



Veille scientifique

Maladies tropicales négligées

Semaine 28
10 au 16 juillet 2023

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Cysticercose

Sexual dimorphism in the murine model of extraparenchymal neurocysticercosis.

Moreira CAA, Murayama LHV, Martins TC, Oliveira VT, Generoso D, Machado VMV, Batah SS, Fabro AT, Bazan R, Zanini MA, Sciutto E, Fleury A, Hamamoto Filho PT.
10-07-2023

Parasitol Res.

<https://pubmed.ncbi.nlm.nih.gov/37428312/>

Neurocysticercosis is a heterogeneous disease, and the patient's sex seems to play a role in this heterogeneity. Hosts' sexual dimorphism in cysticercosis has been largely explored in the murine model of intraperitoneal *Taenia crassiceps* cysticercosis. In this study, we investigated the sexual dimorphism of inflammatory responses in a rat model of extraparenchymal neurocysticercosis caused by *T. crassiceps*. *T. crassiceps* cysticerci were inoculated in the subarachnoid space of Wistar rats (25 females, 22 males). Ninety days later, the rats were euthanized for histologic, immunohistochemistry, and cytokines studies. Ten animals also underwent a 7-T magnetic resonance imaging (MRI). Female rats presented a higher concentration of immune cells in the arachnoid-brain interface, reactive astrogliosis in the periventricular region, in situ pro-inflammatory cytokine (interleukin [IL]-6) and anti-inflammatory cytokine (IL-10), and more intense hydrocephalus on MRI than males. Intracranial hypertension signals were not observed during the observational period. Overall, these results suggest sexual dimorphism in the intracranial inflammatory response that accompanied *T. crassiceps* extraparenchymal neurocysticercosis.

Dengue, chikungunya et maladie à virus Zika

Attitude towards dengue control efforts with the potential of digital technology during COVID-19: partial least squares-structural equation modeling.

Purnama SG, Susanna D, Achmadi UF, Eryando T.
27-06-2023

F1000Res.

<https://pubmed.ncbi.nlm.nih.gov/37441548/>

Background: Dengue fever is still a public health issue in Indonesia, and during the coronavirus disease 2019 (COVID-19) pandemic, integrated digital technology will be required for its control. This study aims to identify critical indicators influencing attitudes towards dengue control related to the potential for implementing digital technology. **Methods:** This was a cross-sectional survey, with 515 people willing to fill out an online questionnaire. The analysis was conducted using Partial Least Square-Structural Equation Modelling (PLS-SEM). There were 46 indicators used to assess attitudes toward dengue control, which were organized into six variables: the need for digital information systems, perceptions of being

threatened with dengue, the benefits of dengue control programs, program constraints, environmental factors and attitudes in dengue control. **Results:** The source of information needed for dengue control was mainly through social media. There was a positive relationship between perception of environmental factors to perception of dengue threat, perception of program constraints, perception of program benefits, and perception of digital technology needs. Perception of program benefits and threatened perception of dengue have a positive relationship with perception of digital technology needs. **Conclusions:** This model showed the variables perception of digital technology and perception of benefits had a positive association with attitude towards dengue control.

Secondary dengue serotype 1 infection causing dengue shock syndrome with rhombencephalitis and bleeding associated with refractory thrombocytopenia: A case report.

Surabotsophon M, Laohachavalit P, Ponglikitmongkol S, Chuncharunee S, Sudsang T, Thanachartwet V, Sahassananda D, Hunsawong T, Klungthong C, Fernandez S, Kalayanaroj S, Desakorn V, Leelasetakul S.
17-06-2032

Heliyon.

<https://pubmed.ncbi.nlm.nih.gov/37441400/>

Abdominal and Chest Ultrasonography: A predictor for disease progression in nonsevere dengue.

Chaudhary S, Manrai K, Dhagat P, Dudeja P, Sen D, Grewal DS, Kakria N.

Juil-Août 2023

Med J Armed Forces India.

<https://pubmed.ncbi.nlm.nih.gov/37441301/>

Background: Dengue is one of the most rapidly spreading arboviral infections in the world. Ultrasound is well established in abdomino-thoracic evaluation of patients with dengue infection. The aim of this study was to explore the role of ultrasound in predicting occurrence of severe infection in dengue patients and in predicting deterioration in patients with nonsevere dengue.

Methods: The serologically proven dengue patients who reported to hospital during the study period were divided into three categories based on the dengue infection severity score. Ultrasound findings of abdomen and chest in these patients were noted in the initial, as well as follow-up scans and inferences drawn. **Results:** 61% belonged to the category of Dengue Fever, 35% were in Dengue Hemorrhagic Fever category, and 4% had Dengue Shock Syndrome. Positive ultrasound findings were seen to be significantly higher in patients with severe dengue. Logistic regression analysis revealed the presence of pericholecystic fluid to be significantly associated with the severe disease, while the presence of gall bladder wall edema, ascites, and any ultrasound finding were significantly associated with the disease progression. The odds of a patient with severe dengue having gall bladder wall edema, ascites, or any ultrasound finding were 2.74,

2.04, and 2.619 times, respectively. **Conclusion:** Our study indicates that positive findings on ultrasound are significantly higher in severe dengue and also that ultrasound can be reliably used to identify the patients with nonsevere dengue who are likely to progress to severe dengue.

Impact of climate change on dengue fever epidemics in South and Southeast Asian settings: A modelling study.

Wang Y, Zhao S, Wei Y, Li K, Jiang X, Li C, Ren C, Yin S, Ho J, Ran J, Han L, Zee BC, Chong KC.

04-06-2023

Infect Dis Model.

<https://pubmed.ncbi.nlm.nih.gov/37440763/>

The potential for dengue fever epidemic due to climate change remains uncertain in tropical areas. This study aims to assess the impact of climate change on dengue fever transmission in four South and Southeast Asian settings. We collected weekly data of dengue fever incidence, daily mean temperature and rainfall from 2012 to 2020 in Singapore, Colombo, Selangor, and Chiang Mai. Projections for temperature and rainfall were drawn for three Shared Socioeconomic Pathways (SSP126, SSP245, and SSP585) scenarios. Using a disease transmission model, we projected the dengue fever epidemics until 2090s and determined the changes in annual peak incidence, peak time, epidemic size, and outbreak duration. A total of 684,639 dengue fever cases were reported in the four locations between 2012 and 2020. The projected change in dengue fever transmission would be most significant under the SSP585 scenario. In comparison to the 2030s, the peak incidence would rise by 1.29 times in Singapore, 2.25 times in Colombo, 1.36 times in Selangor, and >10 times in Chiang Mai in the 2090s under SSP585. Additionally, the peak time was projected to be earlier in Singapore, Colombo, and Selangor, but be later in Chiang Mai under the SSP585 scenario. Even in a milder emission scenario of SSP126, the epidemic size was projected to increase by 5.94%, 10.81%, 12.95%, and 69.60% from the 2030s-2090s in Singapore, Colombo, Selangor, and Chiang Mai, respectively. The outbreak durations in the four settings were projected to be prolonged over this century under SSP126 and SSP245, while a slight decrease is expected in 2090s under SSP585. The results indicate that climate change is expected to increase the risk of dengue fever transmission in tropical areas of South and Southeast Asia. Limiting greenhouse gas emissions could be crucial in reducing the transmission of dengue fever in the future.

Bilateral Internuclear Ophthalmoplegia Caused by Dengue Fever.

Choudhary T, Malviya S, Thakkar H.

13-07-2023

J Binocul Vis Ocul Motil.

<https://pubmed.ncbi.nlm.nih.gov/37440692/>

The Aedes aegypti RNA interference response against Zika virus in the

context of co-infection with dengue and chikungunya viruses.

Leggewie M, Scherer C, Altinli M, Gestuveo RJ, Sreenu VB, Fuss J, Vazeille M, Mousson L, Badusche M, Kohl A, Failloux AB, Schnettler E.

13-07-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/37440582/>

Human exposure risk assessment for infectious diseases due to temperature and air pollution: an overview of reviews.

Song X, Guo X, Hu X, Zhang Y, Wei D, Hu Y, Jiang L, Zhang Y.

13-07-2023

Environ Sci Pollut Res Int.

<https://pubmed.ncbi.nlm.nih.gov/37440140/>

Air pollution and global temperature change are expected to affect infectious diseases. Air pollution usually causes inflammatory response and disrupts immune defense system, while temperature mainly exacerbates the effect of vectors on humans. Yet to date overview of systematic reviews assessing the exposure risk of air pollutants and temperature on infectious diseases is unavailable. This article aims to fill this research gap. PubMed, Embase, the Cochrane Library, Web of Science, and the Cumulative Index to Nursing and Allied Health Literature were searched. Systematic reviews and meta-analyses investigated the exposure risk of pollutants or temperature on infectious diseases were included. Two investigators screened literature, extracted data and performed the risk of bias assessments independently. A total of 23 articles met the inclusion criteria, which 3 (13%) were "low" quality and 20 (87%) were "critically low" quality. COVID-19 morbidity was associated with long-term exposure PM_{2.5} (RR = 1.056 per 1 [Formula: see text], 95% CI: 1.039-1.072) and NO₂ (RR = 1.042 per 1 [Formula: see text], 95% CI: 1.017-1.068). In addition, for each 1 °C increase in temperature, the morbidity risk of dengue increased 13% (RR = 1.130 per 1 °C, 95% CI: 1.120-1.150), infectious diarrhea increased 8% (RR = 1.080 per 1 °C, 95% CI: 1.050-1.200), and hand, foot and mouth disease (HFMD) increased 5% (RR = 1.050 per 1 °C, 95% CI: 1.020-1.080). In conclusion, PM_{2.5} and NO₂ increased the risk of COVID-19 and temperatures were associated with dengue, infectious diarrhoea and HFMD morbidity. Moreover, the exposure risk of temperature on COVID-19 was recommended to be further explored.

Carbonic anhydrase inhibitory activity of phthalimide-capped benzene sulphonamide derivatives.

Shilkar D, Mohd Siddique MU, Bua S, Yasmin S, Patil M, Timiri AK, Supuran CT, Jayaprakash V.

Déc-2023

J Enzyme Inhib Med Chem.

<https://pubmed.ncbi.nlm.nih.gov/37439360/>

A series of phthalimide-capped benzene sulphonamides (1-22) reported by our group for dengue protease

inhibitory activity have been evaluated for their carbonic anhydrase (hCA, EC 4.2.1.1) inhibitory activity against hCA I, hCA II. Compounds **1**, **3**, **10**, and **15** showed hCA I inhibition, whereas **1**, **4**, and **10** showed hCA II inhibition at nanomolar concentrations. Among these compounds, **1** displayed potent inhibitory activity against the hCA I ($K_i = 28.5$ nM) and hCA II ($K_i = 2.2$ nM), being 10 and 6 times more potent than acetazolamide, a standard inhibitor ($K_i = 250$ nM and 12 nM), respectively. Furthermore, this compound displayed 14-fold selectivity towards the hCA II isoform compared to hCA I. Molecular docking and MD simulations were performed to understand the atomic level interactions responsible for the selectivity of compound **1** towards hCA II.

Midgut transcriptomic responses to dengue and chikungunya viruses in the vectors *Aedes albopictus* and *Aedes malayensis*.

Modahl CM, Chowdhury A, Low DHW, Manuel MC, Missé D, Kini RM, Mendenhall IH, Pompon J.

12-07-2023

Sci Rep.

<https://pubmed.ncbi.nlm.nih.gov/37438463/>

Dengue (DENV) and chikungunya (CHIKV) viruses are among the most preponderant arboviruses. Although primarily transmitted through the bite of *Aedes aegypti* mosquitoes, *Aedes albopictus* and *Aedes malayensis* are competent vectors and have an impact on arbovirus epidemiology. Here, to fill the gap in our understanding of the molecular interactions between secondary vectors and arboviruses, we used transcriptomics to profile the whole-genome responses of *A. albopictus* to CHIKV and of *A. malayensis* to CHIKV and DENV at 1 and 4 days post-infection (dpi) in midguts. In *A. albopictus*, 1793 and 339 genes were significantly regulated by CHIKV at 1 and 4 dpi, respectively. In *A. malayensis*, 943 and 222 genes upon CHIKV infection, and 74 and 69 genes upon DENV infection were significantly regulated at 1 and 4 dpi, respectively. We reported 81 genes that were consistently differentially regulated in all the CHIKV-infected conditions, identifying a CHIKV-induced signature. We identified expressed immune genes in both mosquito species, using a de novo assembled midgut transcriptome for *A. malayensis*, and described the immune architectures. We found the JNK pathway activated in all conditions, generalizing its antiviral function to Aedines. Our comprehensive study provides insight into arbovirus transmission by multiple *Aedes* vectors.

Phospholipid binding of the dengue virus envelope E protein segment containing the conserved His residue.

Villalaín J.

10-07-2023

Biochim Biophys Acta Biomembr.

<https://pubmed.ncbi.nlm.nih.gov/37437754/>

Insights into dengue immunity from vaccine trials.

Ooi EE, Kalimuddin S.

12-06-2023

Sci Transl Med.

<https://pubmed.ncbi.nlm.nih.gov/37437017/>

Dengue virus M and E proteins belonging to genotype II (Cosmopolitan) of serotype 2 are influenced by the nature of M residue 36.

Decotter J, Desprès P, Gadea G.

Juil-2023

J Gen Virol.

<https://pubmed.ncbi.nlm.nih.gov/37436433/>

Twenty-two years of dengue outbreaks in Bangladesh: epidemiology, clinical spectrum, serotypes, and future disease risks.

Hossain MS, Noman AA, Mamun SMAA, Mosabbir AA.

11-07-2023

Trop Med Health.

<https://pubmed.ncbi.nlm.nih.gov/37434247/>

Dengue is the most rapidly spreading mosquito-borne disease and has become a major public health threat, particularly for tropical and subtropical countries including Bangladesh. This comprehensive review aims to summarize the overall scenario of dengue, including disease burden, clinical spectrum, seroprevalence, circulating serotypes/genotypes, and spatial distribution since the first recorded outbreak in Bangladesh. Since the first recorded outbreak in 2000, dengue epidemiology has shown the typical epidemic pattern with more frequent and bigger outbreaks and gradual geographic expansion to non-endemic regions in Bangladesh. For instance, highly confined Rohingya refugee camps that provide shelters to nearly 1.2 million forcibly displaced vulnerable Myanmar nationals in Cox's Bazar district confronted a massive outbreak in 2022. Recent major outbreaks are found to be associated with the emergence of serotype DENV-3, which was undetected for a long time. Consequently, changes in serotypes might be attributed to increased severity in clinical manifestation in recent years. The existing weak surveillance and risk management systems are inadequate to deal with impending dengue risks. The healthcare system, particularly at the district level, is not prepared to manage impending large-scale dengue outbreaks in Bangladesh. Our findings would contribute to the development of strategies for dengue control and management in Bangladesh as well as other similar settings elsewhere in the world.

Setting Dengue Fever Epidemic Thresholds Between 2016 and 2021 in the Central Health Region, Burkina Faso: An Ecological Study.

Ouédraogo JCRP, Ilboudo S, Ouédraogo E, Ouédraogo WT, Ouédraogo S, Samadoulougou BC, Kaboré M, Savadogo LGB.

11-07-2023

J Epidemiol Glob Health.

<https://pubmed.ncbi.nlm.nih.gov/37434033/>

Evaluación de la sensibilidad a organofosforados en poblaciones de *Aedes aegypti* (L.) (Diptera: Culicidae) del departamento de La Guajira, Colombia.

Maestre-Serrano R, Flórez-Rivadeneira Z, Castro-Camacho JM, Ochoa-Bohórquez L, Gómez-Camargo D, Pareja-Loaiza P, Ponce-García G, Flores AE.

30-06-2023

Biomedica.

<https://pubmed.ncbi.nlm.nih.gov/37433166/>

Introducción. El dengue es un problema de salud pública para el departamento de La Guajira. El control se ha enfocado en el vector con el uso de insecticidas, entre ellos los organofosforados. Objetivo. Evaluar el estado de la sensibilidad a insecticidas organofosforados de quince poblaciones de *Aedes aegypti* (L.) en el departamento de La Guajira, Colombia. Materiales y métodos. Se realizaron bioensayos para temefos, malatión y metil-pirimifos en larvas de tercer estadio y mosquitos adultos de *Ae. aegypti* en los municipios de Albania, Barrancas, Dibulla, Distracción, El Molino, Fonseca, Hatonuevo, La Jagua del Pilar, Maicao, Manaure, Riohacha, San Juan del Cesar, Uribia, Urumita y Villanueva, siguiendo la metodología de la Organización Mundial de la Salud (OMS) y la técnica de botellas usando la guía de los de los Centers for Disease Control and Prevention, respectivamente. Se determinó la sensibilidad por medio de la razón de resistencia a CL50 y CL95 (RRCL50, RRCL95) para temefos y a dosis y tiempo diagnóstico para temefos, malatión y metilpirimifos en las poblaciones de campo evaluadas, usando como control la cepa sensible Rockefeller. Resultados. Las 15 poblaciones del departamento de La Guajira son sensibles a: temefos (razón de la resistencia a RRCL50<5,0; relación de resistencia a CL95<5,0; 98 a 100 % de mortalidad); metil-pirimifos (99 a 100 % de mortalidad) y malatión (100 % de mortalidad). Conclusión. Con base en los resultados obtenidos, es factible el uso de temefos, malatión y metil-pirimifos para el control de *Ae. aegypti* en las poblaciones evaluadas.

Evaluación de la eficacia biológica y de la sensibilidad de *Aedes aegypti* a los insecticidas piretroides deltametrina y ciflutrina durante el brote del virus Zika en Kuna Yala, Panamá.

Cáceres L, Ayarza C, Bernal D.

30-06-2023

Biomedica.

<https://pubmed.ncbi.nlm.nih.gov/37433163/>

Introducción. El desarrollo de la resistencia a insecticidas de *Aedes aegypti* representa una gran amenaza para la salud pública. La vigilancia y el monitoreo de la eficacia biológica a los insecticidas y la sensibilidad de las poblaciones de *Aedes aegypti* es de fundamental importancia para prolongar la vida útil de estas moléculas. Objetivo. Evaluar la eficacia biológica de los insecticidas deltametrina y ciflutrina y la sensibilidad de poblaciones de *Aedes aegypti* a estos insecticidas durante el brote epidémico de virus del Zika en Kuna Yala, Panamá. Métodos y materiales. Se evaluó la eficacia biológica de la

deltametrina y la ciflutrina, y la sensibilidad a estos insecticidas de poblaciones de la cepa *Aedes aegypti* Ustupo, mediante bioensayos estandarizados por la Organización Mundial de la Salud durante el brote epidémico de virus del Zika en Kuna Yala, Panamá. Resultados. En los bioensayos con *Aedes aegypti* Ustupo se observó posible resistencia a deltametrina y a ciflutrina con un porcentaje de mortalidad del 95,3 y 94 %, respectivamente. Se registró baja eficacia biológica con la cepa *Aedes aegypti* Ustupo para la deltametrina y la ciflutrina, con medias de porcentajes de mortalidad de 75 y 31,1 %, en el intradomicilio, mientras que en el peridomicilio fue de 63,7 y 26,1 %, respectivamente. Conclusión. Los resultados de este estudio representan un desafío que debe enfrentar el Programa Nacional de Control de *Aedes* para lograr cuidar y mantener el efecto tóxico de los insecticidas aplicados contra las poblaciones de *Aedes*. Es necesario que el Programa Nacional de Control de *Aedes* establezca unos lineamientos de manejo de la resistencia para caracterizarla y evaluar la distribución geográfica de las poblaciones afectadas. Lo anterior con el propósito de garantizar la sostenibilidad de las intervenciones antivectoriales contra las poblaciones de *Aedes*.

Inhibition of phosphodiesterase 12 results in antiviral activity against several RNA viruses including SARS-CoV-2.

Thursz M, Sadiq F, Tree JA, Karayiannis P, Beasley DWC, Dejnirattisai W, Mongkolsapaya J, Screaton G, Wand M, Elmore MJ, Carroll MW, Matthews I, Thomas H.

Jul-2023

J Gen Virol.

<https://pubmed.ncbi.nlm.nih.gov/37432877/>

Dengue Fever-Induced Hypokalemic Paralysis in a Pregnant Patient: An Uncommon Presentation of a Common Disease.

Khan AB, Ali MA, Ur Rehman S, Siddique U, Ahmad S.

09-06-2023

Cureus.

<https://pubmed.ncbi.nlm.nih.gov/37431355/>

Human FcγRIIIa activation on splenic macrophages drives dengue pathogenesis in mice.

Yamin R, Kao KS, MacDonald MR, Cantaert T, Rice CM, Ravetch JV, Bournazos S.

10-07-2023

Nat Microbiol.

<https://pubmed.ncbi.nlm.nih.gov/37429907/>

Although dengue virus (DENV) infection typically causes asymptomatic disease, DENV-infected patients can experience severe complications. A risk factor for symptomatic disease is pre-existing anti-DENV IgG antibodies. Cellular assays suggested that these antibodies can enhance viral infection of Fcγ receptor (FcγR)-expressing myeloid cells. Recent studies, however, revealed more complex interactions between anti-DENV

antibodies and specific FcγRs by demonstrating that modulation of the IgG Fc glycan correlates with disease severity. To investigate the in vivo mechanisms of antibody-mediated dengue pathogenesis, we developed a mouse model for dengue disease that recapitulates the unique complexity of human FcγRs. In in vivo mouse models of dengue disease, we discovered that the pathogenic activity of anti-DENV antibodies is exclusively mediated through engagement of FcγRIIIa on splenic macrophages, resulting in inflammatory sequelae and mortality. These findings highlight the importance of IgG-FcγRIIIa interactions in dengue, with important implications for the design of safer vaccination approaches and effective therapeutic strategies.

Identification of alpha-linolenic acid as a broad-spectrum antiviral against zika, dengue, herpes simplex, influenza virus and SARS-CoV-2 infection.

Feng Y, Yang Y, Zou S, Qiu S, Yang H, Hu Y, Lin G, Yao X, Liu S, Zou M.

08-07-2023

Antiviral Res.

<https://pubmed.ncbi.nlm.nih.gov/37429528/>

Zika virus (ZIKV) has garnered global attention due to its association with severe congenital defects including microcephaly. However, there are no licensed vaccines or drugs against ZIKV infection. Pregnant women have the greatest need for treatment, making drug safety crucial. Alpha-linolenic acid (ALA), a polyunsaturated ω-3 fatty acid, has been used as a health-care product and dietary supplement due to its potential medicinal properties. Here, we demonstrated that ALA inhibits ZIKV infection in cells without loss of cell viability. Time-of-addition assay revealed that ALA interrupts the binding, adsorption, and entry stages of ZIKV replication cycle. The mechanism is probably that ALA disrupts membrane integrity of the virions to release ZIKV RNA, inhibiting viral infectivity. Further examination revealed that ALA inhibited DENV-2, HSV-1, influenza virus and SARS-CoV-2 infection dose-dependently. ALA is a promising broad-spectrum antiviral agent.

Downregulation of Microcephaly-Causing Genes as a Mechanism for ZIKV Teratogenesis: A Meta-analysis of RNA-Seq Studies.

Gomes JA, Sgarioni E, Kowalski TW, Giudicelli GC, Recamonde-Mendoza M, Fraga LR, Schüler-Faccini L, Vianna FSL.

10-07-2023

J Mol Neurosci.

<https://pubmed.ncbi.nlm.nih.gov/37428363/>

5'/3' RACE method for sequencing the 5' and 3' untranslated regions of Zika virus.

Álvarez-Díaz DA, Usme-Ciro JA, Corchuelo S, Naizaque JR, Rivera JA, Castiblanco-Martínez HD, Torres-Fernández O, Rengifo AC.

10-07-2023

Arch Virol.

<https://pubmed.ncbi.nlm.nih.gov/37428234/>

The spread of Zika virus (ZIKV) from the African continent to the Americas promoted its molecular evolution, as reflected by mutations in its RNA genome. Most of the ZIKV genome sequences in the GenBank database have incomplete 5' and 3' UTR sequences, reflecting the deficiency of whole-genome sequencing technologies to resolve the sequences of the genome ends. We modified a protocol for rapid amplification of cDNA ends (RACE) to determine the complete sequences of the 5' and 3' UTRs of a previously reported ZIKV isolate (GenBank no. MH544701.1). This strategy is useful for determining 5' and 3' UTR sequences of ZIKV isolates and will be useful for comparative genomics applications.

Methods for Embedding Cell-Free Protein Synthesis Reactions in Macro-Scale Hydrogels.

Kavil S, Laverick A, Whitfield CJ, Banks AM, Howard TP.

23-06-2023

J Vis Exp.

<https://pubmed.ncbi.nlm.nih.gov/37427932/>

Development of a thermochromic lateral flow assay to improve sensitivity for dengue virus serotype 2 NS1 detection.

Trakoolwilaiwan T, Takeuchi Y, Leung TS, Sebek M, Storozhuk L, Nguyen L, Tung LD, Thanh NTK.

10-07-2023

Nanoscale.

<https://pubmed.ncbi.nlm.nih.gov/37427537/>

Dengue disease is a viral infection that has been widespread in tropical regions, such as Southeast Asia, South Asia and South America. A worldwide effort has been made over a few decades to halt the spread of the disease and reduce fatalities. Lateral flow assay (LFA), a paper-based technology, is used for dengue virus detection and identification because of its simplicity, low cost and fast response. However, the sensitivity of LFA is relatively low and is usually insufficient to meet the minimum requirement for early detection. In this study, we developed a colorimetric thermal sensing LFA format for the detection of dengue virus NS1 using recombinant dengue virus serotype 2 NS1 protein (DENV2-NS1) as a model antigen. Plasmonic gold nanoparticles, including gold nanospheres (AuNSPs) and gold nanorods (AuNRs), and magnetic nanoparticles (MNPs), namely iron oxide nanoparticles (IONPs) and zinc ferrite nanoparticles (ZFNPs), were studied for their thermal properties for sensing assays. AuNSPs with 12 nm diameter were chosen due to their great photothermal effect against light-emitting diodes (LEDs). In the thermal sensing assay, a thermochromic sheet is used as a temperature sensor transforming heat into a visible colour. In the typical LFA, the test line is visible at 6.25 ng mL⁻¹ while our thermal sensing LFA offers a visual signal that can be observed at as low as 1.56 ng mL⁻¹. The colorimetric thermal sensing LFA is capable of reducing the limit of detection (LOD) of DENV2-NS1 by 4 times compared to the typical visual readout. The colorimetric thermal sensing LFA can enhance the sensitivity of detection and deliver visually to

the user to translate without the need for an infrared (IR) camera. It has the potential to expand the utilities of LFA and satisfy early diagnostic applications.

Chikungunya outbreak in Africa: a review of the literature.

Chinedu Eneh S, Uwishema O, Nazir A, El Jurdi E, Faith Olanrewaju O, Abbass Z, Mustapha Jolayemi M, Mina N, Kseiry L, Onyeaka H.

19-06-2023

Ann Med Surg (Lond).

<https://pubmed.ncbi.nlm.nih.gov/37427196/>

The Chikungunya virus (CHIKV), transmitted via mosquitoes, exhibits clinical manifestations ranging from headaches, myalgia and arthralgia to debilitating systemic malfunctions. Endemic to Africa, CHIKV has seen an increase in cases since it was first recorded in 1950. There has recently been an outbreak in numerous African nations. The authors aim to review the history and epidemiology of CHIKV in Africa, current outbreaks, strategies adopted by governments and/or international organisations to mitigate such an outbreak, and future recommendations that can be employed. **Methodology:** Data were collected from medical journals published on Pubmed and Google Scholar, and from the official World Health Organisation, African and United States of America's Centres for Disease Control and Prevention websites. All articles considering CHIKV in Africa, including epidemiology, aetiology, prevention and management, were sought after. **Results:** Since 2015, the number of Chikungunya cases in Africa has increased, reaching the highest values ever recorded, especially in 2018 and 2019. Even though numerous vaccination and therapeutic intervention trials are still ongoing, no advancement has been made so far, including drug approval. Current management is supportive, with preventative measures, such as insecticides, repellents, mosquito nets and habitat avoidance, paramount to halting disease spread. **Conclusion:** In light of the recent CHIKV outbreak in Africa, local and global attempts are re-emerging to mitigate the eruption of the case of the lack of vaccines and antivirals, controlling the virus may be an arduous feat. Improving risk assessment, laboratory detection and research facilities should be a priority.

Yellow fever disease severity and endothelial dysfunction are associated with elevated serum levels of viral NS1 protein and syndecan-1.

de Sousa FTG, Warnes CM, Manuli ER, Ng A, Zanella LGFABD, Ho YL, Bhat S, Romano CM, Beatty PR, Biering SB, Kallas EG, Sabino EC, Harris E.

30-06-2023

medRxiv.

<https://pubmed.ncbi.nlm.nih.gov/37425955/>

Immunologically mediated trade-offs shaping transmission of sylvatic dengue and Zika viruses in native and novel non-human primate hosts.

Hanley KA, Cecilia H, Azar SR, Moehn B, Yu W, Yun R, Althouse BM, Vasilakis N, Rossi SL.

27-06-2023

bioRxiv.

<https://pubmed.ncbi.nlm.nih.gov/37425901/>

MGSurvE: A framework to optimize trap placement for genetic surveillance of mosquito population.

Sánchez C HM, Smith DL, Marshall JM.

27-06-2023

bioRxiv.

<https://pubmed.ncbi.nlm.nih.gov/37425729/>

Genetic surveillance of mosquito populations is becoming increasingly relevant as genetics-based mosquito control strategies advance from laboratory to field testing. Especially applicable are mosquito gene drive projects, the potential scale of which leads monitoring to be a significant cost driver. For these projects, monitoring will be required to detect unintended spread of gene drive mosquitoes beyond field sites, and the emergence of alternative alleles, such as drive-resistant alleles or non-functional effector genes, within intervention sites. This entails the need to distribute mosquito traps efficiently such that an allele of interest is detected as quickly as possible - ideally when remediation is still viable. Additionally, insecticide-based tools such as bednets are compromised by insecticide-resistance alleles for which there is also a need to detect as quickly as possible. To this end, we present MGSurvE (Mosquito Gene SurveillanceE): a computational framework that optimizes trap placement for genetic surveillance of mosquito populations such that the time to detection of an allele of interest is minimized. A key strength of MGSurvE is that it allows important biological features of mosquitoes and the landscapes they inhabit to be accounted for, namely: i) resources required by mosquitoes (e.g., food sources and aquatic breeding sites) can be explicitly distributed through a landscape, ii) movement of mosquitoes may depend on their sex, the current state of their gonotrophic cycle (if female) and resource attractiveness, and iii) traps may differ in their attractiveness profile. Example MGSurvE analyses are presented to demonstrate optimal trap placement for: i) an *Aedes aegypti* population in a suburban landscape in Queensland, Australia, and ii) an *Anopheles gambiae* population on the island of São Tomé, São Tomé and Príncipe. Further documentation and use examples are provided in project's documentation. MGSurvE is freely available as an open-source Python package on pypi (<https://pypi.org/project/MGSurvE/>). It is intended as a resource for both field and computational researchers interested in mosquito gene surveillance. **Author summary:** Mosquito-borne diseases such as malaria and dengue fever continue to pose a major health burden throughout much of the world. The impact of currently-available tools, such as insecticides and antimalarial drugs, is stagnating, and gene drive-modified mosquitoes are considered a novel tool that could contribute to continuing reductions in disease transmission. Gene drive approaches are unique in the field of vector control in that they involve transgenes that could potentially spread on a wide scale, and consequently, surveillance is expected to

be a major cost driver for the technology. This is needed to monitor for unintended spread of intact drive alleles, and the emergence of alternative alleles such as homing-resistance alleles and non-functional effector genes. Additionally, surveillance of insecticide-resistance alleles is of interest to support the impact of insecticide-based tools such as bednets. Here, we present MGSurvE, a computational framework that optimizes trap placement for genetic surveillance of mosquito populations in order to minimize the time to detection for an allele of interest. MGSurvE has been tailored to various features of mosquito ecology, and is intended as a resource for researchers to optimize the efficiency of limited surveillance resources.

Wolbachia -mediated resistance to Zika virus infection in *Aedes aegypti* is dominated by diverse transcriptional regulation and weak evolutionary pressures.

Boehm EC, Jaeger AS, Ries HJ, Castañeda D, Weiler AM, Valencia CC, Weger-Lucarelli J, Ebel GD, O'Connor SL, Friedrich TC, Zamanian M, Aliota MT.

26-06-2023

bioRxiv.

<https://pubmed.ncbi.nlm.nih.gov/37425681/>

A promising candidate for arbovirus control and prevention relies on replacing arbovirus-susceptible *Aedes aegypti* populations with mosquitoes that have been colonized by the intracellular bacterium *Wolbachia* and thus have a reduced capacity to transmit arboviruses. This reduced capacity to transmit arboviruses is mediated through a phenomenon referred to as pathogen blocking. Pathogen blocking has primarily been proposed as a tool to control dengue virus (DENV) transmission, however it works against a range of viruses, including Zika virus (ZIKV). Despite years of research, the molecular mechanisms underlying pathogen blocking still need to be better understood. Here, we used RNA-seq to characterize mosquito gene transcription dynamics in *Ae. aegypti* infected with the w Mel strain of *Wolbachia* that are being released by the World Mosquito Program in Medellín, Colombia. Comparative analyses using ZIKV-infected, uninfected tissues, and mosquitoes without *Wolbachia* revealed that the influence of w Mel on mosquito gene transcription is multifactorial. Importantly, because *Wolbachia* limits, but does not completely prevent, replication of ZIKV and other viruses in coinfecting mosquitoes, there is a possibility that these viruses could evolve resistance to pathogen blocking. Therefore, to understand the influence of *Wolbachia* on within-host ZIKV evolution, we characterized the genetic diversity of molecularly barcoded ZIKV virus populations replicating in *Wolbachia*-infected mosquitoes and found that within-host ZIKV evolution was subject to weak purifying selection and, unexpectedly, loose anatomical bottlenecks in the presence and absence of *Wolbachia*. Together, these findings suggest that there is no clear transcriptional profile associated with *Wolbachia*-mediated ZIKV restriction, and that there is no evidence for ZIKV escape from this restriction in our system. **Author summary:** When *Wolbachia* bacteria infect *Aedes aegypti*

mosquitoes, they dramatically reduce the mosquitoes' susceptibility to infection with a range of arthropod-borne viruses, including Zika virus (ZIKV). Although this pathogen-blocking effect has been widely recognized, its mechanisms remain unclear. Furthermore, because *Wolbachia* limits, but does not completely prevent, replication of ZIKV and other viruses in coinfecting mosquitoes, there is a possibility that these viruses could evolve resistance to *Wolbachia*-mediated blocking. Here, we use host transcriptomics and viral genome sequencing to examine the mechanisms of ZIKV pathogen blocking by *Wolbachia* and viral evolutionary dynamics in *Ae. aegypti* mosquitoes. We find complex transcriptome patterns that do not suggest a single clear mechanism for pathogen blocking. We also find no evidence that *Wolbachia* exerts detectable selective pressures on ZIKV in coinfecting mosquitoes. Together our data suggest that it may be difficult for ZIKV to evolve *Wolbachia* resistance, perhaps due to the complexity of the pathogen blockade mechanism.

Corrigendum: Drug repurposing approach against chikungunya virus: an in vitro and in silico study.

Kasabe B, Ahire G, Patil P, Punekar M, Davuluri KS, Kakade M, Alagarasu K, Parashar D, Cherian S.

23-06-2023

Front Cell Infect Microbiol.

<https://pubmed.ncbi.nlm.nih.gov/37424775/>

Insight into the seroepidemiology and dynamics of circulating serotypes of dengue virus over a 4 year period in western Uttar Pradesh, India.

Mustafa Z, Khan HM, Azam M, Sami H, Ali SG, Ahmad I, Raza A, Khan MA.

23-06-2023

Access Microbiol.

<https://pubmed.ncbi.nlm.nih.gov/37424567/>

An important public health problem in India is dengue infection, with every year seeing an increase in cases of dengue fever. Dengue affects all individuals irrespective of their gender and age, although the infection rate is higher among males and younger people. Despite low severity in general, dengue virus can cause severe health conditions in some individuals. Genetic characterization of circulating endemic dengue virus (DENV) serotypes plays a significant role in providing epidemiological knowledge and subsequent vaccine development. In the present study, over a 4 year period, we assessed DENV transmission dynamics in major regions of western Uttar Pradesh in North India. ELISA tests were used to diagnose dengue, and PCRs were used to determine the circulating serotype. We found that dengue infection peaks after the rainy season and affects all sexes and ages. A total of 1277 individuals were found positive for dengue; among them, 61.7 % were male and 38.3 % were female. DEN-1 was found in 23.12 %, DEN-2 in 45 %, DEN-3 in 29.06 % and DEN-4 in 1.5 % of the dengue-infected individuals. All four DENV serotypes were circulating in the study area, and

DENV serotype-2 (DEN-2) was the most prevalent serotype.

Dengue Severity Score for Predicting Severe Dengue in Children: Need to Validate in Different Settings.

Sookaromdee P, Wiwanitkit V.

15-07-2023

Indian Pediatr.

<https://pubmed.ncbi.nlm.nih.gov/37424133/>

Political instability hampering Peruvian dengue response.

Daniels JP.

08-07-2023

Lancet.

<https://pubmed.ncbi.nlm.nih.gov/37423219/>

Design, synthesis, and biological evaluation of a series of new anthraquinone derivatives as anti-ZIKV agents.

Zhu Y, Yu J, Chen T, Liu W, Huang Y, Li J, Zhang B, Zhu G, He Z, Long Y, Yuan J.

03-07-2023

Eur J Med Chem.

<https://pubmed.ncbi.nlm.nih.gov/37421888/>

Nanoliposomes containing three essential oils from the Artemisia genus as effective larvicides against Aedes aegypti and Anopheles stephensi.

Sanei-Dehkordi A, Ghasemian A, Zarenezhad E, Qasemi H, Nasiri M, Osanloo M.

07-07-2023

Sci Rep.

<https://pubmed.ncbi.nlm.nih.gov/37420038/>

Aedes aegypti and *Anopheles stephensi* have challenged human health by transmitting several infectious disease agents, such as malaria, dengue fever, and yellow fever. Larvicides, especially in endemic regions, is an effective approach to the control of mosquito-borne diseases. In this study, the composition of three essential oil from the *Artemisia* L. family was analyzed by Gas Chromatography-Mass Spectrometry. Afterward, nanoliposomes containing essential oils of *A. annua*, *A. dracunculus*, and *A. sieberi* with particle sizes of 137 ± 5 , 151 ± 6 , and 92 ± 5 nm were prepared. Besides, their zeta potential values were obtained at 32 ± 0.5 , 32 ± 0.6 , and 43 ± 1.7 mV. ATR-FTIR analysis (Attenuated Total Reflection-Fourier Transform InfraRed) confirmed the successful loading of the essential oils. Moreover, The LC₅₀ values of nanoliposomes against *Ae. aegypti* larvae were 34, 151, and 197 µg/mL. These values for *An. stephensi* were obtained as 23 and 90, and 140 µg/mL, respectively. The results revealed that nanoliposomes containing *A. dracunculus* exerted the highest potential larvicidal effect against *Ae. aegypti* and *An. stephensi*, which can be considered against other mosquitoes.

Murine typhus is a common cause of acute febrile illness in Bandung, Indonesia.

Riswari SF, Prodjosoeowo S, Mony SR, Megantara I, Iskandar S, Mayasari W, Heryaman H, Mast Q, der Ven AV, Kosasih H, Alisjahbana B.

07-07-2023

PLoS One.

<https://pubmed.ncbi.nlm.nih.gov/37418452/>

Zika Virus Among Department of Defense Service Members and Beneficiaries, 2013-2022.

Touchstone K, Matsumoto K, Seliga N.

20-03-2023

MSMR.

<https://pubmed.ncbi.nlm.nih.gov/37418358/>

Identification of risk factors and mosquito vectors associated with dengue virus infection in American Samoa, 2017.

Sharp TM, Tufa AJ, Cotter CJ, Lozier MJ, Santiago GA, Johnson SS, Mataia'a M, Waterman SH, Muñoz-Jordán JL, Paz-Bailey G, Hemme RR, Schmaedick MA, Anesi S.

07-07-2023

PLOS Glob Public Health.

<https://pubmed.ncbi.nlm.nih.gov/37418355/>

Introduction: The first outbreak of dengue in American Samoa was reported in 1911. Sporadic outbreaks have been reported since, as were outbreaks of other pathogens transmitted by *Aedes* species mosquitoes including Ross River, chikungunya, and Zika viruses. During an outbreak of dengue virus-type 2 (DENV-2) in 2016-2018, we conducted household-based cluster investigations to identify population-specific risk factors associated with infection and performed entomologic surveillance to determine the relative abundance of *Ae. aegypti* and *Ae. polynesiensis*. **Methods and findings:** We contacted dengue patients who had tested positive for DENV infection and offered them as well as their household members participation in household-based cluster investigations. For those that accepted participation, we also offered participation to residents of households within a 50-meter radius of each case-patient's home. Questionnaires were administered and serum specimens collected for testing by RT-PCR and anti-DENV IgM ELISA. Adult female mosquitoes were aspirated from inside and outside participating households and tested by RT-PCR. We analyzed characteristics associated with DENV infection in bivariate analyses. A total of 226 participants was enrolled from 91 households in 20 clusters. Median age of participants was 34 years (range: <1-94), and 56.2% were female. In total, 7 (3.2%) participants had evidence of DENV infection by IgM ELISA (n = 5) or RT-PCR (n = 2). Factors significantly associated with DENV infection were reporting a febrile illness in the past three months (prevalence ratio: 7.5 [95% confidence interval: 1.9-29.8]) and having a household septic tank (Fisher's Exact Test, p = 0.004). Of 93 *Ae. aegypti* and 90 *Ae. polynesiensis* females collected, 90% of *Ae. aegypti* were collected inside homes whereas 83% of *Ae.*

polynesiensis were collected outside homes. DENV nucleic acid was not detected in any mosquito pools. Sequencing of the DENV-2 from patient specimens identified the Cosmopolitan genotype of DENV-2 and was most closely related to virus detected in the Solomon Islands during 2016. **Conclusions:** This investigation demonstrated that dengue is a continuing risk in American Samoa. Increased frequency of infection among residents with a septic tank suggests a need to investigate whether septic tanks serve as larval habitats for mosquito vectors of DENV in American Samoa. Future efforts should also evaluate the role of *Ae. polynesiensis* in DENV transmission in the wild.

Zika virus dumbbell-1 structure is critical for sfRNA presence and cytopathic effect during infection.

Graham ME, Merrick C, Akiyama BM, Szucs MJ, Leach S, Kieft JS, Beckham JD.

07-07-2022

mBio.

<https://pubmed.ncbi.nlm.nih.gov/37417764/>

All flaviviruses contain conserved RNA structures in the 3' untranslated region (3' UTR) that are important for flavivirus RNA replication, translation, and pathogenesis. Flaviviruses like Zika virus (ZIKV) contain multiple conserved RNA structures in the viral 3' UTR, including the structure known as dumbbell-1 (DB-1). Previous research has shown that the DB-1 structure is important for flavivirus positive-strand genome replication, but the functional role of the flavivirus DB-1 structure and the mechanism by which it contributes to viral pathogenesis are not known. Using the recently solved flavivirus DB RNA structural data, we designed two DB-1 mutant ZIKV infectious clones, termed ZIKV-TL.PK and ZIKV-p.2.5', which disrupt DB-1 tertiary folding. We found that viral positive-strand genome replication of both ZIKV DB-1 mutant clones is similar to wild-type (WT) ZIKV, but ZIKV DB-1 mutants exhibit significantly decreased cytopathic effect due to reduced caspase-3 activation. We next show that ZIKV DB-1 mutants exhibit decreased levels of sfRNA species compared to ZIKV-WT during infection. However, ZIKV DB-1 mutant 3' UTRs exhibit unchanged sfRNA biogenesis following XRN1 degradation *in vitro*. We also found that ZIKV DB-1 mutant virus (ZIKV-p.2.5') exhibited enhanced sensitivity to type I interferon treatment, and both ZIKV-DB-1 mutants exhibit reduced morbidity and mortality due to tissue-specific attenuated viral replication in brain tissue of interferon type I/II receptor knockout mice. We propose that the flavivirus DB-1 RNA structure maintains sfRNA levels during infection despite maintained sfRNA biogenesis, and these results indicate that ZIKV DB-dependent maintenance of sfRNA levels support caspase-3-dependent, cytopathic effect, type I interferon resistance, and viral pathogenesis in mammalian cells and in a ZIKV murine model of disease. **IMPORTANCE** The group of viruses termed flaviviruses cause important disease throughout the world and include dengue virus, Zika virus, Japanese encephalitis virus, and many more. All of these flaviviruses have highly conserved RNA structures in the untranslated regions of the virus genome. One of the shared RNA structures, termed the dumbbell region, is not well studied, but mutations in this

region are important for vaccine development. In this study, we made structure-informed targeted mutations in the Zika virus dumbbell region and studied the effect on the virus. We found that Zika virus dumbbell mutants are significantly weakened or attenuated due to a decreased ability to produce non-coding RNA that is needed to support infection, support virus-induced cell death, and support escape from the host immune system. These data show that targeted mutations in the flavivirus dumbbell RNA structure may be an important approach to develop future vaccine candidates.

Threshold dynamics of a stochastic mathematical model for Wolbachia infections.

Yang J, Chen Z, Tan Y, Liu Z, Cheke RA.

Déc-2023

J Biol Dyn.

<https://pubmed.ncbi.nlm.nih.gov/37417698/>

Diagnostic approaches for dengue infection.

Theragarajan G, Sekaran SD.

13-07-2023

Expert Rev Mol Diagn.

<https://pubmed.ncbi.nlm.nih.gov/37417532/>

Introduction: Every year, a significant rise in dengue incidence observed is responsible for 10% of fever episodes in children and adolescents in endemic countries. Considering that the symptoms of dengue are similar to those of many other viruses, early diagnosis of the disease has long been difficult, and lack of sensitive diagnostic tools may be another factor contributing to a rise in dengue incidence. **Areas covered:** This review will highlight dengue diagnostics strategies and discuss other possible targets for dengue diagnosis. Understanding the dynamics of the immune response and how it affects viral infection has enabled informed diagnosis. As more technologies emerge, precise assays that include some clinical markers need to be included. **Expert opinion:** Future diagnostic strategies will require the use both viral and clinical markers in a serial manner with the use of artificial intelligence technology to determine from the first point of illness to better determine severity status and management. A definitive endpoint is not in the horizon as the disease as well as the virus is constantly evolving and hence many developed assays need to be constantly changing some of their reagents periodically as newer genotypes and probably too serotypes emerge.

Sheehan's Syndrome unmasked by dengue fever: A case report and review of literature.

Gutte SH, Pal S, Bhaskar B, Kurian NM, Sanket, Gurjar M.

Avr-Juil 2023

J Vector Borne Dis.

<https://pubmed.ncbi.nlm.nih.gov/37417174/>

Early virus clearance of SARS-CoV-2 among co-infection with malaria.

Rathi PM, Mahajan NN, Srivastava V, Junare PR, Bansal S, Kaushal N, Rathod DB.

Avr-Juil 2023

J Vector Borne Dis.

<https://pubmed.ncbi.nlm.nih.gov/37417172/>

Background and objectives: India has witnessed significant number of cases of co-infection of malaria or dengue with COVID-19, especially during the monsoon season. It has been speculated that anti-malarial immunity might have a protective role in co-infection. Retrospective analysis of co-infection of vector-borne diseases with COVID-19 was done for comparing their remission with matched controls with COVID-19 by means of epidemiological data.

Methods: Medical case records of patients with co-infection of malaria or dengue with COVID-19 admitted at TNMC and BYL Nair Charitable Hospital from 1 March 2020 to 31 October 2020 were analyzed retrospectively. Out of 91 cases of co-infection of SARS-CoV-2 infection with vector-borne diseases, virus clearance (VC) analysis was done for 61 co-infections with malaria. **Results:** Median duration of VC for co-infection with malaria was 8 days whereas, it was 12 days for controls with COVID-19 ($p=0.056$). Young patients (≤ 50 years) with co-infection recovered faster than controls age ($p=0.018$).

Interpretation & conclusion: Co-infection with malaria is associated with less severe disease and early recovery in the form of early VC. Genetic and immunological studies are necessary to confirm malaria protection against SARS-CoV-2 infection.

Impact of COVID-19 lockdown during 2020 on the occurrence of vector-borne diseases in India.

Mayilsamy M, Vijayakumar A, Veeramanocharan R, Rajaiah P, Balakrishnan V, Kumar A.

Avr-Juil 2023

J Vector Borne Dis.

<https://pubmed.ncbi.nlm.nih.gov/37417171/>

Background & objectives: India imposed one of the world's largest nationwide lockdown in the aftermath of COVID-19 pandemic in March 2020 which was partly extended up to December. Some of the impacts of the COVID-19 lockdown on the economy, research, travel, education, and sports were readily apparent; the same was less obvious in the occurrence of vector-borne diseases (VBDs). The objective of this study was to statistically determine the impact of the COVID-19 lockdown on the occurrence of VBDs in India. **Methods:** The reported incidence of VBDs such as malaria, dengue, Chikungunya, Japanese encephalitis, and kala-azar in India during the years 2015-2019 was analyzed by fitting Poisson and negative binomial (NB) models for each VBDs separately. The number of cases reported was compared with the number of cases predicted for each year from 2015 to 2020 for all the VBDs under study to infer whether or not the lockdown had any impact on their prevalence in India.

Results: The percentage of the actual case was lower by 46, 75, 49, 72, and 38 respectively for malaria, dengue, Chikungunya, Japanese encephalitis, and kala-azar when comparing the lockdown period and the year before lockdown (2020 vs. 2019). The number of cases predicted for the year 2020 based on the trend of the five preceding

years (2015-2019) also showed a great variation between actual and predicted cases. The differences in cases were considered as the cases missed in 2020 were largely due to the lockdown. **Interpretation & conclusion:** The analysis showed that the lockdown had a considerable impact on the occurrence of VBDs.

Urban arbovirolos in the state of São Paulo, Brazil: A retrospective study.

Franco BC, Souza BLAC, Leal RM, Maciel LTR, Coêlho MDG.

Avr-Juil 2023

J Vector Borne Dis.

<https://pubmed.ncbi.nlm.nih.gov/37417169/>

Studies on the breeding potential and entomological indices of dengue vector Aedes aegypti and Aedes albopictus in the district Ghaziabad of Uttar Pradesh, India.

Singh SP, Singh H, Saini S, Mishra GK, Sharma SK.

Avr-Juil 2023

J Vector Borne Dis.

<https://pubmed.ncbi.nlm.nih.gov/37417168/>

Genomic characterization and evolutionary analysis of dengue virus from Aedes mosquitoes in Telangana, India.

Sanku P, Ravinuthala VSU, Mopuri R, Mutheneni SR, Addlagatta A.

Avr-Juil 2023

J Vector Borne Dis.

<https://pubmed.ncbi.nlm.nih.gov/37417167/>

Background & objectives: Entomological surveillance for mosquito-borne viruses is vital for monitoring disease transmission and vector control programs. The vector control program is reliant not only on vector density but also on the timely detection of mosquito-borne infections. In the present study, we conducted an entomological surveillance in different locations of Hyderabad, Telangana, India during 2017-2018 and the collected mosquitoes were screened for dengue virus. **Methods:** Reverse transcriptase polymerase chain reaction (RT-PCR) was used for the identification and serotyping of the dengue virus. Bioinformatics analysis was performed using Mega 6.0 software. Followed by phylogenetic analysis, which was based on CprM structural genome sequence, was performed by using the Maximum-Likelihood method.

Results: The TaqMan RT-PCR assay was used to analyze the serotypes of 25 pools of Aedes mosquitoes and found that all four serotypes are circulating in Telangana. DENV1 (50%) was the most commonly detected serotype followed by DENV2 (16.6%), DENV3 (25%), and DENV4 (8.3%). Moreover, DENV1 has the highest MIR (16 per 1000 mosquitoes) compared with DENV2, 3, and 4. The CprM structural gene sequence was used for phylogenetic analysis, revealing that all four strains have a close relationship with strains isolated from India, Pakistan, China and Thailand. Similarly, two variations in amino acid sequence DENV1 at position 43 (K-R) and 86 (S-T) and a

single mutation DENV2 at 111 amino acid position were observed. **Interpretation & conclusion:** The results of the study provide an in-depth transmission dynamic of the dengue virus and persistence of this emerging pathogen in Telangana, India that needs appropriate prevention programs.

Wolbachia infection is widespread in brackish and fresh water *Aedes albopictus* (Diptera: Culicidae) in the coastal Jaffna peninsula of northern Sri Lanka.

Tharsan A, Sivabalakrishnan K, Arthiyan S, Eswaramohan T, Raveendran S, Ramasamy R, Surendran SN.

Avr-Juil 2023

J Vector Borne Dis.

<https://pubmed.ncbi.nlm.nih.gov/37417166/>

Epitope prediction and designing of receptor inhibitor of Dengue Envelope Protein: An in silico approach.

Uttam G, Kumari A, Singh K.

Avr-Juil 2023

J Vector Borne Dis.

<https://pubmed.ncbi.nlm.nih.gov/37417165/>

Background & objectives: Dengue virus (DENV) is the causative agent of dengue fever (DF) and dengue hemorrhagic fever (DHF). It has four distinct serotypes (DENV-1, DENV-2, DENV-3, and DENV-4) based on their antigenic properties. Mostly, the immunogenic epitopes are present in the envelope (E) protein of the virus. Heparan sulfate (HS) acts as a receptor and interacts with the E protein of the virus thus facilitating the entry of dengue virus into human cells. This study focuses on epitope prediction on the E protein of the DENV serotype. The non-competitive inhibitors of HS were designed using bioinformatics. **Methods:** In the present study, epitope prediction of the E protein of DENV serotypes was performed using the ABCpred server and IEDB analysis resource. The interactions of HS and viral E proteins (PDB ID: 3WE1 and PDB ID:1TG8) were evaluated through AutoDock. Subsequently, non-competitive inhibitors were designed to bind the E protein of DENV better than HS. All the docking results were validated by re-docking the ligand-receptor complexes and superimposing them onto their co-crystallized complexes using AutoDock and visualizing them in Discovery Studio. **Results:** The result predicted B-cell and T-cell epitopes on the E protein of DENV serotypes. The designed HS ligand 1 (non-competitive inhibitor) demonstrated potential binding with the DENV E protein, thereby inhibiting HS-E protein binding. The re-docked complexes were superimposed entirely onto the native co-crystallized complexes (low root mean square deviation values), which validates the docking protocols. **Interpretation & conclusion:** The identified B-cell and T-cell epitopes of the E protein and non-competitive inhibitors of HS (ligand 1) could be used in the designing of potential drug candidates against the dengue virus.

Status of insecticide resistance in the dengue vector *Aedes aegypti* in India: A review.

Sumitha MK, Kalimuthu M, Senthil MK, Paramasivan R, Kumar A, Gupta B.

Avr-Juil 2023

J Vector Borne Dis.

<https://pubmed.ncbi.nlm.nih.gov/37417161/>

Epidemic retinitis during pregnancy.

Kawali A, Mahendradas P, Sanjay S, Mishra SB, Shetty B.

Juil-2023

Indian J Ophthalmol.

<https://pubmed.ncbi.nlm.nih.gov/37417121/>

Targeting Type I Interferon Induction and Signaling: How Zika Virus Escapes from Host Innate Immunity.

Hu H, Feng Y, He ML.

04-06-2023

Int J Biol Sci.

<https://pubmed.ncbi.nlm.nih.gov/37416780/>

Zika virus (ZIKV) infection causes neurological disorders and draws great attention. ZIKV infection can elicit a wide range of immune response. Type I interferons (IFNs) as well as its signaling cascade play crucial role in innate immunity against ZIKV infection and in turn ZIKV can antagonize them. ZIKV genome are mainly recognized by Toll-like receptors 3 (TLR3), TLR7/8 and RIG-I-like receptor 1 (RIG-1), which induces the expression of Type I IFNs and interferon-stimulated genes (ISGs). ISGs exert antiviral activity at different stages of the ZIKV life cycle. On the other hand, ZIKV takes multiple strategies to antagonize the Type I IFN induction and its signaling pathway to establish a pathogenic infection, especially by using the viral nonstructural (NS) proteins. Most of the NS proteins can directly interact with the factors in the pathways to escape the innate immunity. In addition, structural proteins also participate in the innate immune evasion and activation of antibody-binding of blood dendritic cell antigen 2 (BDCA2) or inflammasome also be used to enhance ZIKV replication. In this review, we summarize the recent findings about the interaction between ZIKV infection and type I IFNs pathways and suggest potential strategies for antiviral drug development.

First report on knockdown resistance mutations in wild populations of *Aedes aegypti* from Argentina determined by a novel multiplex high-resolution melting polymerase chain reaction method.

Barrera-Illanes AN, Micieli MV, Ibáñez-Shimabukuro M, Santini MS, Martins AJ, Ons S.

06-07-2023

Parasit Vectors.

<https://pubmed.ncbi.nlm.nih.gov/37415215/>

Background: The mosquito *Aedes aegypti* is an urban vector of dengue and other arboviruses. During epidemics of these viruses, pyrethroid insecticides are used for the control of adult mosquitoes. The worldwide resistance of

Ae. aegypti to these insecticides is a cause of failure of vector control campaigns. The primary target of pyrethroids is the voltage-gated sodium channel. Point mutations in the gene coding for this channel, called knockdown resistance (kdr) mutations, are associated with pyrethroid resistance. Two kdr mutations, V1016I and F1534C, have increased in frequency in natural populations of *Ae. aegypti* in the Americas during the last decade. Their association with pyrethroid resistance has been largely demonstrated in field populations throughout the Americas, and in in vitro assays. Diagnostics for kdr polymorphism allow early detection of the spread of insecticide resistance, which is critical for timely decisions on vector management. Given the importance of resistance management, high-throughput methods for kdr genotyping are valuable tools as they can be used for resistance monitoring programs. These methods should be cost-effective, to allow regional-scale surveys. Despite the extensive presence of *Ae. aegypti* and incidence of dengue in Argentina, the presence, abundance, and distribution of kdr mutations in populations of this mosquito have yet to be reported for the country. **Methods:** *Aedes aegypti* samples were collected as immature stages or adults from Buenos Aires Metropolitan Area and northern localities of Tartagal (Salta Province) and Calilegua (Jujuy Province). Immature stages were maintained in the laboratory until they developed into adults. A high-resolution melting assay, based on an analysis of melting temperatures, was developed for the simultaneous genotyping of V1016I and F1534C kdr mutations. We used this method to infer the presence and frequencies of kdr alleles in 11 wild populations from Argentina. **Results:** We demonstrated the presence of kdr mutations in *Ae. aegypti* in Argentina in regions where this species is under different selection pressures due to the use of pyrethroids. The populations under analysis are located in geographically distant regions of the species' distribution in Argentina: the northern provinces of Salta and Jujuy and the Buenos Aires Metropolitan Area. Higher frequencies of resistant-associated alleles were detected in the northern region. We report a multiplex high-throughput assay based on a high-resolution melting polymerase chain reaction method for the simultaneous genotyping of V1016I and F1534C kdr mutations. This assay was shown to be cost-effective, and thus provides an interesting molecular tool for kdr genotyping in *A. aegypti* control campaigns.

Conclusions: We report, to the best of our knowledge for the first time, the presence of kdr mutations in populations of *Ae. aegypti* from geographically distant locations of Argentina that differ with respect to their epidemiological situation and history of mosquito control. We have developed a high-throughput method for the genotyping of kdr mutations in *Ae. aegypti* from the Americas. Given its affordability and short running time, this method can be used in control campaigns to monitor the presence and spread of kdr alleles. The information provided here is relevant for the rational design of control strategies in the context of integrated vector management.

Global emergence of Langya virus: A serious public health concern.

Piracha ZZ, Saeed U, Ahmed RA, Khan FN, Nasir MI.
07-07-2023

J Glob Health.

<https://pubmed.ncbi.nlm.nih.gov/37411008/>

Molecular evolution of dengue virus: a Bayesian approach using 1581 whole-genome sequences from January 1944 to July 2022.

Wolf J, de Souza AP, de Schardosim RF, Pille A, Maccari JG, Mutlaq MP, Nasi LA.

06-06-2023

Arch Virol.

<https://pubmed.ncbi.nlm.nih.gov/37410187/>

Dengue is a viral disease transmitted by mosquitoes that has spread rapidly across all continents in recent years. There are four distinct but closely related serotypes of the virus that causes dengue (DENV-1, DENV-2, DENV-3, and DENV-4). In the present study, we evaluated temporal spreading and molecular evolution of dengue virus (DENV) serotypes. Bayesian coalescent analysis was performed to study viral evolution, and it was estimated that the most recent common ancestor of DENV-1 was present in 1884 in Southeast Asia, that of DENV-2 was present in 1723 in Europe, that of DENV-3 was present in 1921 in Southeast Asia, and that of DENV-4 was present in 1876 in Southeast Asia. DENV appears to have originated in Spain in approximately 1682, and it was disseminated in Asia and Oceania in approximately 1847. After this period, the virus was introduced into North America in approximately 1890. In South America, it was first disseminated to Ecuador in approximately 1897 and then to Brazil in approximately 1910. Dengue has had a significant impact on global health worldwide, and the present study provides an overview of the molecular evolution of DENV serotypes.

Amid Paraguay Chikungunya Outbreak, Vaccine Candidate Safe, Immunogenic.

Harris E.

11-07-2023

JAMA.

<https://pubmed.ncbi.nlm.nih.gov/37342059/>

National surveillance of severe microcephaly in Australia.

Nunez C, Morris A, Elliott EJ.

Àoût-2023

Acta Paediatr.

<https://pubmed.ncbi.nlm.nih.gov/37183370/>

An Observational Study on Pattern of Empirical Acyclovir Therapy in Children With Acute Encephalitis From Northern India.

Adarsha N, Samprathi M, Sankhyan N, Singh MP, Bansal A, Jayashree M, Angurana SK, Nallasamy K.

Juil-2023

Pediatr Crit Care Med.

<https://pubmed.ncbi.nlm.nih.gov/37097038/>

Objectives: To identify the prevalence of herpes simplex encephalitis (HSE), factors influencing the duration of empirical acyclovir and frequency of acute kidney injury (AKI) in children with acute encephalitis syndrome (AES). **Design:** Prospective observational study. **Setting:** Pediatric Emergency Department and PICU of a tertiary hospital in Northern India. **Patients:** All consecutive, eligible children between 1 month and 12 years old presenting with AES, defined as altered consciousness for greater than 24 hours (including lethargy, irritability, or a change in personality) and two or more of the following signs: 1) fever (temperature $\geq 38^{\circ}\text{C}$) during the current illness, 2) seizures or focal neurological signs, 3) cerebrospinal fluid (CSF) pleocytosis, 4) electroencephalogram, and/or 5) neuroimaging suggesting encephalitis, who received at least one dose of acyclovir. **Interventions:** None. **Measurements and main results:** Of the 101 children screened, 83 were enrolled. The median (interquartile range [IQR]) age was 3 years (1-6 yr). Thirty-one children (37.3%) were diagnosed with AES, of which four were labeled as probable HSE (three based on MRI brain, one based on serology). Scrub typhus, dengue, Japanese encephalitis, and mumps were the other infective causes. The median (IQR) duration of acyclovir therapy was 72 hours (24-264 hr); 21 children (25.3%) received acyclovir for less than 24 hours and 11 (13.3%) for greater than or equal to 14 days. New-onset AKI was seen in 18 children (21.7%) but was mostly transient. Death ($n = 8$, 9.6%) and discontinuation of care due to futility or other reasons ($n = 15$, 18%) were noted in 23 children (28%). Factors associated with duration of acyclovir greater than 7 days, on univariable analysis, were lower modified Glasgow Coma Score at admission, requirement of invasive ventilation, invasive intracranial pressure monitoring, and CSF pleocytosis (5-500 cells). On multivariable analysis, only CSF pleocytosis of 5-500 cells was associated with duration of acyclovir greater than 7 days. **Conclusions:** Given the low prevalence of HSE, and the risk of AKI, this study sensitizes the need to review our practice on initiation and stopping of empirical acyclovir in children with acute encephalitis.

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

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

Jul-2023

Rev Med Virol.

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

Incidence rates of childhood asthma with recurrent exacerbations in the US Environmental influences on Child Health Outcomes (ECHO) program.

Miller RL, Schuh H, Chandran A, Aris IM, Bendixsen C, Blossom J, Breton C, Camargo CA Jr, Canino G, Carroll KN, Commodore S, Cordero JF, Dabelea DM, Ferrara A, Fry RC, Ganiban JM, Gern JE, Gilliland FD, Gold DR, Habre R, Hare ME, Harte RN, Hartert T, Hasegawa K, Khurana Hershey GK, Jackson DJ, Joseph C, Kerver JM, Kim H, Litonjua AA, Marsit CJ, McEvoy C, Mendonça EA, Moore

PE, Nkoy FL, O'Connor TG, Oken E, Ownby D, Perzanowski M, Rivera-Spoljaric K, Ryan PH, Singh AM, Stanford JB, Wright RJ, Wright RO, Zanutti A, Zoratti E, Johnson CC; of program collaborators for Environmental influences on Child Health Outcomes.

Jul-2023

J Allergy Clin Immunol.

<https://pubmed.ncbi.nlm.nih.gov/36972767/>

Background: Descriptive epidemiological data on incidence rates (IRs) of asthma with recurrent exacerbations (ARE) are sparse. **Objectives:** This study hypothesized that IRs for ARE would vary by time, geography, age, and race and ethnicity, irrespective of parental asthma history. **Methods:** The investigators leveraged data from 17,246 children born after 1990 enrolled in 59 US with 1 Puerto Rican cohort in the Environmental Influences on Child Health Outcomes (ECHO) consortium to estimate IRs for ARE. **Results:** The overall crude IR for ARE was 6.07 per 1000 person-years (95% CI: 5.63-6.51) and was highest for children aged 2-4 years, for Hispanic Black and non-Hispanic Black children, and for those with a parental history of asthma. ARE IRs were higher for 2- to 4-year-olds in each race and ethnicity category and for both sexes. Multivariable analysis confirmed higher adjusted ARE IRs (aIRRs) for children born 2000-2009 compared with those born 1990-1999 and 2010-2017, 2-4 versus 10-19 years old (aIRR = 15.36; 95% CI: 12.09-19.52), and for males versus females (aIRR = 1.34; 95% CI 1.16-1.55). Black children (non-Hispanic and Hispanic) had higher rates than non-Hispanic White children (aIRR = 2.51; 95% CI 2.10-2.99; and aIRR = 2.04; 95% CI: 1.22-3.39, respectively). Children born in the Midwest, Northeast and South had higher rates than those born in the West ($P < .01$ for each comparison). Children with a parental history of asthma had rates nearly 3 times higher than those without such history (aIRR = 2.90; 95% CI: 2.43-3.46). **Conclusions:** Factors associated with time, geography, age, race and ethnicity, sex, and parental history appear to influence the inception of ARE among children and adolescents.

Dracunculose

Nanoliposomes containing three essential oils from the Artemisia genus as effective larvicides against Aedes aegypti and Anopheles stephensi.

Sanei-Dehkordi A, Ghasemian A, Zarenezhad E, Qasemi H, Nasiri M, Osanloo M.

07-07-2023

Sci Rep.

<https://pubmed.ncbi.nlm.nih.gov/37420038/>

Dynamic gel as artificial interphase layer for ultrahigh-rate and large-capacity lithium metal anode.

Chen C, Zhang J, Hu B, Liang Q, Xiong X.

07-07-2023

Nat Commun.

<https://pubmed.ncbi.nlm.nih.gov/37420038/>

Two residues determine nicotinic acetylcholine receptor requirement for RIC-3.

Noonan JD, Beech RN.

07-07-2023

Protein Sci.

<https://pubmed.ncbi.nlm.nih.gov/37417463/>

Nicotinic acetylcholine receptors (N-AChRs) mediate fast synaptic signalling and are members of the pentameric ligand-gated ion channel (pLGIC) family. They rely on a network of accessory proteins in vivo for correct formation and transport to the cell surface. RIC-3 is an endoplasmic reticulum protein that physically interacts with nascent pLGIC subunits and promotes their oligomerization. It is not known why some N-AChRs require RIC-3 in heterologous expression systems, while others do not. Previously we reported that the ACR-16 N-AChR from the parasitic nematode *Dracunculus medinensis* does not require RIC-3 in *Xenopus laevis* oocytes. This is unusual because all other nematode ACR-16, like the closely related *Ascaris suum* ACR-16, require RIC-3. Their high sequence similarity limits the number of amino acids that may be responsible, and the goal of this study was to identify them. A series of chimeras and point mutations between *A. suum* and *D. medinensis* ACR-16, followed by functional characterization with electrophysiology, identified two residues that account for a majority of the receptor requirement for RIC-3. ACR-16 with R/K159 in the cys-loop and I504 in the C-terminal tail did not require RIC-3 for functional expression. Mutating either of these to R/K159E or I504T, residues found in other nematode ACR-16, conferred a RIC-3 requirement. Our results agree with previous studies showing that these regions interact and are involved in receptor synthesis. Although it is currently unclear what precise mechanism they regulate, these residues may be critical during specific subunit folding and/or assembly cascades that RIC-3 may promote. This article is protected by copyright. All rights reserved.

Sesquiterpenoids from the rhizomes of *Homalomena pendula* and their anti-inflammatory activities.

Nguyen LTK, Hoang HNT, Do TT, Tran TVA, Nguyen HT, Ho DV.

Juillet-Août 2023

Nat Prod Res.

<https://pubmed.ncbi.nlm.nih.gov/35337228/>

Echinococcosis

Application and evaluation of native antigen B from *Echinococcus granulosus sensu stricto* and *E. canadensis* alone or mixture for serodiagnosis of human G1-G3 and G6/G7 genotypes cystic echinococcosis sera, using ELISA and Western blotting.

Sharifi Y, Sadjjadi SM, Jafari SH, Nikoupour Deilami H, Mardani P, Solgi R.

13-07-2023

Parasitol Res.

<https://pubmed.ncbi.nlm.nih.gov/37438467/>

Cystic echinococcosis (CE) is one of the most important helminthic diseases in the world with different genotypes distribution. The application of specific genotype antigens together with sera from patients with specific cyst genotypes have not been reported, so far. The present study aimed to apply and evaluate native AgB from *Echinococcus granulosus sensu stricto* (Eg) and *Echinococcus canadensis* (Ec) alone or mixture for serodiagnosis of human G1-G3 and G6/G7 genotypes cystic echinococcosis sera, using ELISA and Western blotting. A total of 47 human sera along with 47 human CE cysts were collected. CE genotypes were determined. Native AgB were prepared from *E. granulosus* s.s and *E. canadensis* genotypes. ELISA and Western blot were performed on human specific G1-G3 and G6/G7 genotypes sera. Species specific native AgB were used alone or mixed. The sensitivity of ELISA using alone and mixed 1Eg-1Ec, 1Eg-2Ec, and 2Eg-1Ec of native AgB from *E. granulosus* s.s and *E. canadensis* genotypes for human G1-G3 sera were 92.10, 89.47, 97.37, 100, and 100%, respectively; while using AgBs, alone and mixed for human G6/G7 sera were 100%. The sensitivity of Western blotting using native AgB of *E. granulosus* s.s and *E. canadensis* genotypes alone and mixed 2Eg-1Ec were 78.95% and 100% for human G1-G3 and G6/G7 genotypes sera, respectively. The mixture of AgB from *Echinococcus granulosus sensu stricto* and *Echinococcus canadensis* genotypes increased ELISA sensitivity for the diagnosis of human CE. Preparation and application of native AgB from specific and prevalent genotypes of CE in endemic regions is recommended.

Surgical management of a recurrent hydatid cyst in the thoracic spine of a postpartum patient with paraplegia: a rare case report and literature review.

Aleissa RS, Asiri MS, Nasraldeen GH, Konbaz FM, Alassiri SS, Abaalkhail MS, Al Helal FH, Al Eissa SI.

30-06-2023

J Spine Surg.

<https://pubmed.ncbi.nlm.nih.gov/37435332/>

Background: Hydatid disease is a health problem caused by *Echinococcus granulosus*. Spinal hydatidosis is relatively uncommon when compared to hydatid disease of visceral organs, such as the liver. **Case description:** This report details the case of a 26-year-old female who presented acutely with incomplete paraplegia following delivery via cesarean section. She was previously treated for visceral and thoracic spine hydatid cyst disease. On magnetic resonance imaging (MRI), a cystic lesion suggestive of hydatid cyst disease was identified as causing severe cord compression, mainly at T7, raising suspicions of recurrence. Emergency decompression of the thoracic spinal cord via costotransversectomy was performed, as well as the removal of a hydatid cyst and instrumentation from T3-T10. Histopathology findings were consistent with a parasitic infection, specifically *Echinococcus granulosus*. The patient was administered albendazole for treatment and subsequently had full neurological recovery at the final follow-up. **Conclusions:** Diagnosis and treatment of

spinal hydatid disease is challenging. Surgical excision of the cyst for neural decompression and pathological identification of the cyst is the initial treatment of choice, alongside albendazole chemotherapy. In this review, we have analyzed spine cases reported in the literature and present the surgical approach applied to our case, which was the first reported case of spine hydatid cyst disease following delivery and recurrence. Uneventful surgery, avoiding cyst rupture, and treatment with antiparasitic medication are the mainstays of spine hydatid cyst management and avoidance of recurrence.

Incidentally diagnosed multiple intradural extramedullary spinal hydatidosis in a young adult: A case report and review of the literature.

Ahmadi SM, Meibodi KT, Raeesi N, Bitaraf MA, Iranmehr A.

10-07-2023

Clin Case Rep.

<https://pubmed.ncbi.nlm.nih.gov/37434963/>

An unusual site for hydatid cyst on ovary misdiagnosed as an ovarian cyst: a case report.

Bdeiwi H, Sultan H, Mezketli Z, Jouma Al-Hejazi T, Trissi M, Kellawi K, Zayat R, Al-Hammod A.

20-06-2023

Ann Med Surg (Lond).

<https://pubmed.ncbi.nlm.nih.gov/37427247/>

A hydatid cyst is a parasitic infection that can occur in multiple organs of the body, mostly in the liver. The ovary is one of the very rare locations for those cysts. **Case presentation:** The authors report a case of a 43-year-old woman with a primary hydatid cyst, the patient presented with left lower quadrant abdominal pain for 2 months. Ultrasound of the abdomen showed evidence of a multivesicular, fluid-containing cystic lesion in the left adnexa. The mass was excised and a hysterectomy with total left salpingo-oophorectomy was performed. Histopathology confirmed it to be a hydatid cyst. **Clinical discussion:** The clinical presentation of an ovarian hydatid cyst can differ, ranging from asymptomatic for years to dull pain if it compresses on the neighbouring organs or tissues, it may even cause a systemic immunological reaction if it ruptures. **Conclusion:** Cyst excision when possible is the best treatment, percutaneous sterilization techniques, and drug therapy may also be applied in certain cases.

Tension pneumothorax caused by the ruptured hydatid cyst of the lung.

Rezaei R, Sadidi H, Taqanaki PB.

06-06-2023

Clin Case Rep.

<https://pubmed.ncbi.nlm.nih.gov/37426682/>

Filariose lymphatique

The efficacy of the benzimidazoles oxfendazole and flubendazole against *Litomosoides sigmodontis* is dependent on the adaptive and innate immune system.

Risch F, Scheunemann JF, Reichwald JJ, Lenz B, Ehrens A, Gal J, Fercoq F, Koschel M, Fendler M, Hoerauf A, Martin C, Hübner MP.

27-06-2023

Front Microbiol.

<https://pubmed.ncbi.nlm.nih.gov/37440891/>

Filarial nematodes can cause debilitating diseases such as lymphatic filariasis and onchocerciasis. Oxfendazole (OXF) is one promising macrofilaricidal candidate with improved oral availability compared to flubendazole (FBZ), and OXF is currently under preparation for phase 2 clinical trials in filariasis patients. This study aimed to investigate the immune system's role during treatment with OXF and FBZ and explore the potential to boost the treatment efficacy via stimulation of the immune system. Wild type (WT) BALB/c, eosinophil-deficient Δ dblGata1, IL-4r/IL-5-/-, antibody-deficient μ MT and B-, T-, NK-cell and ILC-deficient Rag2/IL-2ry-/- mice were infected with the rodent filaria *Litomosoides sigmodontis* and treated with an optimal and suboptimal regimen of OXF and FBZ for up to 5 days. In the second part, WT mice were treated for 2-3 days with a combination of OXF and IL-4, IL-5, or IL-33. Treatment of WT mice reduced the adult worm burden by up to 94% (OXF) and 100% (FBZ) compared to vehicle controls. In contrast, treatment efficacy was lower in all immunodeficient strains with a reduction of up to 90% (OXF) and 75% (FBZ) for Δ dblGata1, 50 and 92% for IL-4r/IL-5-/-, 64 and 78% for μ MT or 0% for Rag2/IL-2ry-/- mice. The effect of OXF on microfilariae and embryogenesis displayed a similar pattern, while FBZ's ability to prevent microfilaremia was independent of the host's immune status. Furthermore, flow cytometric analysis revealed strain- and treatment-specific immunological changes. The efficacy of a shortened 3-day treatment of OXF (-33% adult worms vs. vehicle) could be boosted to a 91% worm burden reduction via combination with IL-5, but not IL-4 or IL-33. Our results suggest that various components of the immune system support the filaricidal effect of benzimidazoles in vivo and present an opportunity to boost treatment efficacy.

Ivermectin and doxycycline treatments against Onchocerciasis: Adaptations and impact among semi-nomadic population in Massangam Health District, Cameroon.

Nditanchou R, Dixon R, Atekem K, Biholong B, Wilhelm A, Selby R, Oye J, Kamgno J, Boakye D, Schmidt E, Senyonjo L.

12-06-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/37437096/> ,

Socio-economic and environmental factors associated with high lymphatic filariasis morbidity prevalence distribution in Bangladesh.

Williams T, Karim MJ, Uddin S, Jahan S, Asm SM, Forbes SP, Hooper A, Taylor MJ, Kelly-Hope LA.

11-07-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/37432968/>

Background: Lymphatic filariasis (LF) is a vector-borne parasitic disease which affects 70 million people worldwide and causes life-long disabilities. In Bangladesh, there are an estimated 44,000 people suffering from clinical conditions such as lymphoedema and hydrocoele, with the greatest burden in the northern Rangpur division. To better understand the factors associated with this distribution, this study examined socio-economic and environmental factors at division, district, and sub-district levels. **Methodology:** A retrospective ecological study was conducted using key socio-economic (nutrition, poverty, employment, education, house infrastructure) and environmental (temperature, precipitation, elevation, waterway) factors. Characteristics at division level were summarised. Bivariate analysis using Spearman's rank correlation coefficient was conducted at district and sub-district levels, and negative binomial regression analyses were conducted across high endemic sub-districts ($n = 132$). Maps were produced of high endemic sub-districts to visually illustrate the socio-economic and environmental factors found to be significant. **Results:** The highest proportion of rural population (86.8%), poverty (42.0%), tube well water (85.4%), and primary employment in agriculture (67.7%) was found in Rangpur division. Spearman's rank correlation coefficient at district and sub-district level show that LF morbidity prevalence was significantly ($p < 0.05$) positively correlated with households without electricity (district $r_s = 0.818$; sub-district $r_s = 0.559$), households with tube well water (sub-district $r_s = 0.291$), households without toilet (district $r_s = 0.504$; sub-district $r_s = 0.40$), mean annual precipitation (district $r_s = 0.695$; sub-district $r_s = 0.503$), mean precipitation of wettest quarter (district $r_s = 0.707$; sub-district $r_s = 0.528$), and significantly negatively correlated with severely stunted children (district $r_s = -0.723$; sub-district $r_s = -0.370$), mean annual temperature (district $r_s = -0.633$; sub-district $r_s = 0.353$) and mean temperature (wettest quarter) ((district $r_s = -0.598$; sub-district $r_s = 0.316$) Negative binomial regression analyses at sub-district level found severely stunted children ($p = < 0.001$), rural population ($p = 0.002$), poverty headcount ($p = 0.001$), primary employment in agriculture ($p = 0.018$), households without toilet ($p = < 0.001$), households without electricity ($p = 0.002$) and mean temperature (wettest quarter) ($p = 0.045$) to be significant.

Conclusions: This study highlights the value of using available data to identify key drivers associated with high LF morbidity prevalence, which may help national LF programmes better identify populations at risk and implement timely and targeted public health messages and intervention strategies.

Chyloperitoneum After Penetrating Abdominal Trauma: A Report of a Rare Case.

Syrnioti G, Al Awwa G, Eisdorfer J.

09-06-2023

Cureus.

<https://pubmed.ncbi.nlm.nih.gov/37431330/>

The term chyloperitoneum refers to the accumulation of triglyceride-rich fluid in the peritoneal cavity. It is an uncommon clinical condition that usually occurs due to disruption of lymphatic flow secondary to trauma or obstruction. Common causes include penetrating or blunt trauma, iatrogenic injuries, congenital anomalies, malignant neoplasms, infections such as tuberculosis and filariasis, liver cirrhosis, constrictive pericarditis, congestive heart failure, inflammatory conditions, such as sarcoidosis and pancreatitis, and radiation- and drug-related pathologies. We present a case of chyloperitoneum in a 33-year-old woman secondary to penetrating abdominal trauma secondary to a gunshot wound. The patient was successfully managed with total parenteral nutrition and octreotide administration. To our knowledge, this is the only case of chylous ascites caused by a penetrating injury that has been reported in the literature. Conservative management with the initiation of total parenteral nutrition and octreotide led to the resolution of this condition.

A Phase-I pharmacokinetic, safety and food-effect study on flubentylisin, a novel analog of Tylosin-A having potent anti-Wolbachia and antifilarial activity.

Alami N, Carter DC, Kwatra NV, Zhao W, Snodgrass L, Porcalla AR, Klein CE, Cohen DE, Gallenberg L, Neenan M, Carr RA, Marsh KC, Kempf DJ.

10-07-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/37428804/>

Discovery of New Broad-Spectrum Anti-Infectives for Eukaryotic Pathogens Using Bioorganometallic Chemistry.

Lin Y, Jung H, Bulman CA, Ng J, Vinck R, O'Beirne C, Moser MS, Tricoche N, Peguero R, Li RW, Urban JF, Pape PL, Pagniez F, Moretto M, Weil T, Lustigman S, Cariou K, Mitreva M, Sakanari JA, Gasser G.

30-06-2023

bioRxiv.

<https://pubmed.ncbi.nlm.nih.gov/37425761/>

Drug resistance observed with many anti-infectives clearly highlights the need for new broad-spectrum agents to treat especially neglected tropical diseases (NTDs) caused by eukaryotic parasitic pathogens including fungal infections. Since these diseases target the most vulnerable communities who are disadvantaged by health and socio-economic factors, new agents should be, if possible, easy-to-prepare to allow for commercialization based on their low cost. In this study, we show that simple modification of one of the most well-known antifungal drugs, fluconazole, with organometallic moieties not only

improves the activity of the parent drug but also broadens the scope of application of the new derivatives. These compounds were highly effective *in vivo* against pathogenic fungal infections and potent against parasitic worms such as *Brugia*, which causes lymphatic filariasis and *Trichuris*, one of the soil-transmitted helminths that infects millions of people globally. Notably, the identified molecular targets indicate a mechanism of action that differs greatly from the parental antifungal drug, including targets involved in biosynthetic pathways that are absent in humans, offering great potential to expand our armamentarium against drug-resistant fungal infections and NTDs targeted for elimination by 2030. Overall, the discovery of these new compounds with broad-spectrum activity opens new avenues for the development of treatments for several current human infections, either caused by fungi or by parasites, including other NTDs, as well as newly emerging diseases. **One-sentence summary:** Simple derivatives of the well-known antifungal drug fluconazole were found to be highly effective *in vivo* against fungal infections, and also potent against the parasitic nematode *Brugia*, which causes lymphatic filariasis and against *Trichuris*, one of the soil-transmitted helminths that infects millions of people globally.

"Our interventions are still here to support communities during the pandemic": Resuming mass drug administration for neglected tropical diseases after COVID-19 implementation delays.

Itaye T, Matendechero SH, Mbonigaba JB, Gebretsadik FS, Molefi TL, Baayenda G, Ruberanziza E, Kollie KK, Zilabumba J, Dembele M, Deribe K, Adrien EM, Polo MR; Kikundi African NTD Program Managers Community of Practice.

26-06-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/37363911/>

Gale

Culturally supported health promotion to See, Treat, Prevent (SToP) skin infections in Aboriginal children living in the Kimberley region of Western Australia: a qualitative analysis.

McRae T, Leaversuch F, Sibosado S, Coffin J, Carapetis JR, Walker R, Bowen AC.

08-04-2023

Lancet Reg Health West Pac.

<https://pubmed.ncbi.nlm.nih.gov/37424680/>

Background: While there are many skin infections, reducing the burden of scabies and impetigo for remote living Aboriginal people, particularly children remains challenging. Aboriginal children living in remote communities have experienced the highest reported rate of impetigo in the world and are 15 times more likely to be admitted to hospital with a skin infection compared to non-Aboriginal children. Untreated impetigo can develop

into serious disease and may contribute to the development of acute rheumatic fever (ARF) and rheumatic heart disease (RHD). As the largest organ protecting the body and visible to everyone, skin infections are often unsightly and very painful, therefore maintaining healthy skin and reducing the burden of skin infections is important for overall physical and cultural health and well-being. Biomedical treatments alone will not address these factors; therefore, a holistic, strengths-based approach that aligns with the Aboriginal world view of wellness is required to help reduce the prevalence of skin infections and their downstream consequences. **Methods:** Culturally appropriate yarning sessions with community members were conducted between May 2019 and November 2020. Yarning sessions have been identified as a valid method for story sharing and collecting information. Semi-structured, face-to-face interviews and focus groups with school and clinic staff were conducted. When consent was provided, interviews were audio-recorded and saved as a digital recording in a de-identified format; for those yarning sessions not recorded, handwritten notes were scribed. Audio recordings and handwritten notes were uploaded into NVivo software prior to a thematic analysis being conducted. **Findings:** Overall, there was a strong knowledge of recognition, treatment, and prevention of skin infections. However, this did not extend to the role skin infections play in causing ARF, RHD or kidney failure. Our study has confirmed three main findings: 1. The biomedical model of treatment of skin infections remained strong in interviews with staff living in the communities; 2. Community members have a reliance and belief in traditional remedies for skin infections; and 3. Ongoing education for skin infections using culturally appropriate health promotion resources. **Interpretation:** While this study revealed ongoing challenges with service practices and protocols associated with treating and preventing skin infections in a remote setting, it also provides unique insights requiring further investigation. Bush medicines are not currently practiced in a clinic setting, however, using traditional medicines alongside biomedical treatment procedures facilitates cultural security for Aboriginal people. Further investigation, and advocacy to establish these into practice, procedures and protocols is warranted. Establishing protocols and practice procedures focused on improving collaborations between service providers and community members in remote communities is also recommended. **Funding:** Funding was received from the National Health and Medical Research Council [NHMRC] (GNT1128950), Health Outcomes in the Tropical NORTH [HOT NORTH 113932] (Indigenous Capacity Building Grant), and WA Health Department and Healthway grants contributed to this research. A.C.B. receives a NHMRC investigator Award (GNT1175509). T.M. receives a PhD scholarship from the Australian Centre for Elimination of Neglected Tropical Diseases (ACE-NTD), an NHMRC centre of excellence (APP1153727).

Evaluating the role of asymptomatic throat carriage of *Streptococcus pyogenes* in impetigo transmission in remote Aboriginal communities in Northern Territory, Australia: a retrospective genomic analysis.

Lacey JA, Marcato AJ, Chisholm RH, Campbell PT, Zachreson C, Price DJ, James TB, Morris JM, Gorrie CL, McDonald MI, Bowen AC, Giffard PM, Holt DC, Currie BJ, Carapetis JR, Andrews RM, Davies MR, Geard N, McVernon J, Tong SYC.

Jul-2023

Lancet Microbe.

<https://pubmed.ncbi.nlm.nih.gov/37211022/>

Background: Streptococcus pyogenes, or group A Streptococcus (GAS), infections contribute to a high burden of disease in Aboriginal Australians, causing skin infections and immune sequelae such as rheumatic heart disease. Controlling skin infections in these populations has proven difficult, with transmission dynamics being poorly understood. We aimed to identify the relative contributions of impetigo and asymptomatic throat carriage to GAS transmission. **Methods:** In this genomic analysis, we retrospectively applied whole genome sequencing to GAS isolates that were collected as part of an impetigo surveillance longitudinal household survey conducted in three remote Aboriginal communities in the Northern Territory of Australia between Aug 6, 2003, and June 22, 2005. We included GAS isolates from all throats and impetigo lesions of people living in two of the previously studied communities. We classified isolates into genomic lineages based on pairwise shared core genomes of more than 99% with five or fewer single nucleotide polymorphisms. We used a household network analysis of epidemiologically and genomically linked lineages to quantify the transmission of GAS within and between households. **Findings:** We included 320 GAS isolates in our analysis: 203 (63%) from asymptomatic throat swabs and 117 (37%) from impetigo lesions. Among 64 genomic lineages (encompassing 39 emm types) we identified 264 transmission links (involving 93% of isolates), for which the probable source was asymptomatic throat carriage in 166 (63%) and impetigo lesions in 98 (37%). Links originating from impetigo cases were more frequent between households than within households. Households were infected with GAS for a mean of 57 days (SD 39 days), and once cleared, reinfectd 62 days (SD 40 days) later. Increased household size and community presence of GAS and scabies were associated with slower clearance of GAS. **Interpretation:** In communities with high prevalence of endemic GAS-associated skin infection, asymptomatic throat carriage is a GAS reservoir. Public health interventions such as vaccination or community infection control programmes aimed at interrupting transmission of GAS might need to include consideration of asymptomatic throat carriage.

A patient's experience of crusted scabies in the context of immunosuppression.

Duff E, Lyons D, Eustace K, Collins S.

07-07-2023

Clin Exp Dermatol.

<https://pubmed.ncbi.nlm.nih.gov/36994790/>

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

Ascariasis causing small bowel obstruction in an adult female: A case report.

Birhanu AM, Mohammed SH, Gossaye BT, Kebede MA.

08-07-2023

Int J Surg Case Rep.

<https://pubmed.ncbi.nlm.nih.gov/37437322/>

Prevalence of soil-transmitted helminth infections in HIV patients: a systematic review and meta-analysis.

Akanksha K, Kumari A, Dutta O, Prasanth A, Deeba F, Salam N.

08-07-23

Sci Rep.

<https://pubmed.ncbi.nlm.nih.gov/37422549/>

Leishmaniose

A Visceral Leishmaniasis Case from the Black Sea region: Skin Lesions and Leishmania Donovanii Amastigotes in Bone Marrow.

Öneç B, Öztürk CE, Yazıcı A.

13-07-2023

Turk J Haematol.

<https://pubmed.ncbi.nlm.nih.gov/37439507/>

Serological survey of Leishmania infantum in apparently healthy dogs in different areas of Spain.

Baxarias M, Mateu C, Miró G, Solano-Gallego L.

12-07-2023

Vet Med Sci.

<https://pubmed.ncbi.nlm.nih.gov/37438910/>

Background: Canine leishmaniosis caused by Leishmania infantum is an endemic disease in Spain. The dog is considered the main reservoir, and the detection of specific serum antibodies against L. infantum antigen is the most used technique for diagnosing this infection. The LEISCAN LEISHMANIA ELISA test is a commercialized enzyme-linked immunosorbent assay for the detection and measurement of canine anti-Leishmania serum antibodies.

Objectives: The aim of this study was to assess seroprevalence results of apparently healthy dogs in different areas of Spain using LEISCAN. **Methods:** Collection of sera from 5451 apparently healthy dogs was performed between 2020 and 2021 in different areas of Spain. Dogs were of adult age (≥ 12 months), were not previously diagnosed with clinical leishmaniosis or

vaccinated against *Leishmania* and did not present clinical signs compatible with *L. infantum* infection. LEISCAN was performed following the manufacturer's protocol. **Results:** The overall seroprevalence was 5.5%. The highest seroprevalences were found in the Southeast of Spain: Comunidad Valenciana (14%) and Región de Murcia (14%), whereas the lowest seroprevalences were found in Northern Spain: Galicia (1%), Navarra (2%) and Castilla y León (2%) (p-value <0.001). **Conclusions:** In conclusion, the seroprevalence for *L. infantum* in apparently healthy dogs in Spain varied from almost no infection to being over 10%.

Is leishmaniasis the new emerging zoonosis in the world?

Montaner-Angoiti E, Llobat L.

12-07-2023

Vet Res Commun.

<https://pubmed.ncbi.nlm.nih.gov/37438495/>

Leishmania is a genus of parasitic protozoa that causes a disease called leishmaniasis. Leishmaniasis is transmitted to humans through the bites of infected female sandflies. There are several different species of *Leishmania* that can cause various forms of the disease, and the symptoms can range from mild to severe, depending on species of *Leishmania* involved and the immune response of the host. *Leishmania* parasites have a variety of reservoirs, including humans, domestic animals, horses, rodents, wild animals, birds, and reptiles. Leishmaniasis is endemic of 90 countries, mainly in South American, East and West Africa, Mediterranean region, Indian subcontinent, and Central Asia. In recent years, cases have been detected in other countries, and it is already an infection present throughout the world. The increase in temperatures due to climate change makes it possible for sandflies to appear in countries with traditionally colder regions, and the easy movement of people and animals today, facilitate the appearance of *Leishmania* species in new countries. These data mean that leishmaniasis will probably become an emerging zoonosis and a public health problem in the coming years, which we must consider controlling it from a One Health point of view. This review summarizes the prevalence of *Leishmania* spp. around the world and the current knowledge regarding the animals that could be reservoirs of the parasite.

Novel mutations in genes of the IL-12/IFN- γ axis cause susceptibility to tuberculosis.

Ahmad S, Ahmed J, Khalifa EH, Khattak FA, Khan AS, Farooq SU, Osman SMA, Salih MM, Ullah N, Khan TA.

15-06-2023

J Infect Public Health.

<https://pubmed.ncbi.nlm.nih.gov/37437430/>

Background: The IL-12/23/ISG15-IFN- γ pathway is the main immunological pathway for controlling intra-macrophagic microorganisms such as *Mycobacteria*, *Salmonella*, and *Leishmania* spp. Consequently, upon mutations in genes of the IL-12/23/ISG15-IFN- γ pathway cause increased susceptibility to intra-macrophagic pathogens, particularly to *Mycobacteria*. Therefore, the purpose of this study was to characterize the mutations in

genes of the IL-12/23/ISG15-IFN- γ pathway in severe tuberculosis (TB) patients. **Methods:** Clinically suspected TB was initially confirmed in four patients (P) (P1, P2, P3, and P4) using the GeneXpert MTB/RIF and culturing techniques. The patients' Peripheral blood mononuclear cells (PBMCs) were then subjected to ELISA to measure Interleukin 12 (IL-12) and interferon gamma (IFN- γ). Flow cytometry was used to detect the surface expressions of IFN- γ R1 and IFN- γ R2 as well as IL-12R β 1 and IL-12R β 2 on monocytes and T lymphocytes, respectively. The phosphorylation of signal transducer and activator of transcription 1 (STAT1) on monocytes and STAT4 on T lymphocytes were also detected by flow cytometry. Sanger sequencing was used to identify mutations in the IL-12R β 1, STAT1, NEMO, and CYBB genes. **Results:** P1's PBMCs exhibited reduced IFN- γ production, while P2's and P3's PBMCs exhibited impaired IL-12 induction. Low IL-12R β 1 surface expression and reduced STAT4 phosphorylation were demonstrated by P1's T lymphocytes, while impaired STAT1 phosphorylation was detected in P2's monocytes. The impaired I κ B- α degradation and abolished H₂O₂ production in monocytes and neutrophils of P3 and P4 were observed, respectively. Sanger sequencing revealed novel nonsense homozygous mutation: c.191 G>A/p.W64 * in exon 3 of the IL-12R β 1 gene in P1, novel missense homozygous mutation: c.107 A>T/p.Q36L in exon 3 of the STAT1 gene in P2, missense hemizygous mutation: c.950 A>C/p.Q317P in exon 8 of the NEMO gene in P3, and nonsense hemizygous mutation: c.868 C>T/p.R290X in exon 8 of CYBB gene in P4. **Conclusion:** Our findings broaden the clinical and genetic spectra associated with IL-12/23/ISG15-IFN- γ axis anomalies. Additionally, our data suggest that TB patients in Pakistan should be investigated for potential genetic defects due to high prevalence of parental consanguinity and increased incidence of TB in the country.

Clinical, hematological, biochemical, and histopathological evaluations in domestic cats (*Felis catus*) infected by *Leishmania infantum*.

Batista JF, Magalhães Neto FDCR, Lopes KSPDP, Sousa CMG, Alcântara DS, Baêta SAF, Alves MMM, Mendonça IL.

07-07-2023

Rev Bras Parasitol Vet.

<https://pubmed.ncbi.nlm.nih.gov/37436206/>

Auricular cutaneous leishmaniasis: An unusual presentation of *Leishmania* major from Southwest Iran.

Yaghoobi R, Pazyar N, Rafiei A, Saki N.

14-06-2023

Indian J Dermatol Venereol Leprol.

<https://pubmed.ncbi.nlm.nih.gov/37436021/>

Leishmania donovani visceral leishmaniasis diagnosed by metagenomics next-generation sequencing in an infant with acute lymphoblastic leukemia: a case report.

Chang L, Che G, Yang Q, Lai S, Teng J, Duan J, Liu T, Liu F. 220-06-2032

Front Public Health.

<https://pubmed.ncbi.nlm.nih.gov/37435524/>

Background: Visceral leishmaniasis (VL) is a neglected vector-borne tropical disease caused by *Leishmania donovani* (*L. donovani*) and *Leishmania infantum* (*L. infantum*). Due to the very small dimensions of the protozoa impounded within blood cells and reticuloendothelial structure, diagnosing VL remains challenging. **Case presentation:** Herein, we reported a case of VL in a 17-month-old boy with acute lymphoblastic leukemia (ALL). The patient was admitted to West China Second University Hospital, Sichuan University, due to repeated fever after chemotherapy. After admission, chemotherapy-related bone marrow suppression and infection were suspected based on clinical symptoms and laboratory test results. However, there was no growth in the conventional peripheral blood culture, and the patient was unresponsive to routine antibiotics. Metagenomics next-generation sequencing (mNGS) of peripheral blood identified 196123 *L. donovani* reads, followed by *Leishmania* spp. amastigotes using cytomorphology examination of the bone marrow specimen. The patient was given pentavalent antimonials as parasite-resistant therapy for 10 days. After the initial treatment, 356 *L. donovani* reads were still found in peripheral blood by mNGS. Subsequently, the anti-leishmanial drug amphotericin B was administered as rescue therapy, and the patient was discharged after a clinical cure. **Conclusion:** Our results indicated that leishmaniasis still exists in China. Unbiased mNGS provided a clinically actionable diagnosis of a specific infectious disease from an uncommon pathogen that eluded conventional testing.

Case Report: Diffuse Cutaneous Leishmaniasis Successfully Treated with a Combination of Oral Rifampicin and Fluconazole.

Yadav N, Madke B.

10-07-2023

Am J Trop Med Hyg.

<https://pubmed.ncbi.nlm.nih.gov/37429574/>

Case Report: Diagnosis and Treatment of Two Clinical Cases of Visceral Leishmaniasis-Related Hemophagocytic Lymphohistiocytosis.

Wang L, Hu M, Wu X, Ma L, Yang H.

10-07-2023

Am J Trop Med Hyg.

<https://pubmed.ncbi.nlm.nih.gov/37429573/>

Antiprotozoal activity of natural products from Nigerien plants used in folk medicine.

Sevik Kilicaslan O, Cretton S, Hausmann E, Quirós-Guerrero L, Karimou S, Kaiser M, Mäser P, Christen P, Cuendet M.

23-06-2023

Front Pharmacol.

<https://pubmed.ncbi.nlm.nih.gov/37426806/>

In the course of the screening of plants from Niger for antiprotozoal activity, the methanol extract of *Cassia sieberiana*, and the dichloromethane extracts of *Ziziphus mauritiana* and *Sesamun alatum* were found to be active against protozoan parasites, namely *Trypanosoma brucei rhodesiense*, *Trypanosoma cruzi*, *Leishmania donovani* and/or *Plasmodium falciparum*. Myricitrin (**1**), quercitrin (**2**) and 1-palmitoyl-lysophosphatidylcholine (**3**) were isolated from *C. sieberiana*. From *Z. mauritiana*, the three triterpene derivatives **13**, **15**, and **16** are described here for the first time. Their chemical structures were determined by 1D and 2D NMR experiments, UV, IR and HRESIMS data. The absolute configurations were assigned via comparison of the experimental and calculated ECD spectra. In addition, eight known cyclopeptide alkaloids (**4**, **5**, **7-12**), and five known triterpenoids (**6**, **14**, **17-19**) were isolated. The antiprotozoal activity of the isolated compounds, as well as of eleven quinone derivatives (**20-30**) previously isolated from *S. alatum* was determined *in vitro*. The cytotoxicity in L6 rat myoblast cells was also evaluated. Compound **18** showed the highest antiplasmodial activity ($IC_{50} = 0.2 \mu M$) and compound **24** inhibited *T. b. rhodesiense* with an IC_{50} value of $0.007 \mu M$. However, it also displayed significant cytotoxicity in L6 cells ($IC_{50} = 0.4 \mu M$).

Insights into Leishmania donovani potassium channel family and their biological functions.

Paul A, Chumbale SS, Lakra A, Kumar V, Alhat DS, Singh S.

20-07-2023

3 Biotech.

<https://pubmed.ncbi.nlm.nih.gov/37425093/>

The role of natural anti-parasitic guided development of synthetic drugs for leishmaniasis.

Pal R, Teli G, Akhtar MJ, Matada GSP.

30-06-2023

Eur J Med Chem.

<https://pubmed.ncbi.nlm.nih.gov/37421889/>

Leishmaniasis is a parasitic disease and categorised as a neglected tropical disease (NTD). Each year, between 70,000 and 1 million new cases are believed to occur. There are approximately 90 sandfly species which can spread the Leishmania parasites (over 20 species) causing 20,000 to 30,000 death per year. Currently, leishmaniasis has no specific therapeutic treatment available. The prescribed drugs with several drawbacks including high cost, challenging administration, toxicity, and drug resistance led to search for the alternative treatment with less toxicity and selectivity. Introducing the molecular features like that of phytoconstituents for the search of compounds with less toxicity is another promising approach. The current review classifies the synthetic compounds according to the core rings present in the natural phytochemicals for the development of antileishmanial agents (2020-2022). Considering the toxicity and limitations of synthetic analogues, natural

compounds are at the higher notch in terms of effectiveness and safety. Synthesized compounds of chalcones (Compound 8; IC₅₀: 0.03 μ M, 4.7 folds more potent than Amphotericin B; IC₅₀: 0.14 μ M), pyrimidine (compound 56; against *L. tropica*; 0.04 μ M and *L. infantum*; 0.042 μ M as compared to glucantime: *L. tropica*; 8.17 μ M and *L. infantum*; 8.42 μ M), quinazoline and (compound 72; 0.021 μ M, 150 times more potent than miltefosine). The targeted delivery against DHFR have been demonstrated by one of the pyrimidine compounds 62 with an IC₅₀ value of 0.10 μ M against *L. major* as compared to the standard trimethoprim (IC₅₀: 20 μ M). The review covers the medicinal importance of antileishmanial agents from synthetic and natural sources such as chalcone, pyrazole, coumarins, steroids, and alkaloidal-containing drugs (indole, quinolines, pyridine, pyrimidine, carbolines, pyrrole, aurones, and quinazolines). The efforts of introducing the core rings present in the natural phytoconstituents as antileishmanial in the synthetic compounds are discussed with their structural activity relationship. The perspective will support the medicinal chemists in refining and directing the development of novel molecules phytochemicals-based antileishmanial agents.

Structure-Property Optimization of a Series of Imidazopyridines for Visceral Leishmaniasis.

Dichiara M, Simpson QJ, Quotadamo A, Jalani HB, Huang AX, Millard CC, Klug DM, Tse EG, Todd MH, Silva DG, da Silva Emery F, Carlson JE, Zheng SL, Vleminckx M, Matheeußen A, Caljon G, Pollastri MP, Sjö P, Perry B, Ferrins L.

07-07-2023

ACS Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/37417544/>

Leishmaniasis is a collection of diseases caused by more than 20 *Leishmania* parasite species that manifest as either visceral, cutaneous, or mucocutaneous leishmaniasis. Despite the significant mortality and morbidity associated with leishmaniasis, it remains a neglected tropical disease. Existing treatments have variable efficacy, significant toxicity, rising resistance, and limited oral bioavailability, which necessitates the development of novel and affordable therapeutics. Here, we report on the continued optimization of a series of imidazopyridines for visceral leishmaniasis and a scaffold hop to a series of substituted 2-(pyridin-2-yl)-6,7-dihydro-5H-pyrrolo[1,2-a]imidazoles with improved absorption, distribution, metabolism, and elimination properties.

Particulate and non-particle adjuvants in Leishmaniasis vaccine designs: A review.

Kelleci K, Allahverdiyev A, Bağırova M, İhlamur M, Abamor EŞ.

Avr-Juin 2023

J Vector Borne Dis.

<https://pubmed.ncbi.nlm.nih.gov/37417162/>

Ionized alkaline water reduces injury in BALB/c mice infected with *Leishmania amazonensis*.

Retamiro KM, Nunes KC, Zani AP, Zani CP, Beltran LB, Silva SO, Garcia FP, Ueda-Nakamura T, Bergamasco R, Nakamura CV.

06-07-2023

PLoS One.

<https://pubmed.ncbi.nlm.nih.gov/37410769/>

Detection of *Leishmania major* and *Leishmania infantum* in cats during an outbreak of cutaneous leishmaniasis in Southern Israel.

Kleinerman G, Melloul S, Chaim L, Mergy SE, Kaufman RG, Dagan N, Nachum-Biala Y, Kitaichik S, Gross S, Astman N, Baneth G.

Juיל-2023

Comp Immunol Microbiol Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/37356168/>

Prevalence of *Leishmania* spp. infection was studied in stray cats in two military bases in Southern Israel during a cutaneous leishmaniasis (CL) human outbreak caused by *Leishmania major*. Human CL cases increased from 0/100 in 2008 to 1.28/100 in 2022 in camp #1, and from 0.17/100 in 2008 to 6.4/100 in 2022, in camp #2. Eight out of 29 cats sampled were *Leishmania*-seropositive (28 %) and 7/29 (24 %) were internal transcribed spacer 1 (ITS1) PCR-positive, out of which four (14 %) were positive for *L. major* and three (10 %) for *L. infantum*. Five positive-cats had skin lesions including ulcers, alopecia and scabs, and five had eye lesions. This is the first report of *L. major* infection in cats in Israel and one of the first descriptions in felines worldwide. A larger cohort of cats and vector studies are necessary to determine if felids may act as reservoirs or sentinels of human *L. major* infection.

Leishmania donovani Induces Multiple Dynamic Responses in the Metabolome Associated with Amastigote Differentiation and Maturation Inside the Human Macrophage.

Fernández-García M, Mesquita I, Ferreira C, Araújo M, Saha B, Rey-Stolle MF, García A, Silvestre R, Barbas C.

07-07-2023

J Proteome Res.

<https://pubmed.ncbi.nlm.nih.gov/37339249/>

Leishmania donovani infection of macrophages drives profound changes in the metabolism of both the host macrophage and the parasite, which undergoes different phases of development culminating in replication and propagation. However, the dynamics of this parasite-macrophage cometabolome are poorly understood. In this study, a multiplatform metabolomics pipeline combining untargeted, high-resolution CE-TOF/MS and LC-QTOF/MS with targeted LC-QqQ/MS was followed to characterize the metabolome alterations induced in *L. donovani*-infected human monocyte-derived macrophages from different donors at 12, 36, and 72 h post-infection. The set of alterations known to occur during *Leishmania* infection

of macrophages, substantially expanded in this investigation, characterized the dynamics of the glycerophospholipid, sphingolipid, purine, pentose phosphate, glycolytic, TCA, and amino acid metabolism. Our results showed that only citrulline, arginine, and glutamine exhibited constant trends across all studied infection time points, while most metabolite alterations underwent a partial recovery during amastigote maturation. We determined a major metabolite response pointing to an early induction of sphingomyelinase and phospholipase activities and correlated with amino acid depletion. These data represent a comprehensive overview of the metabolome alterations occurring during promastigote-to-amastigote differentiation and maturation of *L. donovani* inside macrophages that contributes to our understanding of the relationship between *L. donovani* pathogenesis and metabolic dysregulation.

Generation of dysbiotic microbiota in cutaneous leishmaniasis and enhancement of skin inflammation.

Naz S, Ali Z, Minhas A, Fatima A, Waseem S.

Aug-2023

Microb Pathog.

<https://pubmed.ncbi.nlm.nih.gov/37327948/>

Enhanced apoptotic index in hepatocytes, Kupffer cells, and inflammatory infiltrate showed positive correlation with hepatic lesion intensity, parasite load, and clinical status in naturally Leishmania-infected dogs.

Verçosa BLA, Muniz-Junqueira MI, Mineiro ALBB, Costa FAL, Melo MN, Vasconcelos AC.

Aug-2023

Microb Pathog.

<https://pubmed.ncbi.nlm.nih.gov/37269879/>

Design, synthesis and biological evaluation of antiparasitic dinitroaniline-ether phospholipid hybrids.

Roussaki M, Magoulas GE, Fotopoulou T, Santarem N, Barrias E, Pöhner I, Luelmo S, Afroudakis P, Georgikopoulou K, Nevado PT, Eick J, Bifeld E, Corral MJ, Jiménez-Antón MD, Ellinger B, Kuzikov M, Fragiadaki I, Scoulca E, Gul S, Clos J, Prousis KC, Torrado JJ, Alunda JM, Wade RC, de Souza W, Cordeiro da Silva A, Calogeropoulou T.

Sept-2023

Bioorg Chem.

<https://pubmed.ncbi.nlm.nih.gov/37244229/>

A series of nine novel ether phospholipid-dinitroaniline hybrids were synthesized in an effort to deliver more potent antiparasitic agents with improved safety profile compared to miltefosine. The compounds were evaluated for their in vitro antiparasitic activity against *L. infantum*, *L. donovani*, *L. amazonensis*, *L. major* and *L. tropica* promastigotes, *L. infantum* and *L. donovani* intracellular amastigotes, *Trypanosoma brucei brucei* and against

different developmental stages of *Trypanosoma cruzi*. The nature of the oligomethylene spacer between the dinitroaniline moiety and the phosphate group, the length of the side chain substituent on the dinitroaniline and the choline or homocholine head group were found to affect both the activity and toxicity of the hybrids. The early ADMET profile of the derivatives did not reveal major liabilities. Hybrid 3, bearing an 11-carbon oligomethylene spacer, a butyl side chain and a choline head group, was the most potent analogue of the series. It exhibited a broad spectrum antiparasitic profile against the promastigotes of New and Old World *Leishmania* spp., against intracellular amastigotes of two *L. infantum* strains and *L. donovani*, against *T. brucei* and against *T. cruzi* Y strain epimastigotes, intracellular amastigotes and trypomastigotes. The early toxicity studies revealed that hybrid 3 showed a safe toxicological profile while its cytotoxicity concentration (CC₅₀) against THP-1 macrophages being >100 µM. Computational analysis of binding sites and docking indicated that the interaction of hybrid 3 with trypanosomatid α-tubulin may contribute to its mechanism of action. Furthermore, compound 3 was found to interfere with the cell cycle in *T. cruzi* epimastigotes, while ultrastructural studies using SEM and TEM in *T. cruzi* showed that compound 3 affects cellular processes that result in changes in the Golgi complex, the mitochondria and the parasite's plasma membrane. The snapshot pharmacokinetic studies showed low levels of 3 after 24 h following oral administration of 100 mg/Kg, while, its homocholine congener compound 9 presented a better pharmacokinetic profile.

Knockout of protein phosphatase 1 in Leishmania major reveals its role during RNA polymerase II transcription termination.

Kieft R, Zhang Y, Yan H, Schmitz RJ, Sabatini R.

07-07-2023

Nucleic Acids Res.

<https://pubmed.ncbi.nlm.nih.gov/37194692/>

Computer-aided drug design approaches applied to screen natural product's structural analogs targeting arginase in Leishmania spp.

Barazorda-Ccahuana HL, Goyzueta-Mamani LD, Candia Puma MA, Simões de Freitas C, de Sousa Viera Tavares G, Pagliara Lage D, Ferraz Coelho EA, Chávez-Fumagalli MA.

24-05-2023

F1000Res.

<https://pubmed.ncbi.nlm.nih.gov/37424744/>

Introduction: Leishmaniasis is a disease with high mortality rates and approximately 1.5 million new cases each year. Despite the new approaches and advances to fight the disease, there are no effective therapies. **Methods:** Hence, this study aims to screen for natural products' structural analogs as new drug candidates against leishmaniasis. We applied Computer-aided drug design (CADD) approaches, such as virtual screening, molecular docking, molecular dynamics simulation, molecular mechanics-generalized

Born surface area (MM-GBSA) binding free estimation, and free energy perturbation (FEP) aiming to select structural analogs from natural products that have shown anti-leishmanial and anti-arginase activities and that could bind selectively against the *Leishmania* arginase enzyme. **Results:** The compounds 2H-1-benzopyran, 3,4-dihydro-2-(2-methylphenyl)-(9CI), echiodinin, and malvidin showed good results against arginase targets from three parasite species and negative results for potential toxicities. The echiodinin and malvidin ligands generated interactions in the active center at pH 2.0 conditions by MM-GBSA and FEP methods. **Conclusions:** This work suggests the potential anti-leishmanial activity of the compounds and thus can be further *in vitro* and *in vivo* experimentally validated.

A RP-HPLC-DAD method for analysis of Brazilian southeast brown propolis and its leishmanicidal properties.

Ribeiro VP, Aldana-Mejia JA, Arruda C, Candido ACBB, Magalhães LG, Oliveira ND, Veneziani RCS, Bastos JK, Ambrósio SR.

Août-2023

Biomed Chromatogr.

<https://pubmed.ncbi.nlm.nih.gov/36977284/>

Propolis is a natural product of great economic and pharmacological importance. The flora surrounding the bee communities is a determining factor in the composition of propolis and therefore in its biological and medicinal properties. Brown propolis is one of the most important types of propolis in Brazil, produced in the southeastern region. The ethanolic extract of a brown propolis sample from Minas Gerais state was chemically characterized for the subsequent development of a RP-HPLC method, validated according to the standards of regulatory agencies. The leishmanicidal activity of this extract was assessed. The brown propolis was characterized by the presence of chemical markers reported on green propolis such as ferulic acid, coumaric acid, caffeic acid, cinnamic acid, baccharin, artemisin and drupanin, indicating a probable origin on *Baccharis dracunculifolia*. The developed method agreed with the parameters established by the validation guidelines, then proved to be reliable for the analysis of this type of propolis. The brown propolis displayed significant activity against *Leishmania amazonensis* with IC₅₀ values of 1.8 and 2.4 µg/ml against the promastigote and amastigote forms, respectively. The studied propolis exhibited promising evidence for use as a natural source against *L. amazonensis*.

Post-kala-azar dermal leishmaniasis manifestation in a Mediterranean immunosuppressed patient: a rare incident.

Panou E, Marinos L, Piperaki E, Migkou M, Stratigos AJ, Nikolaou V.

Clin Exp Dermatol.

07-07-2023

<https://pubmed.ncbi.nlm.nih.gov/36929204/>

Evaluation of the inhibitory potential of Valproic acid against histone deacetylase of *Leishmania donovani* and computational studies of Valproic acid derivatives.

Prasanna P, Joshi T, Pant M, Pundir H, Chandra S.

Juil-Août 2023

J Biomol Struct Dyn.

<https://pubmed.ncbi.nlm.nih.gov/35706132/>

Lèpre

Erythema nodosum leprosum: A rare cause of testicular nodules.

Figueroa-Diaz A, Cordero-Pacheco C, Quintero-Noriega A.

16-05-2023

IDCases.

<https://pubmed.ncbi.nlm.nih.gov/37441582/>

Culture circle with community health workers about (lack of) knowledge and stigma of leprosy.

Aquino DMC, Monteiro EMLM, Coutinho NPS, Soeiro VMDS, Santos TA, Oliveira EM, Pereira DLM, Caldas AJM. 10-07-2023

Rev Gaucha Enferm.

<https://pubmed.ncbi.nlm.nih.gov/37436218/>

Objective: To describe the construction about the (lack of) knowledge and stigma of leprosy by Community Health Workers participating in the Culture Circle. **Method:** Qualitative, action-research type study supported by the Paulo Freire Culture Circle framework, carried out with 21 Community Health Workers. Data collected in November 2021, in the municipality of São Luís, Maranhão. The following categories were evidenced: knowledge about leprosy, signs and symptoms, stigma. **Results:** The participants had knowledge about the disease, but they verbalized people's misinformation about leprosy, disbelief in relation to the cure, and situations of prejudice and stigma that are still present today. **Final considerations:** The culture circle enabled the intertwining of scientific and empirical knowledge in the construction of a critical and reflective knowledge committed to welcoming and comprehensive care for people and families affected by leprosy.

Mucosal syphilide.

Hazarika N, Maisnam S, Azad S.

01-06-2032

Indian J Dermatol Venereol Leprol.

<https://pubmed.ncbi.nlm.nih.gov/37436026/>

Science and art of teaching rounds in dermatology.

Asokan N, Mohan AJ.

06-06-2023

Indian J Dermatol Venereol Leprol.

<https://pubmed.ncbi.nlm.nih.gov/37436025/>

Disease severity scores in dermatology: An update of the various indices.

Chakraborty A.

21-06-2023

Indian J Dermatol Venereol Leprol.

<https://pubmed.ncbi.nlm.nih.gov/37436018/>

Case Report: Diffuse Cutaneous Leishmaniasis Successfully Treated with a Combination of Oral Rifampicin and Fluconazole.

Yadav N, Madke B.

10-07-2023

Am J Trop Med Hyg.

<https://pubmed.ncbi.nlm.nih.gov/37429574/>

Diffuse cutaneous leishmaniasis (DCL) is a rare parasitic infection caused by the *Leishmania* species. Diffuse cutaneous leishmaniasis commonly presents as non-ulcerating papules and nodules over the face, neck, and arms. A middle-aged female presented with multiple nodular lesions on her face, neck, and chest region. Histopathology of the lesions showed multiple amastigotes, confirming the diagnosis of DCL. She was successfully treated with a combination course of rifampicin and fluconazole. Here, we report the first case of DCL in north India, a non-endemic area for cutaneous leishmaniasis.

Polyunsaturated Fatty Acid-Derived Lipid Mediators as Potential Biomarkers for Leprosy Among Individuals with Asymptomatic *Mycobacterium leprae* Infection.

Silva CAM, Graham BG, Webb K, Islam MN, Harton M, de Mello Marques MA, Marques de Carvalho F, Pinheiro RO, Spencer J, Sarno EN, Batista Pereira GM, Vidal Pessolani MC, Santos de Macedo C, Belisle JT.

10-07-2023

ACS Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/37428112/>

Intra-household contacts (HCs) of leprosy patients are at increased risk of infection by *Mycobacterium leprae* and about ~5-10% will develop active disease. A prognostic tool to identify HCs with the greatest risk of progressing to active disease would enhance early leprosy diagnosis and optimize prophylactic intervention. Previous metabolomics studies suggest that host lipid mediators derived from ω -3 and ω -6 polyunsaturated fatty acids (PUFAs) are potential biomarkers for leprosy. In this study, we investigated retrospective sera of leprosy HCs by liquid chromatography-mass spectrometry and enzyme-linked immunoassay to determine whether circulating levels of ω -3 and ω -6 PUFA metabolites were altered in HCs that developed leprosy (HCDL) in comparison to those that did not (HCNDL). Sera were collected from HCs at the time of index case diagnosis and before clinical signs/symptoms of leprosy. Our findings showed that HCDL sera exhibited a distinct metabolic profile in comparison to HCNDL. Specifically, arachidonic acid, leukotriene B₄, 11-hydroxyeicosatetraenoic acid, prostaglandin D₂, and

lipoxin A₄ were elevated in HCDL. In contrast, prostaglandin E₂ levels were reduced in HCDL. The ω -3 PUFAs, docosahexaenoic acid, eicosapentaenoic acid, and the docosahexaenoic acid-derived resolvin D1 and maresin-1 were also elevated in HCDL individuals compared to HCNDL. Principal component analyses provided further evidence that lipid mediators could serve as an early biomarker for progression to active leprosy. A logistic model identified resolvin D1 and D2, and prostaglandin D₂ as having the greatest potential for early detection of HCs that will manifest leprosy.

Renal function impairment might be worsened by SARS-CoV-2 virus: a triple critical care disease causing hypoxemia.

Bereda G.

23-05-2023

Ann Med Surg (Lond).

<https://pubmed.ncbi.nlm.nih.gov/37427226/>

Clinico-Demographic Profiles of Herpes Zoster Cases in Patients With and Without COVID-19 Infection During the Pandemic: A Retrospective Analysis of 32 Cases.

Ahmed G, Ganguly S, Rahim JS, George C A, Karim HMR.

06-06-2023

Cureus.

<https://pubmed.ncbi.nlm.nih.gov/37425608/>

Leprosy among children in an area without primary health care coverage in Caratateua Island, Brazilian Amazon.

Costa ILV, da Costa PF, da Silva SM, Gobbo AR, Pinto PDDC, Spencer JS, da Silva MB, Salgado CG.

22-06-2023

Front Med (Lausanne).

<https://pubmed.ncbi.nlm.nih.gov/37425318/>

Introduction: The detection of leprosy in children is an important epidemiological marker of the disease, indicating the community's early exposure to *Mycobacterium leprae* and active transmission of the infection. **Methods:** In order to detect new cases among children by combining clinical evaluation and laboratory tests, we conducted an active case finding among individuals under 15 years old on Caratateua Island, located in the city of Belém, in the Pará state, an endemic region in the Amazon. Dermato-neurological examination, collection of 5 mL of peripheral blood for IgM anti-PGL-I antibody titration, and intradermal scraping for bacilloscopy and amplification of the specific RLEP region by qPCR were performed. **Results:** Out of the 56 examined children, 28/56 (50%) new cases were identified. At the time of evaluation, 38/56 (67.8%) children presented one or more clinical alterations. Seropositivity was detected in 7/27 (25.9%) new cases and 5/24 (20.8%) undiagnosed children. DNA amplification of *Mycobacterium leprae* was observed in 23/28 (82.1%) of new cases and in 5/26 (19.2%) of non-cases. Out of the total cases, 11/28 (39.2%) were exclusively diagnosed by clinical evaluation performed during the active case finding. Seventeen new

cases (60.8%) were detected considering the clinical alterations found in addition to positive results for qPCR. In this group, 3/17 (17.6%) qPCR-positive children presented significant clinical changes 5.5 months after the first evaluation. **Discussion:** Our research detected a number of cases 5.6 times higher compared to the total number of pediatric cases recorded throughout the year 2021 in the municipality of Belém, which shows a critical scenario of underdiagnosing of leprosy among children under 15 years old in the region. We propose the use of qPCR technique to identify new cases among children with oligosymptomatic or early disease in endemic areas, in addition to the training of Primary Health Care professionals and the implementation of the Family Health Strategy coverage in the visited area.

Unilateral Sweet's syndrome of lymphedematous inferior extremity associated with endometrial carcinoma: a unique presentation.

Zawar VP, Malekar PR, Nikam VV, Telhure BJ.

10-07-2023

Int J Dermatol.

<https://pubmed.ncbi.nlm.nih.gov/37424433/>

Leprosy in Literature and Art: The Covenant of Water.

Alpert JS.

07-7-2032

Am J Med.

<https://pubmed.ncbi.nlm.nih.gov/37423434/>

The leprosy reaction is associated with salivary anti-Porphyromonas gingivalis IgA antibodies.

Falcão MML, Passos-Soares JS, Machado PRL, Gomes-Filho IS, de Carvalho LP, de Campos EJ, Calheira MC, de Miranda PM, Santos RPB, Rocha Filho JTR, de Farias APF, Peixoto T, Nascimento RM, Seymour GJ, Trindade SC.

07-07-2023

AMB Express.

<https://pubmed.ncbi.nlm.nih.gov/37418096/>

The aim of the study was to evaluate the association between salivary anti-Porphyromonas gingivalis IgA antibodies and the leprosy reaction. The levels of salivary anti - P. gingivalis IgA antibodies, together with salivary flow and pH were measured in individuals diagnosed with leprosy and associated with the development of the leprosy reaction. Saliva was collected from 202 individuals diagnosed with leprosy at a reference leprosy treatment center, 106 cases with the leprosy reaction and 96 controls without the leprosy reaction. Anti - P. gingivalis IgA was evaluated by indirect immunoenzyme assay. Non-conditional logistic regression analysis was employed to estimate the association between antibody levels and the leprosy reaction. There was a positive statistically significant association between the levels of anti - P. gingivalis IgA and the presence of the leprosy reaction, controlling for confounders: age, sex, level of education and alcoholic beverage consumption: OR_{adjusted}: 2.55; IC 95%: 1.34-4.87. Individuals with leprosy who had high

levels of salivary anti - P. gingivalis IgA had approximately twice as many chances of developing the leprosy reaction. The findings suggest a possible relationship between salivary anti - P. gingivalis IgA antibodies and the leprosy reaction.

Contact sensitizers in commercial hair dye products in the Indian market: A consumer exposure study.

Palaniappan V, Murthy AB, Sadhasivamohan A, Karthikeyan K.

Aug-2023

Contact Dermatitis.

<https://pubmed.ncbi.nlm.nih.gov/37227133/>

A Change in the Trend of Quality Reporting in Leprosy Trials: A Systematic Review.

Thangaraju P, Sheth PG, Velmurugan H, Venkatesan S, Balan AK.

2023

Infect Disord Drug Targets.

<https://pubmed.ncbi.nlm.nih.gov/36843257/>

Background: Leprosy is a communicable disease caused by bacteria Mycobacterium leprae. Despite all attempts, it has not been eradicated in several underdeveloped nations since the start of the antibiotic age. It's a social issue as well as a stigmatised disease. Due to these restrictions, randomised controlled trials in leprosy confront numerous obstacles, which are reflected in the quality of study reporting. **Objectives:** The objective of this study is to use the Consolidated Standard for Reporting Trials (CONSORT) 2010 checklist to assess the quality of leprosy trial reporting. **Methods:** We assess the quality of reporting of randomised control trials on leprosy conducted after 2010 in the PubMed database, using the CONSORT checklist 2010. Second, we compare the quality of RCT reporting before and after the release of the CONSORT guidelines in 2010. **Results:** A total of 19 full-text eligible articles were examined and included in the final list of articles, which were then evaluated further. 4 out of 19 trials had a compliance percentage of more than 75%. 6 out of 19 trials had compliance percentage of 50% to 75%. 9 trials had a compliance percentage of below 50%. Highest compliance was 86.48% and the lowest compliance was 32.43%. When compared with trials before 2010, we could see an improvement in some criteria showing a statistically significant rise in comparison with trials conducted before 2010. **Conclusion:** Leprosy is still a concern in developing countries, which have failed to eradicate the disease despite their best efforts and resources. The compliance of leprosy related RCTs has improved since the introduction of the CONSORT guidelines, but the quality of reporting still remains on the lower side.

Alice Augusta Ball: The African-American chemist who pioneered the first viable treatment for Hansen's Disease.

Mushtaq S, Wermager P.

Morsures de serpent

The Association Between Ambient Temperature and Snakebite in Georgia, USA: A Case-Crossover Study.

Landry M, D'Souza R, Moss S, Chang HH, Ebelt S, Wilson L, Scovronick N.

11-07-2023

Geohealth.

<https://pubmed.ncbi.nlm.nih.gov/37441711/>

The World Health Organization has identified snakebite envenoming as a highest priority neglected tropical disease, yet there is a dearth of epidemiologic research on environmental risk factors, including outdoor temperature. Temperature may affect snakebites through human behavior or snake behavior; snakes are ectotherms, meaning outdoor temperatures influence their internal body temperature and thus their behavior. Here we investigate the relationship between short-term temperature and snakebites in Georgia, one of the most biodiverse US states in terms of herpetofauna. We acquired emergency department (ED) visit data for Georgia between 1 January 2014 and 31 December 2020. Visits for venomous and non-venomous snakebites were identified using diagnosis codes. For comparison, we also considered visits for non-snake (e.g., insects, spiders, scorpions) envenomation. Daily meteorology from the Daymet 1 km product was linked to patient residential ZIP codes. We applied a case-crossover design to estimate associations of daily maximum temperature and snakebite ED visits. During the 7-year study period, there were 3,908 visits for venomous snakebites, 1,124 visits for non-venomous bites and 65,187 visits for non-snake envenomation. Across the entire period, a 1°C increase in same-day maximum temperature was associated with a 5.6% (95%CI: 4.0-7.3) increase in the odds of venomous snakebite and a 5.8% (95%CI: 3.0-8.8) increase in non-venomous snakebite. Associations were strongest in the spring. We also observed a positive and significant ($p < 0.05$) association for non-snake envenomation, albeit slightly smaller and more consistent across seasons compared to those for snakebites.

Glutamine ameliorates Bungarus multicinctus venom-induced lung and heart injury through HSP70: NF-κB p65 and P53/PUMA signaling pathways involved.

Li Y, Guan Z, Hu S, Huang Z, He D, Cheng X, Song T, Mo C, Xiao M, Huang Y, Wei Y, Zhou Y, Zhang X, Liao M.

10-07-2023

J Venom Anim Toxins Incl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/37441002/>

Background: *Bungarus multicinctus* is one of the most dangerous venomous snakes prone to cardiopulmonary damage with extremely high mortality. In our previous

work, we found that glutamine (Gln) and glutamine synthetase (GS) in pig serum were significantly reduced after *Bungarus multicinctus* bite. In the present study, to explore whether there is a link between the pathogenesis of cardiopulmonary injury and Gln metabolic changes induced by *Bungarus multicinctus* venom. We investigated the effect of Gln supplementation on the lung and heart function after snakebite. **Methods:** We supplemented different concentrations of Gln to mice that were envenomated by *Bungarus multicinctus* to observe the biological behavior, survival rate, hematological and pathological changes. Gln was supplemented immediately or one hour after the venom injection, and then changes in Gln metabolism were analyzed. Subsequently, to further explore the protective mechanism of glutamine on tissue damage, we measured the expression of heat-shock protein70 (HSP70), NF-κB P65, P53/PUMA by western blotting and real-time polymerase in the lung and heart. **Results:** Gln supplementation delayed the envenoming symptoms, reduced mortality, and alleviated the histopathological changes in the heart and lung of mice bitten by *Bungarus multicinctus*. Additionally, Gln increased the activity of glutamine synthetase (GS), glutamate dehydrogenase (GDH) and glutaminase (GLS) in serum. It also balanced the transporter SLC7A11 expression in heart and lung tissues. *Bungarus multicinctus* venom induced the NF-κB nuclear translocation in the lung, while the HO-1 expression was suppressed. At the same time, venom activated the P53/PUMA signaling pathway and the BAX expression in the heart. Gln treatment reversed the above phenomenon and increased HSP70 expression. **Conclusion:** Gln alleviated the glutamine metabolism disorder and cardiopulmonary damage caused by *Bungarus multicinctus* venom. It may protect lungs and heart against venom by promoting the expression of HSP70, inhibiting the activation of NF-κB and P53/PUMA, thereby delaying the process of snake venom and reducing mortality. The present results indicate that Gln could be a potential treatment for *Bungarus multicinctus* bite.

Thromboelastography Use to Guide Resuscitation and Antivenom Administration after Gaboon Viper Bite.

Faulkner JD, Carballo CJ, Acquista E, Baughman SD Jr, Powers WF 4th, Novosel TJ, Yon JR.

11-07-2032

Am Surg.

<https://pubmed.ncbi.nlm.nih.gov/37431298/>

The Gaboon viper (*Bitis gabonica*) is an exotic snake native to sub-Saharan Africa. Gaboon viper venom is an extremely toxic hemotoxin, causing severe coagulopathy and local tissue necrosis. These are not aggressive snakes and therefore bites involving humans are rare and there is not a substantial amount of literature documenting how to manage these injuries and resultant coagulopathies. We report a 29-year-old male presenting 3 hours after a Gaboon viper envenomation resulting in coagulopathy requiring massive resuscitation and multiple doses of antivenom. The patient received various blood products based on thromboelastography (TEG) and also underwent early continuous renal replacement therapy (CRRT) to

assist in correction of severe acidosis and acute renal failure. The combination of TEG to guide resuscitation, administration of antivenom, and early implementation of CRRT allowed our team to correct venom-induced consumptive coagulopathy and ultimately allow the patient to survive following this extremely deadly Gaboon viper envenomation.

Intravenous snake bite: A catastrophic snake envenomation.

Naik SB.

Juil-Sep 2023

Ann Afr Med.

<https://pubmed.ncbi.nlm.nih.gov/37417008/>

Diagnostic characteristics of the 20-minute whole blood clotting test in detecting venom-induced consumptive coagulopathy following carpet viper envenoming.

Tianyi FL, Hamza M, Abubakar SB, Al Solaiss J, Trelfa A, Abdullahi HL, Ilyasu G, Mohammed N, Mohammed SA, Casewell NR, Harrison RA, Lalloo DG, Stienstra Y, Habib AG.

26-06-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/37363905/>

Introduction: Envenoming by *Echis* spp. (carpet or saw-scaled vipers) causes haemorrhage and coagulopathy and represents a significant proportion of snakebites in the savannah regions of West Africa. Early diagnosis of envenoming is crucial in the management of these patients and there is limited evidence on the utility of the 20-minute whole blood clotting test (20WBCT) in diagnosing venom-induced consumptive coagulopathy (VICC) following envenoming by *Echis ocellatus*. **Methods:** A prospective observational cohort study was conducted at the Kaltungo General Hospital in North-eastern Nigeria from September 2019 to September 2021. Standardised 20WBCTs were conducted by trained hospital staff and citrated plasma samples were collected at numerous timepoints. Prothrombin time (PT) and international normalised ratio (INR) were determined using a semi-automated analyser and INR values were calculated using international sensitivity indices (ISI). The sensitivity, specificity, positive predictive values (PPV), negative predictive values (NPV), and likelihood ratios of the 20WBCT compared to an INR ≥ 1.4 were calculated, alongside 95% confidence intervals. **Results:** We enrolled 121 patients into our study, with a median age of 26 (18.0-35.0) years and a male predominance (75.2%). The 20WBCT was positive (abnormal) in 101 out of 121 patients at timepoint 0h, of which 95 had an INR ≥ 1.4 , giving a sensitivity of 87.2% (95%CI 79.4-92.8). Among patients with a negative 20WBCT (normal), six had an INR < 1.4 giving a specificity of 50% (95%CI 21.1-78.9). The positive and negative likelihood ratios were 1.7 (95%CI 1.6-1.9) and 0.3 (95%CI 0.1-0.4) respectively. **Conclusion:** The 20WBCT is a simple, cheap, and easily accessible bedside test with a high sensitivity for the detection of patients with venom induced consumptive coagulopathy

(VICC) following envenoming by *E. ocellatus*, although false positives do occur. Repeated 20WBCTs can identify patients with new, persistent, and rebound coagulopathy.

Mycétome

Sinonasal Oxalosis due to Fungal Rhinosinusitis: A Unique Case of a Destructive Pseudotumor.

Christensen D, Tuluc M, Faro SH, Udare A, Gargano S.

10-07-2023

Int J Surg Pathol.

<https://pubmed.ncbi.nlm.nih.gov/37424352/>

Diagnostic capacities and treatment practices on implantation mycoses: Results from the 2022 WHO global online survey.

Milani B, Dagne DA, Choi HL, Schito M, Stone HA.

28-06-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/37379338/>

Between January and March 2022, WHO conducted a global online survey to collect data on diagnostic capacities and treatment practices in different settings for four implantation mycoses: eumycetoma, actinomycetoma, cutaneous sporotrichosis and chromoblastomycosis. The survey investigated the type of diagnostic methods available in countries at various health system levels (tertiary, secondary, primary level) and the medicines used to treat implantation mycoses, with a view to understanding the level of drug repurposing for treatment of these diseases. 142 respondents from 47 countries, including all continents, contributed data: 60% were from middle-income countries, with 59% working at the tertiary level of the health system and 30% at the secondary level. The results presented in this article provide information on the current diagnostic capacity and treatment trends for both pharmacological and non-pharmacological interventions. In addition, the survey provides insight on refractory case rates, as well as other challenges, such as availability and affordability of medicines, especially in middle-income countries. Although the study has limitations, the survey-collected data confirms that drug repurposing is occurring for all four surveyed implantation mycoses. The implementation of an openly accessible global and/or a national treatment registry for implantation mycoses could contribute to address the gaps in epidemiological information and collect valuable observational data to inform treatment guidelines and clinical research.

Rage

Therapeutic effects of engineered exosome-based miR-25 and miR-181a treatment in spinocerebellar ataxia type 3 mice by silencing ATXN3.

Tang Z, Hu S, Wu Z, He M.

12-07-2023

Mol Med.

<https://pubmed.ncbi.nlm.nih.gov/37438701/>

Background: Spinocerebellar ataxia type 3 (SCA3) is the most common autosomal dominant hereditary ataxia worldwide, which is however in a lack of effective treatment. In view of that engineered exosomes are a promising non-invasive gene therapy transporter that can overcome the traditional problem of poor drug delivery, the aim of this study was to evaluate, for the first time, the value of exosome-based microRNA therapy in SCA3 and the therapeutic effects of intravenously administrated ATXN3 targeting microRNAs in transgenic SCA3 mouse models. **Methods:** The rabies virus glycoprotein (RVG) peptide-modified exosomes loaded with miR-25 or miR-181a were peripherally injected to enable targeted delivery of miRNAs to the brain of SCA3 mice. The behaviors, ATXN3 level, purkinje cell and other neuronal loss, and neuroinflammation were evaluated 4 weeks after initial treatment. **Results:** The targeted and efficient delivery of miR-25 and miR-181a by modified exosomes substantially inhibited the mutant ATXN3 expression, reduced neuron apoptosis and induced motor improvements in SCA3 mouse models without increasing the neuroinflammatory response. **Conclusions:** Our study confirmed the therapeutic potential of engineered exosome-based miR-25 and miR-181a treatment in substantially reducing ATXN3 aggregation and cytotoxicity by relying on its targeted and efficient drug delivery performance in SCA3 mice. This treatment method shows a promising prospect for future clinical applications in SCA3.

Molecular Engineering of AIE Photosensitizers for Inactivation of Rabies Virus.

Bai Y, Yu EY, Liu Y, Jin H, Liu X, Wu X, Zhang M, Feng N, Huang P, Zhang H, Kwok RTK, Xia X, Li Y, Tang BZ, Wang H.

10-07-2023

Small.

<https://pubmed.ncbi.nlm.nih.gov/37431212/>

Rabies is a zoonotic neurological disease caused by the rabies virus (RABV) that is fatal to humans and animals. While several post-infection treatment have been suggested, developing more efficient and innovative antiviral methods are necessary due to the limitations of current therapeutic approaches. To address this challenge, a strategy combining photodynamic therapy and immunotherapy, using a photosensitizer (TPA-Py-PhMe) with high type I and type II reactive oxygen species (ROS) generation ability is proposed. This approach can inactivate the RABV by killing the virus directly and activating the immune response. At the cellular level, TPA-Py-PhMe can reduce the virus titer under preinfection prophylaxis and postinfection treatment, with its antiviral effect mainly dependent on ROS and pro-inflammatory factors. Intriguingly, when mice are injected with TPA-Py-PhMe and exposed to white light irradiation at three days post-infection, the onset of disease is delayed, and survival rates improved to some extent. Overall, this study shows

that photodynamic therapy and immunotherapy open new avenues for future antiviral research.

Author Correction: Unmodified rabies mRNA vaccine elicits high cross-neutralizing antibody titers and diverse B cell memory responses.

Hellgren F, Cagigi A, Arcoverde Cerveira R, Ols S, Kern T, Lin A, Eriksson B, Dodds MG, Jasny E, Schwendt K, Freuling C, Müller T, Corcoran M, Karlsson Hedestam GB, Petsch B, Loré K.

10-07-2023

Nat Commun.

<https://pubmed.ncbi.nlm.nih.gov/37429868/>

Dog Population Rabies Immunity before a Mass Vaccination Campaign in Lima, Peru: Vulnerabilities for Virus Reestablishment.

Chuquista-Alcarraz O, Falcón N, Vigilato MAN, Rocha F, Toledo-Barone G, Amorim-Conselheiro J, Recuenco SE, Castillo-Neyra R.

10-07-2023

Am J Trop Med Hyg.

<https://pubmed.ncbi.nlm.nih.gov/37429572/>

Lima, Peru, has not had a case of canine rabies since 1999. However, Lima remains at risk of rabies reintroduction due to the free movement of dogs from nearby rabies-endemic areas. In Latin America, rabies vaccination campaigns must reach 80% of dogs to halt transmission, but estimates of vaccine coverage are often unavailable, unreliable, or inaccurate. Quantifying virus neutralizing antibodies (VNA) allows monitoring of the immunological status of the canine population, evaluation of the degree of humoral protection to the virus, and assessing, partially, the population response to vaccination. We evaluated the dog population's immunity level against the rabies virus before a mass vaccination campaign in Lima. We collected 141 canine blood samples in the district of Surquillo and quantified rabies virus neutralizing antibody titers using the fluorescent antibody virus neutralization test). We surveyed dogs owners to reconstruct canine vaccination histories. Among dogs previously vaccinated, 73.9% exceeded the seroconversion threshold of > 0.5 IU/mL. Among all dogs, only 58.2% reached the titer limit for seroconversion. Dogs ≤ 1 year old constituted 26.2% of the total canine population and had lower levels of VNA than dogs > 1 year old ($\chi^2 = 9.071$; $P = 0.028$). Importantly, dogs vaccinated with single-pathogen vaccines had higher levels of VNA than those who received combined-pathogen vaccines ($\chi^2 = 7.721$; $P = 0.005$). We provide an important and timely glimpse to the immunity status of the dog population in urban areas of Lima, a metropolis near a dog rabies-endemic region.

Expert consensus on the clinical application of ormutivimab injection for use against the rabies virus.

Chen R, Li H, Zhu W, Cheng H, Li Y, Li X, Li F, Liu X, Hu S, Yan B, Zheng Y, Zuo Y, Dong G, Li X.

12-07-2023

Expert Opin Drug Saf.
<https://pubmed.ncbi.nlm.nih.gov/37427985/>

One Health for Rabies Elimination: China Rabies Annual Conference in 2023.

[No authors listed]
20-07-2023
Biomed Environ Sci.
<https://pubmed.ncbi.nlm.nih.gov/37424254/>

Whole-brain monosynaptic inputs to lateral periaqueductal gray glutamatergic neurons in mice.

Ma WX, Li L, Kong LX, Zhang H, Yuan PC, Huang ZL, Wang YQ.
09-07-2023
CNS Neurosci Ther.
<https://pubmed.ncbi.nlm.nih.gov/37424163/>

Objective: The lateral periaqueductal gray (LPAG), which mainly contains glutamatergic neurons, plays an important role in social responses, pain, and offensive and defensive behaviors. Currently, the whole-brain monosynaptic inputs to LPAG glutamatergic neurons are unknown. This study aims to explore the structural framework of the underlying neural mechanisms of LPAG glutamatergic neurons. **Methods:** This study used retrograde tracing systems based on the rabies virus, Cre-LoxP technology, and immunofluorescence analysis. **Results:** We found that 59 nuclei projected monosynaptic inputs to the LPAG glutamatergic neurons. In addition, seven hypothalamic nuclei, namely the lateral hypothalamic area (LH), lateral preoptic area (LPO), substantia innominata (SI), medial preoptic area, ventral pallidum, posterior hypothalamic area, and lateral globus pallidus, projected most densely to the LPAG glutamatergic neurons. Notably, we discovered through further immunofluorescence analysis that the inputs to the LPAG glutamatergic neurons were colocalized with several markers related to important neurological functions associated with physiological behaviors. **Conclusion:** The LPAG glutamatergic neurons received dense projections from the hypothalamus, especially nuclei such as LH, LPO, and SI. The input neurons were colocalized with several markers of physiological behaviors, which show the pivotal role of glutamatergic neurons in the physiological behaviors regulation by LPAG.

Schistosomiasis

A planetary health innovation for disease, food and water challenges in Africa.

Rohr JR, Sack A, Bakhom S, Barrett CB, Lopez-Carr D, Chamberlin AJ, Civitello DJ, Diatta C, Doruska MJ, De Leo GA, Haggerty CJE, Jones IJ, Jouanard N, Lund AJ, Ly AT, Ndione RA, Remais JV, Riveau G, Schacht AM, Seck M, Senghor S, Sokolow SH, Wolfe C.
12-07-2023

Nature.
<https://pubmed.ncbi.nlm.nih.gov/37438520/>

Low prevalence of *Schistosoma haematobium* infection in pregnant women in Buffalo City district.

Peters RPH, Mdingi M, Jung H, Mukomana F, Gigi RMS, Medina-Marino A, Klausner JD.
15-07-2023
S Afr J Infect Dis.
<https://pubmed.ncbi.nlm.nih.gov/37435116/>

Investigation on birth weight outcomes in schistosomiasis and praziquantel research: a correspondence.

Holtfreter MC, Mischlinger J, Davi SD, Schleenvoigt BT.
12-07-2023
Eur J Med Res.
<https://pubmed.ncbi.nlm.nih.gov/37434209/>

Infection with *Schistosoma* sp. during pregnancy can cause low birth weight of the newborn. To allow a better differentiation between newborns with low birth weight and those with normal weight, the terms of intrauterine growth restriction (IUGR), small for gestational age (SGA) or fetal growth restriction (FGR) should be used. FGR describes the relationship between birth weight and gestational age and is defined as the incapability of a fetus to achieve expected growth with birth weight below the 10th percentile for gestational age. Additional investigations of the proportion of newborns with FGR should obtain more certainty about the effect of praziquantel and schistosomiasis on fetal growth.

TREM2 expression promotes liver and peritoneal M2 macrophage polarization in mice infected with *Schistosoma japonicum*.

Zhu D, Huang M, Shen P, Zhang B, Chen G, Chen J, Duan L, Duan Y.
10-07-2023
J Cell Mol Med.
<https://pubmed.ncbi.nlm.nih.gov/37430471/>

Oxamniquine derivatives overcome Praziquantel treatment limitations for Schistosomiasis.

Alwan SN, Taylor AB, Rhodes J, Tidwell M, McHardy SF, LoVerde PT.
10-07-2023
PLoS Pathog.
<https://pubmed.ncbi.nlm.nih.gov/37428793/>

Human schistosomiasis is a neglected tropical disease caused by *Schistosoma mansoni*, *S. haematobium*, and *S. japonicum*. Praziquantel (PZQ) is the method of choice for treatment. Due to constant selection pressure, there is an urgent need for new therapies for schistosomiasis. Previous treatment of *S. mansoni* included the use of oxamniquine (OXA), a drug that is activated by a schistosome sulfotransferase (SULT). Guided by data from X-ray crystallography and *Schistosoma* killing assays more

than 350 OXA derivatives were designed, synthesized, and tested. We were able to identify CIDD-0150610 and CIDD-0150303 as potent derivatives in vitro that kill (100%) of all three *Schistosoma* species at a final concentration of 71.5 μ M. We evaluated the efficacy of the best OXA derivatives in an in vivo model after treatment with a single dose of 100 mg/kg by oral gavage. The highest rate of worm burden reduction was achieved by CIDD -150303 (81.8%) against *S. mansoni*, CIDD-0149830 (80.2%) against *S. haematobium* and CIDD-066790 (86.7%) against *S. japonicum*. We have also evaluated the ability of the derivatives to kill immature stages since PZQ does not kill immature schistosomes. CIDD-0150303 demonstrated (100%) killing for all life stages at a final concentration of 143 μ M in vitro and effective reduction in worm burden in vivo against *S. mansoni*. To understand how OXA derivatives fit in the SULT binding pocket, X-ray crystal structures of CIDD-0150303 and CIDD-0150610 demonstrate that the SULT active site will accommodate further modifications to our most active compounds as we fine tune them to increase favorable pharmacokinetic properties. Treatment with a single dose of 100 mg/kg by oral gavage with co-dose of PZQ + CIDD-0150303 reduced the worm burden of PZQ resistant parasites in an animal model by 90.8%. Therefore, we conclude that CIDD-0150303, CIDD-0149830 and CIDD-066790 are novel drugs that overcome some of PZQ limitations, and CIDD-0150303 can be used with PZQ in combination therapy.

Emerging biomedical tools for biomarkers detection and diagnostics in schistosomiasis.

Lima RRM, Lima JVA, Ribeiro JFF, Nascimento JB, Oliveira WF, Cabral Filho PE, Fontes A.

01-07-2023

Talanta.

<https://pubmed.ncbi.nlm.nih.gov/37423177/>

Influence of a chronic *Schistosoma mansoni* infection on the outcomes of a SARS-CoV-2 infection in the hamster model.

Rissmann M, Veldhuis Kroeze EJB, Tielens AGM, Rockx B, van Hellemond JJ.

05-07-2023

J Infect.

<https://pubmed.ncbi.nlm.nih.gov/37419283/>

Schistosoma mansoni egg-derived thioredoxin and Sm14 drive the development of IL-10 producing regulatory B cells.

Chayé MAM, Gasan TA, Ozir-Fazalalikhani A, Scheenstra MR, Zawistowska-Deniziak A, van Hengel ORJ, Gentenaar M, Manurung MD, Harvey MR, Codée JDC, Chiodo F, Heijke AM, Kalinowska A, van Diepen A, Hensbergen PJ, Yazdanbakhsh M, Guigas B, Hokke CH, Smits HH.

26-06-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/37363916/>

During chronic schistosome infections, a complex regulatory network is induced to regulate the host immune system, in which IL-10-producing regulatory B (Breg) cells play a significant role. *Schistosoma mansoni* soluble egg antigens (SEA) are bound and internalized by B cells and induce both human and mouse IL-10 producing Breg cells. To identify Breg-inducing proteins in SEA, we fractionated SEA by size exclusion chromatography and found 6 fractions able to induce IL-10 production by B cells (out of 18) in the high, medium and low molecular weight (MW) range. The high MW fractions were rich in heavily glycosylated molecules, including multi-fucosylated proteins. Using SEA glycoproteins purified by affinity chromatography and synthetic glycans coupled to gold nanoparticles, we investigated the role of these glycan structures in inducing IL-10 production by B cells. Then, we performed proteomics analysis on active low MW fractions and identified a number of proteins with putative immunomodulatory properties, notably thioredoxin (SmTrx1) and the fatty acid binding protein Sm14. Subsequent splenic murine B cell stimulations and hock immunizations with recombinant SmTrx1 and Sm14 showed their ability to dose-dependently induce IL-10 production by B cells both in vitro and in vivo. Identification of unique Breg cells-inducing molecules may pave the way to innovative therapeutic strategies for inflammatory and auto-immune diseases.

The FMRF-NH₂ gated sodium channel of *Biomphalaria glabrata*: Localization and expression following infection by *Schistosoma mansoni*.

Vicente-Rodríguez LC, Torres-Arroyo AC, Hernández-Vázquez A, Rosa-Casillas M, Bracho-Rincón DP, de Jesús PM, Behra ML, Habib MR, Zhou XN, Rosenthal JJC, Miller MW.

23-06-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/37352363/>

The neglected tropical disease schistosomiasis impacts over 700 million people globally. *Schistosoma mansoni*, the trematode parasite that causes the most common type of schistosomiasis, requires planorbid pond snails of the genus *Biomphalaria* to support its larval development and transformation to the cercarial form that can infect humans. A greater understanding of neural signaling systems that are specific to the *Biomphalaria* intermediate host could lead to novel strategies for parasite or snail control. This study examined a *Biomphalaria glabrata* neural channel that is gated by the neuropeptide FMRF-NH₂. The *Biomphalaria glabrata* FMRF-NH₂ gated sodium channel (Bgl-FaNaC) amino acid sequence was highly conserved with FaNaCs found in related gastropods, especially the planorbid *Planorbella trivolvis* (91% sequence identity). In common with the *P. trivolvis* FaNaC, the *B. glabrata* channel exhibited a low affinity (EC₅₀: 3 x 10⁻⁴ M) and high specificity for the FMRF-NH₂ agonist. Its expression in the central nervous system, detected with immunohistochemistry and in situ hybridization, was widespread, with the protein localized mainly to neuronal fibers and the mRNA confined to cell bodies. Colocalization of the Bgl-FaNaC message with its FMRF-NH₂ agonist

precursor occurred in some neurons associated with male mating behavior. At the mRNA level, Bgl-FaNaC expression was decreased at 20 and 35 days post infection (dpi) by *S. mansoni*. Increased expression of the transcript encoding the FMRF-NH2 agonist at 35 dpi was proposed to reflect a compensatory response to decreased receptor levels. Altered FMRF-NH2 signaling could be vital for parasite proliferation in its intermediate host and may therefore present innovative opportunities for snail control.

Trachome

The conjunctival transcriptome in Ethiopians after trichiasis surgery: associations with the development of eyelid contour abnormalities and the effect of oral doxycycline treatment.

Derrick T, Habtamu E, Tadesse Z, Callahan EK, Worku A, Gashaw B, Macleod D, Mabey DCW, Holland MJ, Burton MJ.

11-11-2022

Wellcome Open Res.

<https://pubmed.ncbi.nlm.nih.gov/37426632/>

Changes in trachoma indicators in Kiribati with two rounds of azithromycin mass drug administration, measured in serial population-based surveys.

Goodhew EB, Taoaba R, Harding-Esch EM, Gwyn SE, Bakhtiari A, Butcher R, Cama A, Guagliardo SAJ, Jimenez C, Mpyet CD, Tun K, Wickens K, Solomon AW, Martin DL, Tekeraoi R.

07-07-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/37418501/>

Baseline mapping in the two major population centers of Kiribati showed that trachoma was a public health problem in need of programmatic interventions. After conducting two annual rounds of antibiotic mass drug administration (MDA), Kiribati undertook trachoma impact surveys in 2019, using standardized two-stage cluster surveys in the evaluation units of Kiritimati Island and Tarawa. In Kiritimati, 516 households were visited and in Tarawa, 772 households were visited. Nearly all households had a drinking water source and access to an improved latrine. The prevalence of trachomatous trichiasis remained above the elimination threshold (0.2% in ≥15-year-olds) and was virtually unchanged from baseline. The prevalence of trachomatous inflammation-follicular (TF) in 1-9-year-olds decreased by approximately 40% from baseline in both evaluation units but remained above the 5% TF prevalence threshold for stopping MDA. TF prevalence at impact survey was 11.5% in Kiritimati and 17.9% in Tarawa. Infection prevalence in 1-9-year-olds by PCR was 0.96% in Kiritimati and 3.3% in Tarawa. Using a multiplex bead assay to measure antibodies to the *C. trachomatis* antigen Pgp3, seroprevalence in 1-9-year-olds was 30.2% in Kiritimati and 31.4% in Tarawa. The seroconversion rate, in seroconversion events/100 children/year, was 9.0 in Kiritimati and 9.2 in Tarawa.

Seroprevalence and seroconversion rates were both assessed by four different assays, with strong agreement between tests. These results show that, despite decreases in indicators associated with infection at impact survey, trachoma remains a public health problem in Kiribati, and provide additional information about changes in serological indicators after MDA.

Trachoma, the world's leading infectious cause of blindness: The remaining gap in care and access to basic handwashing facilities.

Wu TJ, Reynolds MM.

Jul-2023

Eur J Ophthalmol.

<https://pubmed.ncbi.nlm.nih.gov/36726295/>

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

The global prevalence of human fascioliasis: a systematic review and meta-analysis.

Rosas-Hostos Infantes LR, Paredes Yataco GA, Ortiz-Martínez Y, Mayer T, Terashima A, Franco-Paredes C, Gonzalez-Diaz E, Rodriguez-Morales AJ, Bonilla-Aldana DK, Vargas Barahona L, Grimshaw AA, Chastain DB, Sillau S, Marcos LA, Henao-Martínez AF.

08-07-2023

Ther Adv Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/37434654/>

Background: Fascioliasis is a parasitic zoonosis that can infect humans and be a source of significant morbidity. The World Health Organization lists human fascioliasis as a neglected tropical disease, but the worldwide prevalence of fascioliasis data is unknown. **Objective:** We aimed to estimate the global prevalence of human fascioliasis. **Data sources and methods:** We performed a systematic review and prevalence meta-analysis. We used the following inclusion criteria: articles published in the English, Portuguese, or Spanish languages from December 1985 to October 2022 and studies assessing the prevalence of *Fasciola* in the general population with an appropriate diagnostic methodology, including longitudinal studies, prospective and retrospective cohorts, case series, and randomized clinical trials (RCTs). We excluded animal studies. Two reviewers independently reviewed the selected studies for methodological quality, performing critical standard measures from JBI SUMARI. A random-effects model was conducted of the summary extracted data on the prevalence proportions. We reported the estimates according to the GATHER statement. **Results:** In all, 5617 studies were screened for

eligibility. Fifty-five studies from 15 countries were selected, including 154,697 patients and 3987 cases. The meta-analysis revealed a pooled prevalence of 4.5% [95% confidence interval (CI): 3.1-6.1; $I^2 = 99.4\%$; $T^2 = 0.07$]. The prevalence in South America, Africa, and Asia was 9.0%, 4.8%, and 2.0%, respectively. The highest prevalence was found in Bolivia (21%), Peru (11%), and Egypt (6%). Subgroup analysis showed higher prevalence estimates in children, in studies from South America, and when Fas2-enzyme-linked immunosorbent assay (ELISA) was used as a diagnostic method. A larger study sample size ($p = 0.027$) and an increase in female percentage ($p = 0.043$) correlated with a decrease in prevalence. Multiple meta-regression showed a higher prevalence for hyperendemic than hypoendemic ($p = 0.002$) or mesoendemic ($p = 0.013$) regions. **Conclusion:** The estimated prevalence and projected disease burden of human fascioliasis are high. Study findings support that fascioliasis continues to be a globally neglected tropical disease. Strengthening epidemiological surveillance and implementing measures to control and treat fascioliasis is imperative in the most affected areas.

ON LIVER FLUKE (FASCIOLA HEPATICA) IN CAPTIVE VICUÑAS (VICUGNA VICUGNA) AT KNOWSLEY SAFARI, PRESCOT, UNITED KINGDOM.

Juhasz A, Chapman E, Martin A, Cunningham LJ, Jones S, Johnson B, Walsh ND, Quayle J, Cracknell J, LaCourse EJ, Stothard JR.

Jul-2023

J Zoo Wildl Med.

<https://pubmed.ncbi.nlm.nih.gov/37428698>

Trypanosomes (trypanosomiasis et maladie de Chagas)

Characterization of Latin American migrants at risk for Trypanosoma cruzi infection in a non-endemic setting. Insights into initial evaluation of cardiac and digestive involvement.

Layne-Roldán P, Losada-Galván I, Posada E, de la Torre Ávila L, Casellas A, Sanz S, Subirá C, Rodríguez-Valero N, Camprubí-Ferrer D, Vera I, Roldán M, Aldasoro E, Oliveira-Souto I, Calvo-Cano A, Valls ME, Álvarez-Martínez MJ, Gállego M, Abras A, Ballart C, Muñoz J, Gascón J, Pinazo MJ.

13-07-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/37440480/>

Background: Trypanosoma cruzi causes Chagas disease (CD), a potentially fatal disease characterized by cardiac disorders and digestive, neurological or mixed alterations. T. cruzi is transmitted to humans by the bite of triatomine vectors; both the parasite and disease are endemic in Latin America and the United States. In the last decades, population migration has changed the classic

epidemiology of T. cruzi, contributing to its global spread to traditionally non-endemic countries. Screening is recommended for Latin American populations residing in non-endemic countries. **Methods:** The present study analyzes the epidemiological characteristics of 2,820 Latin American individuals who attended the International Health Service (IHS) of the Hospital Clinic de Barcelona between 2002 and 2019. The initial assessment of organ damage among positive cases of T. cruzi infection was analyzed, including the results of electrocardiogram (ECG), echocardiogram, barium enema and esophagogram. **Results:** Among all the screened individuals attending the clinic, 2,441 (86.6%) were born in Bolivia and 1,993 (70.7%) were female. Of individuals, 1,517 (81.5%) reported previous exposure to the vector, which is a strong risk factor associated with T. cruzi infection; 1,382 individuals were positive for T. cruzi infection. The first evaluation of individuals with confirmed T. cruzi infection, showed 148 (17.1%) individuals with Chagasic cardiomyopathy, the main diagnostic method being an ECG and the right bundle branch block (RBBB) for the most frequent disorder; 16 (10.8%) individuals had a normal ECG and were diagnosed of Chagasic cardiomyopathy by echocardiogram. **Conclusions:** We still observe many Latin American individuals who were at risk of T. cruzi infection in highly endemic areas in their countries of origin, and who have not been previously tested for T. cruzi infection. In fact, even in Spain, a country with one of the highest proportion of diagnosis of Latin American populations, T. cruzi infection remains underdiagnosed. The screening of Latin American populations presenting with a similar profile as reported here should be promoted. ECG is considered necessary to assess Chagasic cardiomyopathy in positive individuals, but echocardiograms should also be considered as a diagnostic approach given that it can detect cardiac abnormalities when the ECG is normal.

Molecular and genetic diversity in isolates of Trypanosoma evansi from naturally infected horse and dogs by using RoTat 1.2 VSG gene in Madhya Pradesh, India.

Verma R, Das G, Singh AP, Kumar S, Nath S, Sengupta PP, Sankar M, Tiwari A, Gupta V, Srivastava S.

13-07-2023

Mol Biol Rep.

<https://pubmed.ncbi.nlm.nih.gov/37439897/>

Background: Trypanosoma evansi is a protozoan parasite that can infect a wide range of animals and is widespread around the world. In this study, we analyzed four fatal cases of T. evansi infection using clinical, parasitological, and molecular approaches. We also explored the genetic diversity, demographic history, and population-genetic structure of T. evansi using available Rode Trypanozoon antigenic type (RoTat) 1.2 gene sequences. **Methods and results:** Clinical findings of infected animals revealed high fever, anemia, weakness, and anorexia. The animals were treated with diminazene aceturate, which was moderately effective, and hematobiochemical parameters showed changes in hemoglobin and glucose levels. The molecular and genetic diversity of T. evansi was analyzed using the RoTat 1.2 VSG gene. Phylogenetic and haplotype analysis

revealed two distinct clusters of *T. evansi* circulating in India. The genetic diversity indices, neutrality tests, gene flow, and genetic differentiation outcomes confirmed the genetic diversity of the *T. evansi* population, with a lack of uniformity. The identification of two distinct clusters, exhibiting differential demographic histories and evolutionary forces, implies that the clusters may have undergone independent evolutionary trajectories or experienced different environmental pressures.

Conclusion: The present findings underlined the need of an early and precise diagnosis in order to treat and control *T. evansi* infections, and the RoTat 1.2 VSG gene is an important genetic marker for understanding the genetic diversity and evolutionary history of *T. evansi*. This knowledge can be used to create tailored strategies to control and manage the infection in an endemic region.

Validation of in vitro-produced and freeze-dried whole cell lysate antigens for ELISA Trypanosoma evansi antibody detection in camels.

Bossard G, Desquesnes M.

04-07-2023

Vet Parasitol.

<https://pubmed.ncbi.nlm.nih.gov/37437407/>

Development of the livestock pathogen Trypanosoma (Nannomonas) simiae in the tsetse fly with description of putative sexual stages from the proboscis.

Peacock L, Kay C, Collett C, Bailey M, Gibson W.

11-07-2023

Parasit Vectors.

<https://pubmed.ncbi.nlm.nih.gov/37434196/>

Structure-Activity Relationships, Tolerability and Efficacy of Microtubule-Active 1,2,4-Triazolo[1,5-a]pyrimidines as Potential Candidates to Treat Human African Trypanosomiasis.

Monti L, Liu LJ, Varricchio C, Lucero B, Alle T, Yang W, Bem-Shalom I, Gilson M, Brunden KR, Brancale A, Caffrey CR, Ballatore C.

10-07-2023

ChemMedChem.

<https://pubmed.ncbi.nlm.nih.gov/37429821/>

Tubulin and microtubules (MTs) are potential protein targets to treat parasitic infections and our previous studies have shown that the triazolopyrimidine (TPD) class of MT-active compounds hold promise as antitrypanosomal agents. MT-targeting TPDs include structurally related but functionally diverse congeners that interact with mammalian tubulin at either one or two distinct interfacial binding sites; namely, the seventh and vinca sites, which are found within or between α,β -tubulin heterodimers, respectively. Evaluation of the activity of 123 TPD congeners against cultured *Trypanosoma brucei* enabled a robust quantitative structure-activity relationship (QSAR) model and the prioritization of two congeners for in vivo pharmacokinetics (PK), tolerability and efficacy studies. Treatment of *T. brucei*-infected mice

with tolerable doses of TPDs 3 and 4 significantly decreased blood parasitemia within 24 h. Further, two once-weekly doses of 4 at 10 mg/kg significantly extended the survival of infected mice relative to infected animals treated with vehicle. Further optimization of dosing and/or the dosing schedule of these CNS-active TPDs may provide alternative treatments for human African trypanosomiasis.

Comparative proteomic analysis of Trypanosoma cruzi TcI lineage epimastigotes unveils metabolic and phenotypic differences between fast- and slow-dividing strains.

Telleria J, Tibayrenc M, Mendoza MDS, Seveno M, Costales JA.

08-07-2023

Exp Parasitol.

<https://pubmed.ncbi.nlm.nih.gov/37429537/>

Trypanosoma cruzi, the causative agent of Chagas disease, is a genetically and phenotypically diverse species, divided into 5 main phylogenetic lineages (TcI to TcVI). TcI is the most widespread lineage in the Americas. Proteomics is a suitable tool to study the global protein expression dynamics in pathogens. Previous proteomic studies have revealed a link between (i) the genetic variability; (ii) the protein expression; and (iii) the biological characteristics of *T. cruzi*. Here, two-dimensional electrophoresis (2DE) and mass spectrometry were used to characterize the overall protein expression profiles of epimastigotes from four distinct TcI strains displaying different growth kinetics. Ascending hierarchical clustering analysis based on the global 2DE protein expression profiles grouped the strains under study into two clusters that were congruent with their fast or slow growth kinetics. A subset of proteins differentially expressed by the strains in each group were identified by mass spectrometry. Biological differences between the two groups, including use of glucose as an energy source, flagellum length, and metabolic activity, were predicted by proteomic analysis and confirmed by metabolic tests and microscopic measurements performed on the epimastigotes of each strain. Our results show that protein expression profiles are correlated with parasite phenotypes, which may in turn influence the parasite's virulence and transmission capacity.

Alterations in energy metabolism of Rhodnius prolixus induced by Trypanosoma rangeli infection.

Andrade LC, Majerowicz D, Oliveira PL, Guarneri AA.

08-07-2023

Insect Biochem Mol Biol.

<https://pubmed.ncbi.nlm.nih.gov/37429385/>

DIAGNOSIS AND TREATMENT OF A NATURAL INFECTION WITH TRYPANOSOMA CRUZI (CHAGAS DISEASE) IN A SYMPTOMATIC DE BRAZZA'S MONKEY (CERCOPITHECUS NEGLECTUS) IN ALABAMA.

McCain S, Sim RR, Weidner B, Rivas AE, White B, Auckland LD, Tarleton RL, Hamer S.

Jul-2023

J Zoo Wildl Med.

<https://pubmed.ncbi.nlm.nih.gov/37428708/>

Histone divergence in trypanosomes results in unique alterations to nucleosome structure.

Deák G, Wapenaar H, Sandoval G, Chen R, Taylor MRD, Burdett H, Watson JA, Tuijtel MW, Webb S, Wilson MD.

10-07-2023

Nucleic Acids Res.

<https://pubmed.ncbi.nlm.nih.gov/37427792/>

Eukaryotes have a multitude of diverse mechanisms for organising and using their genomes, but the histones that make up chromatin are highly conserved. Unusually, histones from kinetoplastids are highly divergent. The structural and functional consequences of this variation are unknown. Here, we have biochemically and structurally characterised nucleosome core particles (NCPs) from the kinetoplastid parasite *Trypanosoma brucei*. A structure of the *T. brucei* NCP reveals that global histone architecture is conserved, but specific sequence alterations lead to distinct DNA and protein interaction interfaces. The *T. brucei* NCP is unstable and has weakened overall DNA binding. However, dramatic changes at the H2A-H2B interface introduce local reinforcement of DNA contacts. The *T. brucei* acidic patch has altered topology and is refractory to known binders, indicating that the nature of chromatin interactions in *T. brucei* may be unique. Overall, our results provide a detailed molecular basis for understanding evolutionary divergence in chromatin structure.

Antiprotozoal activity of natural products from Nigerien plants used in folk medicine.

Sevik Kilicaslan O, Cretton S, Hausmann E, Quirós-Guerrero L, Karimou S, Kaiser M, Mäser P, Christen P, Cuendet M.

23-06-2023

Front Pharmacol.

<https://pubmed.ncbi.nlm.nih.gov/37426806/>

In the course of the screening of plants from Niger for antiprotozoal activity, the methanol extract of *Cassia sieberiana*, and the dichloromethane extracts of *Ziziphus mauritiana* and *Sesamun alatum* were found to be active against protozoan parasites, namely *Trypanosoma brucei rhodesiense*, *Trypanosoma cruzi*, *Leishmania donovani* and/or *Plasmodium falciparum*. Myricitrin (**1**), quercitrin (**2**) and 1-palmitoyl-lysocleithin (**3**) were isolated from *C. sieberiana*. From *Z. mauritiana*, the three triterpene derivatives **13**, **15**, and **16** are described here for the first time. Their chemical structures were determined by 1D and 2D NMR experiments, UV, IR and HRESIMS data. The absolute configurations were assigned via comparison of the experimental and calculated ECD spectra. In addition, eight known cyclopeptide alkaloids (**4**, **5**, **7-12**), and five known triterpenoids (**6**, **14**, **17-19**) were isolated. The antiprotozoal activity of the isolated compounds, as well

as of eleven quinone derivatives (**20-30**) previously isolated from *S. alatum* was determined *in vitro*. The cytotoxicity in L6 rat myoblast cells was also evaluated. Compound **18** showed the highest antiplasmodial activity (IC₅₀ = 0.2 µM) and compound **24** inhibited *T. b. rhodesiense* with an IC₅₀ value of 0.007 µM. However, it also displayed significant cytotoxicity in L6 cells (IC₅₀ = 0.4 µM).

Molecular identification of *Trypanosoma theileri* (Laveran, 1902) in cattle from two slaughterhouses in Ecuador and its relation with other haematropic agents.

Chávez-Larrea MA, Cholota-Iza C, Cueva-Villavicencio J, Yugcha-Díaz M, Ron-Román JW, Rodríguez-Cabezas A, Saegerman C, Reyna-Bello A.

23-06-2023

Front Vet Sci.

<https://pubmed.ncbi.nlm.nih.gov/37426080/>

Trypanosoma theileri is a worldwide distributed haemoparasite that has been reported throughout the American continent in various species, including bovines, buffaloes and bats. In bovines, high incidence of *T. theileri* can be harmful when associated with other infections or under stress situations. There is little information on this hemoflagellate in Ecuador, which prompted the study and molecular identification of the trypanosomes collected in two slaughtering centers. Between February and April 2021, a total of 218 samples of bovine blood were collected in abattoirs located in the Andean region of Quito ($n = 83$) and in the coastal region, in Santo Domingo ($n = 135$). Quito public Slaughterhouse is the biggest in Ecuador, and for that, they receive animals from all country; on the other hand, Santo Domingo's Slaughterhouse is a small one where mainly females from the region are sacrificed and some males. The samples were evaluated using two molecular tests, the PCR cathepsin L-like (CatL) specific for *T. theileri* and for the positive samples, a Nested PCR that targets the ITS of the 18S gene. The corresponding PCR products were sequenced, analyzed by BLAST/NCBI and the sequences were used to build a concatenated phylogenetic tree, using the MEGA XI software. Overall, 34 out of the 218 samples, (15.6%) were positive to *T. theileri* by PCR CatL, resulting from 20/83 (24.1%) positives from the Quito abattoir and 14/135 (10.4%) from the Santo Domingo slaughterhouse. These prevalence rates were found to be significantly different ($p = 0.006$). According to the phylogenetic tree based on the CatL and ITS concatenated sequences ($n = 13$), the two novel Equatorial *T. theileri* isolates, ThI ($n = 7$) and ThII ($n = 6$) are closely related and associated to the IC, IB and IIB genotypes, present in Brazil, Venezuela and Colombia. Thirty-one out of the thirty-four *T. theileri*-positive bovines were co-infected with other haematropic pathogens, *Anaplasma marginale*, *Babesia* spp and *T. vivax*. This coinfection could be responsible for additional pathologies and harmful effects on the affected cattle. This study presents the molecular identification and genotypification of *T. theileri* isolated from cattle in Ecuador through the analysis of *CATL* and *ITS* sequences,

and the high frequency of coinfection of this hemoflagellate with other blood haematotropic organisms.

Persistent biofluid small molecule alterations induced by *Trypanosoma cruzi* infection are not restored by antiparasitic treatment.

Dean DA, Roach J, vonBargen RU, Xiong Y, Kane SS, Klechka L, Wheeler K, Sandoval MJ, Lesani M, Hossain E, Katemauswa M, Schaefer M, Harris M, Barron S, Liu Z, Pan C, McCall LI.

03-07-2023

bioRxiv.

<https://pubmed.ncbi.nlm.nih.gov/37425694/>

Biochemical characterization of GAF domain of free-R-methionine sulfoxide reductase from *Trypanosoma cruzi*.

Gonzalez LN, Cabeza MS, Robello C, Guerrero SA, Iglesias AA, Arias DG.

07-07-2023

Biochimie.

<https://pubmed.ncbi.nlm.nih.gov/37423556/>

Trypanosoma cruzi is the causal agent of Chagas Disease and is a unicellular parasite that infects a wide variety of mammalian hosts. The parasite exhibits auxotrophy by L-Met; consequently, it must be acquired from the extracellular environment of the host, either mammalian or invertebrate. Methionine (Met) oxidation produces a racemic mixture (R and S forms) of methionine sulfoxide (MetSO). Reduction of L-MetSO (free or protein-bound) to L-Met is catalyzed by methionine sulfoxide reductases (MSRs). Bioinformatics analyses identified the coding sequence for a free-R-MSR (fRMSR) enzyme in the genome of *T. cruzi* Dm28c. Structurally, this enzyme is a modular protein with a putative N-terminal GAF domain linked to a C-terminal TIP41 motif. We performed detailed biochemical and kinetic characterization of the GAF domain of fRMSR in combination with mutant versions of specific cysteine residues, namely, Cys¹², Cys⁹⁸, Cys¹⁰⁸, and Cys¹³². The isolated recombinant GAF domain and full-length fRMSR exhibited specific catalytic activity for the reduction of free L-Met(R)SO (non-protein bound), using trypanodioxins as reducing partners. We demonstrated that this process involves two Cys residues, Cys⁹⁸ and Cys¹³². Cys¹³² is the essential catalytic residue on which a sulfenic acid intermediate is formed. Cys⁹⁸ is the resolutive Cys, which forms a disulfide bond with Cys¹³² as a catalytic step. Overall, our results provide new insights into redox metabolism in *T. cruzi*, contributing to previous knowledge of L-Met metabolism in this parasite.

Atypical network topologies enhance the reductive capacity of pathogen thiol antioxidant defense networks.

Pillay CS, John N, Barry CJ, Mthethwa LMDC, Rohwer JM.

04-07-2023

Redox Biol.

<https://pubmed.ncbi.nlm.nih.gov/37423162/>

Comparative study of three novel ion exchange resins with DEAE-cellulose for the purification of *Trypanosoma evansi*.

Marques J, das Neves GB, Ungri AM, de Souza Franco C, Galdino NAL, Ribeiro BG, Borges GK, Miletti LC.

06-07-2023

Anal Biochem.

<https://pubmed.ncbi.nlm.nih.gov/37422062/>

Intracellular ROS production and apoptotic effect of Quinoline and Isoquinoline alkaloids on the growth of *Trypanosoma evansi*.

Rani R, Sethi K, Gupta S, Virmani N, Kumar S, Kumar R.

05-07-2023

Acta Trop.

<https://pubmed.ncbi.nlm.nih.gov/37419379/>

Trypanosoma evansi, a hemoflagellate poses huge economic threat to the livestock industry of several countries of Asia, Africa, South America and Europe continents of the world. Limited number of available chemical drugs, incidents of growing drug resistance, and related side effects encouraged the use of herbal substitutes. In the present investigation, the impact of six alkaloids of quinoline and isoquinoline group was evaluated on the growth and multiplication of *Trypanosoma evansi* and their cytotoxic effect was examined on horse peripheral blood mononuclear cells in an in vitro system. Quinine, quinidine, cinchonine, cinchonidine, berbamine and emetine showed potent trypanocidal activities with IC₅₀/24 h values 6.631 ± 0.244, 8.718 ± 0.081, 16.96 ± 0.816, 33.38 ± 0.653, 2.85 ± 0.065, and 3.12 ± 0.367 µM, respectively, which was comparable to the standard anti-trypanosomal drug, quinapyramine sulfate (20 µM). However, in the cytotoxicity assay, all the drugs showed dose dependent cytotoxic effect and quinine, berbamine and emetine showed selectivity index more than 5, based on ratio of CC₅₀ to IC₅₀. Among the selected alkaloids, quinidine, berbamine and emetine exhibited higher apoptotic effects in *T. evansi*. Likewise, drug treated parasites showed a dose-dependent and time-dependent increase in reactive oxygen species (ROS) production. Therefore, increased apoptosis in combination with ROS generation could be responsible for the observed trypanocidal effect which could be further evaluated in *T. evansi*-infected mice model.

Kinetic and Structural Characterization of *Trypanosoma cruzi* Hypoxanthine-Guanine-Xanthine Phosphoribosyltransferases and Repurposing of Transition-State Analogue Inhibitors.

Glockzin K, Meneely KM, Hughes R, Maatouk SW, Piña GE, Suthagar K, Clinch K, Buckler JN, Lamb AL, Tyler PC, Meek TD, Katzfuss A.

07-07-2023

Biochemistry.

<https://pubmed.ncbi.nlm.nih.gov/37418678/>

Molecular and hematological investigation of *Trypanosoma evansi* infection in Iranian one-humped camels (*Camelus dromedarius*).

Jafari S, Sharifiyazdi H, Yaghoobpour T, Ghane M, Nazifi S.

12-07-2023

Parasitol Res.

<https://pubmed.ncbi.nlm.nih.gov/37433937/>

Trypanosoma species cause animal trypanosomiasis that infects many animals. *Trypanosoma evansi* is an organism that infects camels. There are many economic problems associated with this disease, including lower milk and meat yields and abortions. The purpose of the current survey was molecular study of the presence of *Trypanosoma* in dromedary camel blood in the south of Iran, and its effects on the hematologic, and some acute-phase protein changes. Blood samples were aseptically collected from the jugular vein of dromedary camels ($n = 100$; aged from 1 to 6 years) originating from Fars Province in EDTA-coated vacutainers. Genomic DNA from 100 μ L of the whole blood was extracted and amplified using a PCR assay based on ITS1, 5.8S, and ITS2 ribosomal regions. Also, the PCR products obtained were sequenced. Moreover, the changes in hematological parameters and serum acute-phase proteins (serum amyloid A, alpha-1 acid glycoprotein, and haptoglobin) were measured. Among 100 tested blood, nine samples (9%, 95% CI: 4.2-16.4%) were found positive by the PCR assay. The phylogenetic tree and blast analysis showed four different genotypes closely related to the strains (accession numbers: JN896754 and JN896755) previously reported from dromedary camels in Yazd Province, center Iran. Based on hematological analysis, normocytic and normochromic anemia and lymphocytosis were detected in the PCR-positive cases compared with the negative group. Furthermore, alpha-1 acid glycoprotein was significantly increased in the positive cases. There was a substantial and positive relation between the number of lymphocytes, and the levels of alpha-1 acid glycoprotein and serum amyloid A in the blood ($p = 0.045$, $r = 0.223$ and $p = 0.036$, $r = 0.234$, respectively). A noticeable frequency of *T. evansi* infection was reported in dromedary camels in south Iran. This is the first report on the genetic diversity of *T. evansi* in this region. There was a significant association among *Trypanosoma* infection, lymphocytosis, and alpha-1 acid glycoprotein. *Trypanosoma*-positive camels had a significant decrease in hematocrit (HCT), hemoglobin (Hb), and red blood cell (RBC) values compared to the non-infected group. Further experimental studies are needed to elucidate the hematological and acute-phase protein alteration during a different phase of *Trypanosoma* spp. infection.

TRYPANOSOMA CRUZI INFECTION IN THREE SLENDER-TAILED MEERKATS (*SURICATA SURICATTA*).

Valdés-Soto M, Burgdorf-Moisuk A, Raines J, Connolly M, Allen KE, Lineberry MW, Garner MM.

Jul-2023

J Zoo Wildl Med.

<https://pubmed.ncbi.nlm.nih.gov/37428705/>

Trypanosoma cruzi is a protozoan parasite primarily transmitted by triatomine insects (Hemiptera: subfamily Reduviidae) and is the cause of Chagas disease (CD). This report describes three cases of CD in a mob of five slender-tailed meerkats (*Suricata suricatta*) living in an outdoor exhibit at one zoological institution in Texas. The index case was a 9.5-yr-old female that presented with ataxia, lethargy, and pleural effusion. This case was diagnosed with CD postmortem via cytology, *T. cruzi* PCR of whole blood and lung fluid, and histology. Blood was opportunistically collected from the remaining four meerkats 28 d after the death of the index case and tested by PCR and serology. The second case was a clinically normal 7.5-yr-old male that tested PCR and antibody positive and the third case was a clinically normal 9-yr-old female that tested PCR positive. The second animal presented depressed, with pneumonia, and with continuous shivering 53 d after blood collection, and clinically improved after treatment with antibiotics and supportive care. Fifteen days later, the animal was found minimally responsive and died shortly thereafter. Histologic examination revealed *Trypanosoma* sp. amastigotes in the myocardium and the tissue was positive for *T. cruzi* DNA. The third meerkat, which received two separate courses of benznidazole over a span of almost 2 yr, was monitored routinely by PCR and serology and appeared clinically normal until found dead on exhibit 93 d after completion of the second treatment. Myocardium was positive for *T. cruzi* DNA. To the authors' knowledge, this case series is the first to document Chagas disease in meerkats and features associated cytologic and histologic findings.

Comparative microRNA profiling of *Trypanosoma cruzi* infected human cells.

Rego N, Libisch MG, Rovira C, Tosar JP, Robello C.

21-06-2023

Front Cell Infect Microbiol.

<https://pubmed.ncbi.nlm.nih.gov/37424776/>

Ulcère de Buruli

Type-I interferons promote innate immune tolerance in macrophages exposed to *Mycobacterium ulcerans* vesicles.

Bernard Q, Goumeidane M, Chaumond E, Robbe-Saule M, Boucaud Y, Esnault L, Croué A, Jullien J, Marsollier L, Marion E.

10-07-2023

PLoS Pathog.

<https://pubmed.ncbi.nlm.nih.gov/37428812/>

Buruli ulcer is a chronic infectious disease caused by *Mycobacterium ulcerans*. The pathogen persistence in host skin is associated with the development of ulcerative and necrotic lesions leading to permanent disabilities in most patients. However, few of diagnosed cases are thought to resolve through an unknown self-healing

process. Using in vitro and in vivo mouse models and *M. ulcerans* purified vesicles and mycolactone, we showed that the development of an innate immune tolerance was only specific to macrophages from mice able to heal spontaneously. This tolerance mechanism depends on a type I interferon response and can be induced by interferon beta. A type I interferon signature was further detected during in vivo infection in mice as well as in skin samples from patients under antibiotics regiment. Our results indicate that type I interferon-related genes expressed in macrophages may promote tolerance and healing during infection with skin damaging pathogen.