knowledge on native Brazilian medicinal plants traditionally used as anthelmintic agents - A review.

Kuhn Agnes KN, Boeff DD, de Oliveira Carvalho L, Konrath EL.

10-04-2023

*Exp Parasitol.*

<https://pubmed.ncbi.nlm.nih.gov/37044282/>

### A 14-year follow-up of ultrasound-detected urinary tract pathology associated with urogenital schistosomiasis in women living in the Msambweni region of coastal Kenya.

Joeke E, McMonnies K, Blanshard A, Mutuku FM, Ileri E, Mungai P, Stothard JR, Bustinduy AL, King CH.

12-04-2023

*Trans R Soc Trop Med Hyg.*

<https://pubmed.ncbi.nlm.nih.gov/37042291/>

**Background:** Complications of urogenital schistosomiasis include acute inflammatory and chronic fibrotic changes within the urogenital tract. Disease burden of this neglected tropical disease is often underestimated, as only active, urine egg-patent *Schistosoma* infection is formally considered. Previous studies have focussed on short-term effects of praziquantel treatment on urinary tract pathology, demonstrating that acute inflammation is reversible. However, the reversibility of chronic changes is less well studied. **Methods:** Our study compared, at two time points 14 y apart, urine egg-patent infection and urinary tract pathology in a cohort of women living in a highly endemic area having intermittent praziquantel treatment(s). In 2014 we matched 93 women to their findings in a previous study in 2000. **Results:** Between 2000 and 2014 the rate of egg-patent infection decreased from 34% (95% confidence interval [CI] 25 to 44) to 9% (95% CI 3 to 14). However, urinary tract pathology increased from 15% (95% CI 8 to 22) to 19% (95% CI 11 to 27), with the greatest increase seen in bladder thickening and shape

abnormality. **Conclusions:** Despite praziquantel treatment, fibrosis from chronic schistosomiasis outlasts the presence of active infection, continuing to cause lasting morbidity. We suggest that future efforts to eliminate persistent morbidity attributable to schistosomiasis should include intensified disease management.

### A duplex tetra-primer ARMS-PCR assay to discriminate three species of the *Schistosoma haematobium* group: *Schistosoma curassoni*, *S. bovis*, *S. haematobium* and their hybrids.

Blin M, Dametto S, Agniwo P, Webster BL, Angora E, Dabo A, Boissier J.

07-04-2023

*Parasit Vectors.*

<https://pubmed.ncbi.nlm.nih.gov/37029440/>

**Background:** The use of applications involving single nucleotide polymorphisms (SNPs) has greatly increased since the beginning of the 2000s, with the number of associated techniques expanding rapidly in the field of molecular research. Tetra-primer amplification refractory mutation system-PCR (T-ARMS-PCR) is one such technique involving SNP genotyping. It has the advantage of amplifying multiple alleles in a single reaction with the inclusion of an internal molecular control. We report here the development of a rapid, reliable and cost-effective duplex T-ARMS-PCR assay to distinguish between three *Schistosoma* species, namely *Schistosoma haematobium* (human parasite), *Schistosoma bovis* and *Schistosoma curassoni* (animal parasites), and their hybrids. This technique will facilitate studies of population genetics and the evolution of introgression events. **Methods:** During the development of the technique we focused on one of the five inter-species internal transcribed spacer (ITS) SNPs and one of the inter-species 18S SNPs which, when combined, discriminate between all three *Schistosoma* species and their hybrid forms. We designed T-ARMS-PCR primers to amplify amplicons of specific lengths for each species, which in turn can then be visualized on an electrophoresis gel. This was further tested using laboratory and field-collected adult worms and field-collected larval stages (miracidia) from Spain, Egypt, Mali, Senegal and Ivory Coast. The combined duplex T-ARMS-PCR and ITS + 18S primer set was then used to differentiate the three species in a single reaction. **Results:** The T-ARMS-PCR assay was able to detect DNA from both species being analysed at the maximum and minimum levels in the DNA ratios (95/5) tested. The duplex T-ARMS-PCR assay was also able to detect all hybrids tested and was validated by sequencing the ITS and the 18S amplicons of 148 of the field samples included in the study. **Conclusions:** The duplex tetra-primer ARMS-PCR assay described here can be applied to differentiate between *Schistosoma* species and their hybrid forms that infect humans and animals, thereby providing a method to investigate the epidemiology of these species in endemic areas. The addition of several markers in a single reaction saves considerable time and is of long-standing interest for investigating genetic populations.

## The epidemiology of *Schistosoma mansoni* in the Lake Tana Basin (Ethiopia): Review with retrospective data analyses.

Abera B.

27-03-2023

*Heliyon*.

<https://pubmed.ncbi.nlm.nih.gov/37025815/>

## A randomized, controlled Phase 1b trial of the Sm-TSP-2 Vaccine for intestinal schistosomiasis in healthy Brazilian adults living in an endemic area.

Diemert DJ, Correa-Oliveira R, Fraga CG, Talles F, Silva MR, Patel SM, Galbiati S, Kennedy JK, Lundeen JS, Gazzinelli MF, Li G, Hoeweler L, Deye GA, Bottazzi ME, Hotez PJ, El Sahly HM, Keitel WA, Bethony J, Atmar RL.

30-03-2023

*PLoS Negl Trop Dis*.

<https://pubmed.ncbi.nlm.nih.gov/36996185/>

**Background:** Recombinant *Schistosoma mansoni* Tetraspanin-2 formulated on Alhydrogel (Sm-TSP-2/Alhydrogel) is being developed to prevent intestinal and hepatic disease caused by *S. mansoni*. The tegumentary Sm-TSP-2 antigen was selected based on its unique recognition by cytophilic antibodies in putatively immune individuals living in areas of ongoing *S. mansoni* transmission in Brazil, and preclinical studies in which vaccination with Sm-TSP-2 protected mice following infection challenge. **Methods:** A randomized, observer-blind, controlled, Phase 1b clinical trial was conducted in 60 healthy adults living in a region of Brazil with ongoing *S. mansoni* transmission. In each cohort of 20 participants, 16 were randomized to receive one of two formulations of Sm-TSP-2 vaccine (adjuvanted with Alhydrogel only, or with Alhydrogel plus the Toll-like receptor-4 agonist, AP 10-701), and 4 to receive Euvax B hepatitis B vaccine. Successively higher doses of antigen (10 µg, 30 µg, and 100 µg) were administered in a dose-escalation fashion, with progression to the next dose cohort being dependent upon evaluation of 7-day safety data after all participants in the preceding cohort had received their first dose of vaccine. Each participant received 3 intramuscular injections of study product at intervals of 2 months and was followed for 12 months after the third vaccination. IgG and IgG subclass antibody responses to Sm-TSP-2 were measured by qualified indirect ELISAs at pre- and post-vaccination time points through the final study visit. **Results:** Sm-TSP-2/Alhydrogel administered with or without AP 10-701 was well-tolerated in this population. The most common solicited adverse events were mild injection site tenderness and pain, and mild headache. No vaccine-related serious adverse events or adverse events of special interest were observed. Groups administered Sm-TSP-2/Alhydrogel with AP 10-701 had higher post-vaccination levels of antigen-specific IgG antibody. A significant dose-response relationship was seen in those administered Sm-TSP-2/Alhydrogel with AP 10-701. Peak anti-Sm-TSP-2 IgG levels were observed approximately 2 weeks following the third dose, regardless of Sm-TSP-2

formulation. IgG levels fell to low levels by Day 478 in all groups except the 100 µg with AP 10-701 group, in which 57% of subjects (4 of 7) still had IgG levels that were  $\geq 4$ -fold higher than baseline. IgG subclass levels mirrored those of total IgG, with IgG1 being the predominant subclass response. **Conclusions:** Vaccination of adults with Sm-TSP-2/Alhydrogel in an area of ongoing *S. mansoni* transmission was safe, minimally reactogenic, and elicited significant IgG and IgG subclass responses against the vaccine antigen. These promising results have led to initiation of a Phase 2 clinical trial of this vaccine in an endemic region of Uganda.

## MALDI-TOF: A new tool for the identification of *Schistosoma cercariae* and detection of hybrids.

Huguenin A, Kincaid-Smith J, Depaquit J, Boissier J, Fertié H.

28-03-2023

*PLoS Negl Trop Dis*.

<https://pubmed.ncbi.nlm.nih.gov/36976804/>

Schistosomiasis is a neglected water-born parasitic disease caused by *Schistosoma* affecting more than 200 million people. Introgressive hybridization is common among these parasites and raises issues concerning their zoonotic transmission. Morphological identification of *Schistosoma cercariae* is difficult and does not permit hybrids detection. Our objective was to assess the performance of MALDI-TOF (Matrix Assisted Laser Desorption-Ionization-Time Of Flight) mass spectrometry for the specific identification of cercariae in human and non-human *Schistosoma* and for the detection of hybridization between *S. bovis* and *S. haematobium*. Spectra were collected from laboratory reared molluscs infested with strains of *S. haematobium*, *S. mansoni*, *S. bovis*, *S. rodhaini* and *S. bovis* x *S. haematobium* natural (Corsican hybrid) and artificial hybrids. Cluster analysis showed a clear separation between *S. haematobium*, *S. bovis*, *S. mansoni* and *S. rodhaini*. Corsican hybrids are classified with those of the parental strain of *S. haematobium* whereas other hybrids formed a distinct cluster. In blind test analysis the developed MALDI-TOF spectral database permits identification of *Schistosoma cercariae* with high accuracy (94%) and good specificity (*S. bovis*: 99.59%, *S. haematobium* 99.56%, *S. mansoni* and *S. rodhaini*: 100%). Most misidentifications were between *S. haematobium* and the Corsican hybrids. The use of machine learning permits to improve the discrimination between these last two taxa, with accuracy, F1 score and Sensitivity/Specificity > 97%. In multivariate analysis the factors associated with obtaining a valid identification score (> 1.7) were absence of ethanol preservation ( $p < 0.001$ ) and a number of 2-3 cercariae deposited per well ( $p < 0.001$ ). Also, spectra acquired from *S. mansoni* cercariae are more likely to obtain a valid identification score than those acquired from *S. haematobium* ( $p < 0.001$ ). MALDI-TOF is a reliable technique for high-throughput identification of *Schistosoma cercariae* of medical and veterinary importance and could be useful for field survey in endemic areas.

## 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.

24-03-2023

*PLoS Negl Trop Dis*.

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

---

## Trachome

### Prevalence of and factors associated with childhood anaemia in remote villages of the Peruvian Amazon: a cross-sectional study and geospatial analysis.

Morocho-Alburquerque N, Quincho-Lopez A, Neseemann JM, Cañari-Casaño JL, Elorreaga OA, Muñoz M, Talero S, Harding-Esch EM, Saboyá-Díaz MI, Honorio-Morales HA, Durand S, Carey-Angeles CA, Klausner JD, Keenan JD, Lescano AG.

11-04-2023

*Trans R Soc Trop Med Hyg*.

<https://pubmed.ncbi.nlm.nih.gov/37039044/>

**Background:** Anaemia is a public health problem in Peru. In the Loreto region of the Amazon,  $\geq 50\%$  of children may be anaemic, although insufficient information exists for rural villages. **Methods:** To generate more data about childhood anaemia in the Peruvian Amazon, haemoglobin was measured as part of a trachoma survey in 21 randomly selected villages. All children 1-9 y of age from 30 randomly selected households per village were recruited. Anaemia was classified according to the World Health Organization guidelines and a socio-economic status (SES) index was created for each household using principal component analysis. Spatial autocorrelation was determined using Moran's I and Ripley's K function. **Results:** Of 678 children with complete haemoglobin data, 25.4% (95% confidence interval [CI] 21.2 to 30.1) had mild-or-worse anaemia and 22.1% (95% CI 15.6 to 30.3) had moderate-or-worse anaemia. Mild-or-worse anaemia was more common among children whose primary source of drinking water was surface water (prevalence ratio [PR] 1.26 [95% CI 1.14 to 1.40],  $p < 0.001$ ) and who were in the lowest SES tercile (PR 1.16 [95% CI 1.02 to 1.32],  $p = 0.021$ ). Moderate-or-worse anaemia was more common among boys (PR 1.32 [95% CI 1.09 to 1.60],  $p = 0.005$ ). No evidence of geospatial clustering was found. **Conclusions:** Remote villages of the Amazon would benefit from interventions for childhood anaemia and the poorest households would have the most to gain. Integrating anaemia screening into neglected tropical diseases surveys is an opportunity to use public health resources more efficiently.

### 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.



# Trématodoses d'origine alimentaire (clonorchiose, opisthorchiose, fasciolose et paragonimose)

## A taxonomic re-evaluation of five stomiiform fish species described by August Brauer (1902) with lectotype designations.

Gon O, Assel E, Anderson E, MacLaine J.

18-10-2023

*Zootaxa*.

<https://pubmed.ncbi.nlm.nih.gov/37044400/>

A study of the type series of *Stylophthalmus paradoxus* and *Idiacanthus atlanticus* (Stomiidae), and *Cyclothone livida*, *C. obscura* and *C. pallida* (Gonostomatidae), uncovered errors in the synonymy of *Idiacanthus* and inconsistencies regarding the number of type specimens of the three species of *Cyclothone*. The syntypes of *S. paradoxus* were matched with the illustrations of this species in Brauer (1906) and the specimen used in the description was identified and designated as a lectotype of this species. A comparison of these syntypes with specimens of *Idiacanthus atlanticus*, including its syntypes, and of *I. fasciola* indicated that *S. paradoxus* is most likely a junior synonym of *I. fasciola*. In addition, the research resulted in a reliable way to distinguish between *I. fasciola* and *I. atlanticus* and in the identification of the primary type of the latter species. Mismatches were found in the information Brauer (1906) provided about the material he had for the three species of *Cyclothone* as well as with published data about the type series of these species. It seems that the whereabouts of many of the type series specimens is unknown. We therefore propose that the individual specimens Brauer singled out for measurements in his original descriptions of *C. livida*, *C. obscura* and *C. pallida* be recognized as lectotypes.

## Prevalence, coinfection, and risk factors associated with *Fasciola hepatica* and other gastrointestinal parasites in cattle from the Peruvian Amazon.

Frias H, Maraví C, Arista-Ruiz MA, Yari-Briones DI, Paredes-Valderrama JR, Bravo YR, Cortez JV, Segura GT, Ruiz RE, Lapa RML, Valderrama NLM.

Mar-2023

*Vet World*.

<https://pubmed.ncbi.nlm.nih.gov/37041847/>

## Adaptive evolution characteristics of mitochondrial genomes in genus *Aparapotamon* (Brachyura, Potamidae) of freshwater crabs.

Ji YT, Zhou XJ, Yang Q, Lu YB, Wang J, Zou JX.

12-04-2023

*BMC Genomics*.

<https://pubmed.ncbi.nlm.nih.gov/37041498/>

**Background:** *Aparapotamon*, a freshwater crab genus endemic to China, includes 13 species. The distribution of *Aparapotamon* spans the first and second tiers of China's terrain ladder, showing great altitudinal differences. To study the molecular mechanisms of adaptive evolution in *Aparapotamon*, we performed evolutionary analyses, including morphological, geographical, and phylogenetic analyses and divergence time estimation. We sequenced the mitogenomes of *Aparapotamon binchuanense* and *Aparapotamon huizeense* for the first time and resequenced three other mitogenomes of *Aparapotamon grahami* and *Aparapotamon gracilipedum*. These sequences were combined with NCBI sequences to perform comparative mitogenome analysis of all 13 *Aparapotamon* species, revealing mitogenome arrangement and the characteristics of protein-coding and tRNA genes. **Results:** A new species classification scheme of the genus *Aparapotamon* has been detected and verified by different aspects, including geographical, morphological, phylogenetics and comparative mitogenome analyses. Imprints from adaptive evolution were discovered in the mitochondrial genomes of group A, including the same codon loss at position 416 of the ND6 gene and the unique arrangement pattern of the tRNA-Ile gene. Multiple tRNA genes conserved or involved in adaptive evolution were detected. Two genes associated with altitudinal adaptation, ATP8 and ND6, which experienced positive selection, were identified for the first time in freshwater crabs. **Conclusions:** Geological movements of the Qinghai-Tibet Plateau and Hengduan Mountains likely strongly impacted the speciation and differentiation of the four *Aparapotamon* groups. After some group A species dispersed from the Hengduan Mountain Range, new evolutionary characteristics emerged in their mitochondrial genomes, facilitating adaptation to the low-altitude environment of China's second terrain tier. Ultimately, group A species spread to high latitudes along the upper reaches of the Yangtze River, showing faster evolutionary rates, higher species diversity and the widest distribution.

## Polymorphism of genes encoding drug-metabolizing and inflammation-related enzymes for susceptibility to cholangiocarcinoma in Thailand.

You G, Zeng L, Tanaka H, Ohta E, Fujii T, Ohshima K, Tanaka M, Hamajima N, Viwatthanassittiphong C, Muangphot M, Chenvidhya D, Jedpiyawongse A, Sripa B, Miwa M, Honjo S.

22-03-2023

*World J Gastrointest Pathophysiol*.

<https://pubmed.ncbi.nlm.nih.gov/37035273/>

**Background:** Cholangiocarcinoma (CCA) is an intractable cancer, and its incidence in northeastern Thailand is the highest worldwide. Infection with the liver fluke *Opisthorchis viverrini* (OV) has been associated with CCA risk. However, animal experiments have suggested that OV alone does not induce CCA, but its combination with a chemical carcinogen like nitrosamine can cause

experimentally induced CCA in hamsters. Therefore, in humans, other environmental and genetic factors may also be involved. **Aim:** To examine relations between risk for CCA and genetic polymorphisms in carcinogen-metabolizing and inflammation-related genes. **Methods:** This hospital-based case-control study enrolled 95 case-control pairs matched by age ( $\pm 5$  years) and sex. We examined relations between risk for CCA and genetic polymorphisms in carcinogen-metabolizing and inflammation-related genes, serum anti-OV, alcohol consumption, and smoking. Polymorphisms of *CYP2E1*, *IL-6* (-174 and -634), *IL-10* (-819), and *NF- $\kappa$ B* (-94) and their co-occurrence with polymorphisms in the drug-metabolizing enzyme gene *GSTT1* or *GSTM1* were also analyzed. **Results:** Although CCA risk was not significantly associated with any single polymorphism, persons with the *GSTT1* wild-type and *CYP2E1* c1/c2 + c2/c2 genotype had an increased risk (OR = 3.33, 95%CI: 1.23-9.00) as compared with persons having the *GSTT1* wild-type and *CYP2E1* c1/c1 wild genotype. The presence of anti-OV in serum was associated with a 7- to 11-fold increased risk, and smoking level was related to an OR of 1.5-1.8 in multivariable analyses adjusted for each of the seven genetic polymorphisms. **Conclusion:** In addition to infection with OV, gene-gene interactions may be considered as one of the risk factors for CCA development.

### Ovine gastrointestinal parasite burden and the impact of strategic anthelmintic treatment in community-based breeding sites in Ethiopia.

Molla W, Moliso MM, Gizaw S, Nane T, Arke A, Ayele F, Knight-Jones T.  
21-03-2023  
*Front Vet Sci.*  
<https://pubmed.ncbi.nlm.nih.gov/37026099/>

## Trypanosomes (trypanosomiasis et maladie de Chagas)

### Lethal and repellent effect of amitraz, eugenol and thymol against *Triatoma infestans*, the main vector of *Trypanosoma cruzi* in the southern of America.

Dadé MM, Daniele M, Reyes-Novelo E, Rodriguez-Vivas RI.  
13-04-2023  
*Med Vet Entomol.*  
<https://pubmed.ncbi.nlm.nih.gov/37052250/>

The lethal and repellent effect of the synthetic insecticide amitraz and the botanical insecticides eugenol and thymol separately and together in binary mixtures was tested against late-stage nymphs of a susceptible strain of *Triatoma infestans*, the main vector of *Trypanosoma cruzi*, the etiological agent of Chagas disease, in the Southern Cone of America. For the lethality study, the LD50 was determined for each insecticide alone and in binary

mixture by topical application. The combination index (CI) was established to quantify interactions occurring between the insecticides. The repellent effect was tested using the area preference technique. The lethal effect of amitraz was 11 and 34 times more potent than that of thymol and eugenol, respectively. Only the combination of eugenol and amitraz at high concentrations showed a synergistic effect (CI: 0.3). The repellent activity of monoterpenes after 30 min of exposure was significant at 780 and 78  $\mu$ g/cm<sup>2</sup> for eugenol and thymol, respectively. The residual repellent effect of eugenol lasted for one week at the concentrations of 1170 and 1560  $\mu$ g/cm<sup>2</sup>, whereas thymol managed to retain its repellent effect for two weeks at concentrations of 1560 and 3900  $\mu$ g/cm<sup>2</sup>.

### Frequency Variation and Dose Modification of Benznidazole Administration for the Treatment of *Trypanosoma cruzi* Infection in Mice, Dogs, and Nonhuman Primates.

Bustamante JM, White BE, Wilkerson GK, Hodo CL, Auckland LD, Wang W, McCain S, Hamer SA, Saunders AB, Tarleton RL.  
11-04-2023  
*Antimicrob Agents Chemother.*  
<https://pubmed.ncbi.nlm.nih.gov/37039666/>

*Trypanosoma cruzi* naturally infects a broad range of mammalian species and frequently results in the pathology that has been most extensively characterized in human Chagas disease. Currently employed treatment regimens fail to achieve parasitological cure of *T. cruzi* infection in the majority of cases. In this study, we have extended our previous investigations of more effective, higher dose, intermittent administration protocols using the FDA-approved drug benznidazole (BNZ), in experimentally infected mice and in naturally infected dogs and nonhuman primates (NHP). Collectively, these studies demonstrate that twice-weekly administration of BNZ for more than 4 months at doses that are ~2.5-fold that of previously used daily dosing protocols, provided the best chance to obtain parasitological cure. Dosing less frequently or for shorter time periods was less dependable in all species. Prior treatment using an ineffective dosing regimen in NHPs did not prevent the attainment of parasitological cure with an intensified BNZ dosing protocol. Furthermore, parasites isolated after a failed BNZ treatment showed nearly identical susceptibility to BNZ as those obtained prior to treatment, confirming the low risk of induction of drug resistance with BNZ and the ability to adjust the treatment protocol when an initial regimen fails. These results provide guidance for the use of BNZ as an effective treatment for *T. cruzi* infection and encourage its wider use, minimally in high value dogs and at-risk NHP, but also potentially in humans, until better options are available.

### Concurrent Trypanosomosis, Babesiosis and Toxocarosis in a Dog: a Case Report.

Abbas H, Rizwan HM, Younus M, Sajid MS, Farooqi SH, Iqbal Z, Imran M, Amanat U, Wazir N, Naeem MA.  
30-06-2023

### **In silico and in vitro assessment of anti-Trypanosoma cruzi efficacy, genotoxicity and pharmacokinetics of pentasubstituted pyrrolic Atorvastatin-aminoquinoline hybrid compounds.**

Araujo-Lima CF, Carvalho RCC, Peres RB, Fiuza LFA, Galvão BVD, Castelo-Branco FS, Bastos MM, Boechat N, Felzenszwalb I, Soeiro MNC.

08-04-2023

*Acta Trop.*

<https://pubmed.ncbi.nlm.nih.gov/37037291/>

### **Candimine from Hippeastrum escoipense (Amaryllidaceae): Anti-Trypanosoma cruzi activity and synergistic effect with benznidazole.**

Ortiz JE, Piñeiro M, Martinez-Peinado N, Barrera P, Sosa M, Bastida J, Alonso-Padilla J, Feresin GE.

29-03-2023

*Phytomedicine.*

<https://pubmed.ncbi.nlm.nih.gov/37037085/>

**Background:** Chagas disease (CD), caused by *Trypanosoma cruzi*, represents a health threat to around 20 million people worldwide. Side effects of benznidazole (Bzn) cause 15-20% of patients to discontinue their treatment. Evidence has increased in favor of the use of drug combinations to improve the efficacy and tolerance of the treatment. Natural products are well known to provide structures that could serve as new drugs or scaffolds for CD treatment. Spp of the Amaryllidoideae sub family of Amaryllidaceae family are known by their bioactives alkaloids, which have been reported by their antiparasitic activities. **Purpose:** To evaluate the anti-T. cruzi activity of the isolated alkaloid candimine (Cnd) from *Hippeastrum escoipense* Slanis & Huaylla; and to assess the combination effect between Cnd and Bzn against different life stages of T. cruzi parasites. **Methods:** The chemical profile of H. escoipense alkaloids extract (AE-H. escoipense), including quantitation of Cnd was performed through GC/MS and UPLC-MS/MS techniques. Subsequently, Cnd was isolated using Shephadex LH-20. Then, the AE-H. escoipense and Cnd were tested against T. cruzi, (epimastigotes, trypomastigotes, and amastigotes) by in vitro proliferation and viability assays. The cytotoxicity was evaluated against Vero and HepG2 mammalian cells. The ultrastructural analysis was performed by transmission electron microscopy (TEM) and mitochondrial activity was carried out by MTT assay. Drug combination assay between Cnd and Bzn was evaluated using the Chou-Talalay method. **Results:** The AE-H. escoipense and Cnd showed high and specific anti-T. cruzi activity, comparable to Bzn. Cnd induces ultrastructural changes in T. cruzi, such as vacuolization, membrane blebs, and increased mitochondrial activity. Regarding the interaction between Cnd and Bzn, it generates synergism in the combinations of 0.25×IC<sub>50</sub> in epimastigotes, 2×IC<sub>50</sub> in trypomastigotes+amastigotes, and 0.25, 2, and 4×IC<sub>50</sub> in amastigotes. **Conclusion:** The synergism between Cnd and

Bzn indicates that the combination at the concentration of 4×IC<sub>50</sub> could be useful as an effective new therapy against CD in the chronic stage. Thus, Cnd isolated from the leaves of H. escoipense emerges as potential candidate for the development of a new drug for the treatment of CD.

### **A spatially resolved elemental nanodomain organization within acidocalcisomes in Trypanosoma cruzi.**

Girard-Dias W, Augusto I, V A Fernandes T, G Pascutti P, de Souza W, Miranda K.

18-04-2023

*Proc Natl Acad Sci U S A.*

<https://pubmed.ncbi.nlm.nih.gov/37036984/>

How are ions distributed in the three-dimensional (3D) volume confined in a nanoscale compartment? Regulation of ionic flow in the intracellular milieu has been explained by different theoretical models and experimentally demonstrated for several compartments with microscale dimensions. Most of these models predict a homogeneous distribution of ions seconds or milliseconds after an initial diffusion step formed at the ion translocation site, leaving open questions when it comes to ion/element distribution in spaces/compartments with nanoscale dimensions. Due to the influence of compartment size on the regulation of ionic flow, theoretical variations of classical models have been proposed, suggesting heterogeneous distributions of ions/elements within nanoscale compartments. Nonetheless, such assumptions have not been fully proven for the 3D volume of an organelle. In this work, we used a combination of cutting-edge electron microscopy techniques to map the 3D distribution of diffusible elements within the whole volume of acidocalcisomes in trypanosomes. Cryofixed cells were analyzed by scanning transmission electron microscopy tomography combined with elemental mapping using a high-performance setup of X-ray detectors. Results showed the existence of elemental nanodomains within the acidocalcisomes, where cationic elements display a self-excluding pattern. These were validated by Pearson correlation analysis and in silico molecular dynamic simulations. Formation of element domains within the 3D space of an organelle is demonstrated. Distribution patterns that support the electrodiffusion theory proposed for nanophysiology models have been found. The experimental pipeline shown here can be applied to a variety of models where ion mobilization plays a crucial role in physiological processes.

### **Macrophage-infectivity potentiator of Trypanosoma cruzi (TcMIP) is a new pro-type 1 immuno-stimulating protein for neonatal human cells and vaccines in mice.**

Radwanska M, de Lemos Esteves F, Linsen L, Coltel N, Cencig S, Widart J, Massart AC, Colson S, Di Paolo A, Percier P, Ait Djebbara S, Guillonnet F, Flamand V, De Pauw E, Frère JM, Carlier Y, Truysens C.

23-03-2023

*Front Immunol.*

<https://pubmed.ncbi.nlm.nih.gov/37033946/>

### Protective effects of Theracurmin treatment during experimental infection of the Colombian strain of *Trypanosoma cruzi* at the testicular site.

Pimenta BL, Menezes TP, Louise V, Dias FCR, Machado BAA, Ribeiro L, Pinto KMC, Talvani A.

24-03-2023

*Front Cell Infect Microbiol.*

<https://pubmed.ncbi.nlm.nih.gov/37033490/>

**Introduction:** Chagas' disease is a tropical neglected illness caused by *Trypanosoma cruzi* and remains one of the most significant causes of morbidity and mortality in South and Central Americas. The disease is caused by a moderate to intense and persistent inflammatory response characterized by local upregulated expression and production of inflammatory mediators that favors the activation and recruitment of distinct cells of the immune system into different tissues to eliminate the parasites. Theracurmin is a curcumin's derived formulation of nanoparticles. Its anti-inflammatory properties make this bioactive compound a mitigating factor in pathological cases after an overwhelming inflammatory response.

**Methods:** Our research focused on the testicular investigation in 28 mice infected by 103 trypomastigote forms of Colombian strain of *T. cruzi* and preventively treated with Theracurmin. The mice were treated with 30 mg/Kg of Theracurmin during the period of 30 days. At the 30th day post infection animals were euthanized, and its testicles were collected to morphological and immunological assays. **Results:** The animals infected and treated with Theracurmin presented a reduction in the testicular levels of IL-15 and IL-6. The volume density (%) of the tunica propria was also higher in all infected animals, but Theracurmin decreased this parameter in the treated animals. In the intertubular area, the percentage of some intertubular components was decreased in the infected animals such as the percentage and volume of Leydig cells, connective tissue, and macrophages.

**Discussion:** Furthermore, our data pointed to the daily use of Theracurmin in the diet as a protective element of the testicular function.

### Antiprotozoal drugs: challenges and opportunities.

Supuran CT.

11-04-2023

*Expert Opin Ther Pat.*

<https://pubmed.ncbi.nlm.nih.gov/37029480/>

### Effectiveness of the repurposed drug isotretinoin in an experimental murine model of Chagas disease.

Rial MS, Reigada C, Prado N, Bua J, Esteva M, Pereira CA, Fichera LE.

05-04-2023

*Acta Trop.*

<https://pubmed.ncbi.nlm.nih.gov/37028584/>

Benznidazole and nifurtimox are the drugs currently used for the treatment of Chagas disease, however its side effects may affect patient adherence. In the search for

new alternative therapies, we previously identified isotretinoin (ISO), an FDA-approved drug widely used for the treatment of severe acne through a drug repurposing strategy. ISO shows a strong activity against *Trypanosoma cruzi* parasites in the nanomolar range, and its mechanism of action is through the inhibition of *T. cruzi* polyamine and amino acid transporters from the Amino Acid/Auxin Permeases (AAAP) family. In this work, a murine model of chronic Chagas disease (C57BL/6 J mice), intraperitoneally infected with *T. cruzi* Nicaragua isolate (DTU TcI), were treated with different oral administrations of ISO: daily doses of 5 mg/kg/day for 30 days and weekly doses of 10 mg/kg during 13 weeks. The efficacy of the treatments was evaluated by monitoring blood parasitemia by qPCR, anti-*T. cruzi* antibodies by ELISA, and cardiac abnormalities by electrocardiography. No parasites were detected in blood after any of the ISO treatments. The electrocardiographic study of the untreated chronic mice showed a significant decrease in heart rate, while in the treated mice this negative chronotropic effect was not observed. Atrioventricular nodal conduction time in untreated mice was significantly longer than in treated animals. Mice treated even with ISO 10 mg/kg dose every 7 days, showed a significant reduction in anti-*T. cruzi* IgG levels. In conclusion, the intermittent administration of ISO 10 mg/kg would improve myocardial compromise during the chronic stage.

---

## Ulcère de Buruli

### Profiling *Mycobacterium ulcerans*: sporulation, survival strategy and response to environmental factors.

Ayerakwa EA, Abban MK, Isawumi A, Mosi L.

23-03-2023

*Future Sci OA.*

<https://pubmed.ncbi.nlm.nih.gov/37026027/>