Réseau MTN Francophone

# Veille scientifique
# Maladies tropicales négligées

**Semaine 40**
*02 au 08 octobre 2023*

# Cysticercose

## Case Report: Three-Day Albendazole Regimen for Orbital Cysticercosis and the Stardust Sign.

**Lokdarshi G, Durgapal P.**
02-10-2023
*Am J Trop Med Hyg*.
https://pubmed.ncbi.nlm.nih.gov/37783462/

Ultrasonography findings have been used to diagnose and treat 10 cases of orbital cysticercosis. Although oral prednisolone has a key role in symptomatic alleviation, 3-day albendazole has been demonstrated to be curative without any recurrence.

## Surgical Debulking Before Medical Management in a Patient With Massive Racemose Neurocysticercosis.

**Wahlster S, Zunt J, Bonow R.**
03-10-2023
*Neurology*.
https://pubmed.ncbi.nlm.nih.gov/37414569/

# Dengue, chikungunya et maladie à virus Zika

## Validation of flavivirus infectious clones carrying fluorescent markers for antiviral drug screening and replication studies.

**Cherkashchenko L, Gros N, Trausch A, Neyret A, Hénaut M, Dubois G, Villeneuve M, Chable-Bessia C, Lyonnais S, Merits A, Muriaux D.**
15-09-2023
*Front Microbiol.*
https://pubmed.ncbi.nlm.nih.gov/37779700/

## Frequent outbreaks of dengue fever in South Asian countries-A correspondence analyzing causative factors and ways to avert.

**Urmi TJ, Mosharrafa RA, Hossain MJ, Rahman MS, Kadir MF, Islam MR.**
28-09-2023
*Health Sci Rep*.
https://pubmed.ncbi.nlm.nih.gov/37414569/

## Spontaneous retroperitoneal haematoma in severe dengue: A case report.

**Ab Rahman SS, Nik Mazian A, Samad SZ.**
01-10-2023
*Trop Med Int Health*.
https://pubmed.ncbi.nlm.nih.gov/37778744/

Dengue is endemic in over 100 countries worldwide, predominantly in the subtropical and tropical regions and the incidence has been increasing globally. Patients with severe dengue may develop massive bleeding, disseminated intravascular coagulopathy and multi-organ failure. Bleeding may occur in various body cavities and muscles; however, bleeding in the retroperitoneal space is uncommon. We report a case of a 37-year-old gentleman who presented with a 4-day history of fever associated with chills and rigours. On Day 6 of illness, he complained of left lumbar and left iliac fossa pain which was aggravated by movement. A computed tomography angiography scan of the abdomen showed the presence of a retroperitoneal haematoma, left iliopsoas and quadratus lumbarum intramuscular haematoma with active bleeding and left abdominal wall muscles haematoma. His condition gradually improved after multiple blood transfusions and he gained full recovery. Spontaneous retroperitoneal haematoma is an uncommon complication of severe dengue infection. Early diagnosis based on high index of clinical suspicion using appropriate imaging will aid in prompt management of these cases and may prevent deaths.

## L-Dopa decarboxylase modulates autophagy in hepatocytes and is implicated in dengue virus-caused inhibition of autophagy completion.

**Tsopela V, Korakidis E, Lagou D, Kalliampakou KI, Milona RS, Kyriakopoulou E, Mpekoulis G, Gemenetzi I, Stylianaki EA, Sideris CD, Sioli A, Kefallinos D, Sideris DC, Aidinis V, Eliopoulos AG, Kambas K, Vassilacopoulou D, Vassilaki N.**
29-09-2023
*Biochim Biophys Acta Mol Cell Res.*
https://pubmed.ncbi.nlm.nih.gov/37778471/

## Knowledge, Attitude and Practice towards Dengue Fever: a Study among the Inhabitants of Cumilla Cantonment area of Bangladesh.

**Hamid MA.**
Oct-2023
*Mymensingh Med J*.
https://pubmed.ncbi.nlm.nih.gov/37777917/

## The Dengue-in-Dhaka Initiative: results from a phase 2 trial evaluating the TV005 tetravalent dengue vaccine in Bangladesh.

**Wilder-Smith A.**
27-09-2023
*Lancet Infect Dis*.
https://pubmed.ncbi.nlm.nih.gov/37776878/

## Safety and durable immunogenicity of the TV005 tetravalent dengue vaccine, across serotypes and age groups, in dengue-endemic Bangladesh: a randomised, controlled trial.

**Walsh MR, Alam MS, Pierce KK, Carmolli M, Alam M, Dickson DM, Bak DM, Afreen S, Nazib F, Golam K, Qadri**

**F, Diehl SA, Durbin AP, Whitehead SS, Haque R, Kirkpatrick BD.**
27-09-2023
*Lancet Infect Dis*.
https://pubmed.ncbi.nlm.nih.gov/37776876/

**Background:** Morbidity and mortality from dengue virus (DENV) is rapidly growing in the large populations of south Asia. Few formal evaluations of candidate dengue vaccine candidates have been undertaken in India, Pakistan, or Bangladesh. Tetravalent vaccines must be tested for safety and immunogenicity in all age groups and in those previously exposed and naive to DENV infections. TV005 is a live, attenuated tetravalent dengue vaccine. We evaluated the safety and immunogenicity of a single dose of TV005 across age groups in dengue-endemic Bangladesh. **Methods:** We performed a randomised, placebo-controlled age de-escalating clinical trial of TV005 at a single clinical site in dengue-endemic Dhaka, Bangladesh, following a technology transfer from the USA. Healthy (as determined by history, clinical examination, and safety laboratory test results) volunteers aged 1-50 years were randomly assigned 3:1 (stratified by four age groups) to receive a single dose of TV005 vaccine or placebo. Participants were followed up for 3 years. The study was double blind and was unmasked at day 180; outcome assessors, clinic staff, and volunteers remained blind throughout. Primary outcomes were safety, evaluated per-protocol as proportion of volunteers with solicited related adverse events of any severity through 28 days post dosing, and post-vaccination seropositivity by day 180 using serotype-specific neutralising antibodies ($PRNT_{50}$ ≥10). Secondary outcomes included viremia, impact of past dengue exposure, and durability of antibody responses. This study is registered with Clinicaltrials.gov, NCT02678455, and is complete. **Findings:** Between March 13, 2016, and Feb 14, 2017, 192 volunteers were enrolled into four age groups (adults [18-50 years; 20 male and 28 female], adolescents [11-17 years; 27 male and 21 female], children [5-10 years; 15 male and 33 female], and young children [1-4 years; 29 male and 19 female]) with 48 participant per group. All participants were Bangladeshi. Vaccination was well tolerated and most adverse events were mild. Rash was the most common vaccine-associated solicited adverse event, in 37 (26%) of 144 vaccine recipients versus six (12%) of 48 placebo recipients; followed by fever in seven (5% of 144) and arthralgias in seven (6% of 108), which were only observed in vaccine recipients. Post-vaccine, volunteers of all ages (n=142) were seropositive to most serotypes with 118 (83%) seropositive to DENV 1, 141 (99%) to DENV 2, 137 (96%) to DENV 3, and 124 (87%) to DENV 4, overall by day 180. Post-vaccination, viraemia was not consistently found and antibody titres were higher (10-15-fold for DENV 1-3 and 1·6-fold for DENV 4) in individuals with past dengue exposure compared with the dengue-naive participants (DENV 1 mean 480 [SD 4·0] vs 32 [2·4], DENV 2 1042 [3·2] vs 105 [3·1], DENV 3 1406 [2·8] vs 129 [4·7], and DENV 4 105 [3·3] vs 65 [3·1], respectively). Antibody titres to all serotypes remained stable in most adults (63-86%) after 3 years of follow-up. However, as expected for individuals without past exposure to dengue, titres for DENV 1, 3, and 4 waned by 3 years in the youngest (1-4 year old) cohort (69% seropositive for DENV 2 and 22-28% seropositive for DENV 1, 3, and 4). **Interpretation:** With 3 years of follow-up, the single-dose tetravalent dengue vaccine, TV005, was well tolerated and immunogenic for all four serotypes in young children to adults, including individuals with no previous dengue exposure. **Funding:** National Institutes of Health-National Institute of Allergy and Infectious Diseases Intramural Research Program and Johns Hopkins University. **Translation:** For the Bangla translation of the abstract see Supplementary Materials section.

## HSPA13 modulates type I interferon antiviral pathway and NLRP3 inflammasome to restrict dengue virus infection in macrophages.

**Wang Q, Yang J, Li X, Wang W, Wu Y, Li Z, Huang X.**
28-09-2023
*Int Immunopharmacol.*
https://pubmed.ncbi.nlm.nih.gov/37776769/

## Metabolic response to CNS infection with flaviviruses.

**Dobrzyńska M, Moniuszko-Malinowska A, Skrzydlewska E.**
29-09-2023
*J Neuroinflammation.*
https://pubmed.ncbi.nlm.nih.gov/37775774/

## Can we control dengue?

**The Lancet Infectious Diseases.**
Oct-2023
*Lancet Infect Dis*.
https://pubmed.ncbi.nlm.nih.gov/37775220/

## The 3' terminal region of Zika virus RNA contains a conserved G-quadruplex and is unfolded by human DDX17.

**Gemmill D, Nelson C, Badmalia M, Pereira HS, Kerr L, Wolfinger MT, Patel TR.**
29-09-2023
*Biochem Cell Biol*.
https://pubmed.ncbi.nlm.nih.gov/37774422/

Zika virus (ZIKV) infection remains a worldwide concern, and currently, no effective treatments or vaccines are available. Novel therapeutics are an avenue of interest that could probe viral RNA-human protein communication to stop viral replication. One specific RNA structure, G-quadruplexes (G4s), possess various roles in viruses and all domains of life, including transcription and translation regulation, genome stability, and serving as nucleation points for RNA liquid-liquid phase separation. Previous G4 studies on ZIKV using a Quadruplex forming G-Rich Sequences (QGRS) Mapper located a potential G-quadruplex sequence (PQS) in the 3' terminal region (TR) and was validated structurally using a 25-mer oligo. It is currently unknown if this structure is conserved and maintained in a large ZIKV RNA transcript, and its specific roles in viral replication. Using bioinformatic analysis and biochemical assays, we demonstrate that the ZIKV 3' TR G4 is conserved across all ZIKV isolates and maintains its

structure in a 3' TR full-length transcript. We further established the G4 formation using Pyridostatin (PDS) and the BG4 G4-recognizing antibody binding assays. Our work also demonstrates that the human DEAD-box helicases, DDX3X132-607 and DDX17135-555, bind to the 3' TR, and that DDX17135-555 unfolds the G4 present in the 3' TR. These findings provide a path forward in potential therapeutic targeting of DDX3X or DDX17's binding to the 3' TR G4 region for novel treatments against ZIKV.

## Maternally derived antibody titer dynamics and risk of hospitalized infant dengue disease.

**O'Driscoll M, Buddhari D, Huang AT, Waickman A, Kaewhirun S, Iamsirithaworn S, Khampaen D, Farmer A, Fernandez S, Rodriguez-Barraquer I, Srikiatkhachorn A, Thomas S, Endy T, Rothman AL, Anderson K, Cummings DAT, Salje H.**
10-10-2023
*Proc Natl Acad Sci U S A*.
https://pubmed.ncbi.nlm.nih.gov/37774093/

Infants less than 1 y of age experience high rates of dengue disease in dengue virus (DENV) endemic countries. This burden is commonly attributed to antibody-dependent enhancement (ADE), whereby concentrations of maternally derived DENV antibodies become subneutralizing, and infection-enhancing. Understanding antibody-related mechanisms of enhanced infant dengue disease risk represents a significant challenge due to the dynamic nature of antibodies and their imperfect measurement processes. Further, key uncertainties exist regarding the impact of long-term shifts in birth rates, population-level infection risks, and maternal ages on the DENV immune landscape of newborns and their subsequent risks of severe dengue disease in infancy. Here, we analyze DENV antibody data from two infant cohorts (N = 142 infants with 605 blood draws) and 40 y of infant dengue hospitalization data from Thailand. We use mathematical models to reconstruct maternally derived antibody dynamics, accounting for discretized measurement processes and limits of assay detection. We then explore possible antibody-related mechanisms of enhanced infant dengue disease risk and their ability to reconstruct the observed age distribution of hospitalized infant dengue cases. We find that ADE mechanisms are best able to reconstruct the observed data. Finally, we describe how the shifting epidemiology of dengue in Thailand, combined with declining birth rates, have decreased the absolute risk of infant dengue disease by 88% over a 40-y period while having minimal impact on the mean age of infant hospitalized dengue disease.

## Systemic and Ophthalmic Manifestations of Chikungunya Fever.

**Mahendradas P, Patil A, Kawali A, Rathinam SR.**
29-09-2023
*Ocul Immunol Inflamm*.
https://pubmed.ncbi.nlm.nih.gov/37773977/

**Purpose:** Chikungunya is a re-emerging viral infection across the globe. The purpose of this article is to review the systemic and ophthalmic manifestations associated with chikungunya fever. Method: A review of literature was conducted using online databases. Results: In this report, we have reviewed the presently available literature on uveitis caused by chikungunya and highlighted the current knowledge of its clinical manifestations, imaging features, laboratory diagnostics, and the available therapeutic modalities from the systemic and ophthalmic standpoint. Conclusions: Ocular involvement in chikungunya infection may occur at the time of systemic manifestations or it may occur as a delayed presentation many weeks after the fever. Treatment relies on a supportive therapy for systemic illness. Treatment of ocular manifestation depends on the type of manifestations and usually includes a combination of topical and oral steroids.

## Phylodynamics of dengue virus 2 in Nicaragua leading up to the 2019 epidemic reveals a role for lineage turnover.

**Thongsripong P, Edgerton SV, Bos S, Saborío S, Kuan G, Balmaseda A, Harris E, Bennett SN.**
28-09-2023
*BMC Ecol Evol*.
https://pubmed.ncbi.nlm.nih.gov/37770825/

## Associations between Dengue Incidence, Ecological Factors, and Anthropogenic Factors in Singapore.

**Tewari P, Guo P, Dickens B, Ma P, Bansal S, Lim JT.**
13-09-2023
*Viruses.*
https://pubmed.ncbi.nlm.nih.gov/37766323/

## Broad-Spectrum Antiviral Activity of Influenza A Defective Interfering Particles against Respiratory Syncytial, Yellow Fever, and Zika Virus Replication In Vitro.

**Pelz L, Piagnani E, Marsall P, Wynserski N, Hein MD, Marichal-Gallardo P, Kupke SY, Reichl U.**
04-09-2023
*Viruses.*
https://pubmed.ncbi.nlm.nih.gov/37766278/

## Production of Recombinant Zika Virus Envelope Protein by Airlift Bioreactor as a New Subunit Vaccine Platform.

**da Costa HHM, Bielavsky M, Orts DJB, Araujo S, Adriani PP, Nogueira JS, Astray RM, Pandey RP, Lancellotti M, Cunha-Junior JP, Prudencio CR.**
11-09-2023
*Int J Mol Sci*.
https://pubmed.ncbi.nlm.nih.gov/37762254/

The Zika Virus (ZIKV) is an emerging arbovirus of great public health concern, particularly in the Americas after its last outbreak in 2015. There are still major challenges regarding disease control, and there is no ZIKV vaccine currently approved for human use. Among many different vaccine platforms currently under study, the recombinant

envelope protein from Zika Virus (rEZIKV) constitutes an alternative option for vaccine development and has great potential for monitoring ZIKV infection and antibody response. This study describes a method to obtain a bioactive and functional rEZIKV using an *E. coli* expression system, with the aid of a 5-L airlift bioreactor and following an automated fast protein liquid chromatography (FPLC) protocol, capable of obtaining high yields of approximately 20 mg of recombinant protein per liter of bacterium cultures. The purified rEZIKV presented preserved antigenicity and immunogenicity. Our results show that the use of an airlift bioreactor for the production of rEZIKV is ideal for establishing protocols and further research on ZIKV vaccines bioprocess, representing a promising system for the production of a ZIKV envelope recombinant protein-based vaccine candidate.

## Susceptibility to Zika virus in a Collaborative Cross mouse strain is induced by Irf3 deficiency in vitro but requires other variants in vivo.

**Bourdon M, Manet C, Conquet L, Ramaugé Parra C, Kornobis E, Bonnefoy E, Montagutelli X.**
21-09-2023
*PLoS Pathog.*
https://pubmed.ncbi.nlm.nih.gov/37733807/

## Quantitative proteomics analysis of permethrin and temephos-resistant Ae. aegypti revealed diverse differentially expressed proteins associated with insecticide resistance from Penang Island, Malaysia.

**Shettima A, Ishak IH, Lau B, Abu Hasan H, Miswan N, Othman N.**
18-09-2023
*PLoS Negl Trop Dis*.
https://pubmed.ncbi.nlm.nih.gov/37721966/

Synthetic insecticides are the primary vector control method used globally. However, the widespread use of insecticides is a major cause of insecticide-resistance in mosquitoes. Hence, this study aimed at elucidating permethrin and temephos-resistant protein expression profiles in Ae. aegypti using quantitative proteomics. In this study, we evaluated the susceptibility of Ae. aegypti from Penang Island dengue hotspot and non-hotspot against 0.75% permethrin and 31.25 mg/l temephos using WHO bioassay method. Protein extracts from the mosquitoes were then analysed using LC-ESI-MS/MS for protein identification and quantification via label-free quantitative proteomics (LFQ). Next, Perseus 1.6.14.0 statistical software was used to perform differential protein expression analysis using ANOVA and Student's t-test. The t-test selected proteins with≥2.0-fold change (FC) and ≥2 unique peptides for gene expression validation via qPCR. Finally, STRING software was used for functional ontology enrichment and protein-protein interactions (PPI). The WHO bioassay showed resistance with 28% and 53% mortalities in adult mosquitoes exposed to permethrin from the hotspot and non-hotspot areas. Meanwhile, the susceptibility of Ae. aegypti larvae revealed high resistance to temephos in hotspot and non-hotspot regions with 80% and 91% mortalities. The LFQ analyses revealed 501 and 557 (q-value <0.05) differentially expressed proteins in adults and larvae Ae. aegypti. The t-test showed 114 upregulated and 74 downregulated proteins in adult resistant versus laboratory strains exposed to permethrin. Meanwhile, 13 upregulated and 105 downregulated proteins were observed in larvae resistant versus laboratory strains exposed to temephos. The t-test revealed the upregulation of sodium/potassium-dependent ATPase β2 in adult permethrin resistant strain, H15 domain-containing protein, 60S ribosomal protein, and PB protein in larvae temephos resistant strain. The downregulation of troponin I, enolase phosphatase E1, glucosidase 2β was observed in adult permethrin resistant strain and tubulin β chain in larvae temephos resistant strain. Furthermore, the gene expression by qPCR revealed similar gene expression patterns in the above eight differentially expressed proteins. The PPI of differentially expressed proteins showed a p-value at <1.0 x 10-16 in permethrin and temephos resistant Ae. aegypti. Significantly enriched pathways in differentially expressed proteins revealed metabolic pathways, oxidative phosphorylation, carbon metabolism, biosynthesis of amino acids, glycolysis, and citrate cycle. In conclusion, this study has shown differentially expressed proteins and highlighted upregulated and downregulated proteins associated with insecticide resistance in Ae. aegypti. The validated differentially expressed proteins merit further investigation as a potential protein marker to monitor and predict insecticide resistance in field Ae. aegypti. The LC-MS/MS data were submitted into the MASSIVE database with identifier no: MSV000089259.

## Clinical, Virological, and Immunological Features in Cosmopolitan Genotype DENV-2-Infected Patients during a Large Dengue Outbreak in Sri Lanka in 2017.

**Nwe KM, Ngwe Tun MM, Muthugala R, Nabeshima T, Balingit JC, Rajamanthri L, Jayawardana D, Attanayake S, Inoue S, Takamatsu Y, Urano T, Morita K.**
11-09-2023
*Am J Trop Med Hyg*.
https://pubmed.ncbi.nlm.nih.gov/37696512/

In 2017, Sri Lanka experienced its largest dengue epidemic and reported severe and unusual presentations of dengue with high morbidity. This outbreak was associated with the reemergence of dengue virus-2 (DENV-2), with the responsible strain identified as a variant of the previously circulating DENV-2 cosmopolitan genotype. In this study, we characterized the DENV-2 cosmopolitan genotype from patients during this epidemic. Also, we identified host factors that contributed to the severity of dengue infection in patients infected with this particular virus. Ninety-one acute serum samples from patients at the National Hospital in Kandy were randomly selected. Of these, 40.2% and 48.9% were positive for dengue IgM and IgG, respectively. NS1 antigen levels were significantly higher in primary infections. The severe dengue (SD) and dengue with warning signs (DWWS) groups exhibited significantly higher viral genome and infectivity titers than

the dengue without warning signs (DWoWS) group. The highest viremia level was observed in SD patients. As for host cytokine response, interferon α (IFN-α) levels were significantly higher in the DWoWS group than in the DWWS and SD groups, whereas interleukin (IL)-12p40 and tumor necrosis factor α (TNF-α) levels in SD patients were significantly higher than in the other two groups. The TNF-α, IL-4, and monocyte chemoattractant protein-1 concentrations were positively correlated with NS1 antigen levels. From whole-genome analysis, NS4 had the highest frequency of amino acid variants, followed by the E gene. Our study suggests that viremia levels and immune responses contributed to SD outcomes, and these findings may help in identifying an effective therapeutic strategy against SD infection.

## Chikungunya virus virus-like particle vaccine is well tolerated and immunogenic in chikungunya seropositive individuals.

**McCarty JM, Bedell L, Mendy J, Coates EE, Chen GL, Ledgerwood JE, Tredo SR, Warfield KL, Richardson JS.**
06-10-2023
*Vaccine.*
https://pubmed.ncbi.nlm.nih.gov/37690874/

## A tale of 141 municipalities: the spatial distribution of dengue in Mato Grosso, Brazil.

**Fernandes KAP, de Almeida Filho AR, Moura Alves TV, Bernardo CSS, Montibeller MJ, Mondini A, Bronzoni RVM.**
03-10-2023
*Trans R Soc Trop Med Hyg*.
https://pubmed.ncbi.nlm.nih.gov/37665762/

## Aedes aegypti container preference for oviposition and its possible implications for dengue vector surveillance in Delhi, India.

**Prasad P, Lata S, Gupta SK, Kumar P, Saxena R, Arya DK, Singh H.**
2023
*Epidemiol Health*.
https://pubmed.ncbi.nlm.nih.gov/37641822/

Objectives: Dengue is a mosquito-borne viral disease globally transmitted by Aedes aegypti. The most effective method to prevent the transmission of the disease is proficient vector control. Understanding the breeding behaviour of the responsible vectors is very pertinent in this regard; therefore, the present study was conducted to understand Ae. aegypti behaviour regarding the selection of containers for oviposition in the megacity of Delhi. Methods: A household survey in different localities within Delhi was carried out during 2018-2019. All available containers were inspected for the presence of immature Ae. aegypti. In entomological surveillance, the ovipositional preference of Aedes was computed using the breeding preference ratio, container index in the field, and laboratory settings, and associations of dengue cases with monthly variation in environmental factors and container type were also calculated. Results: The household larval survey in 40 localities showed that 40% of 27,776 water-holding containers in 3,400 houses were plastic, followed by overhead tanks (26.2%), and coolers (12.1%). The most preferred breeding habitat was clay pots (9.3%), followed by metallic containers (8.5%) and solid waste (7.1%). A laboratory-based study showed that Aedes preferred clay containers (81.8%) over 4 other types of containers (plastic, paper, metal, and glass). Conclusions: The present study provides a rationale for using clay containers as a possible surveillance tool (ovitraps) or as a vector control tool. This information might aid researchers in developing novel traps and targeting preferred containers for larval control activities during transmission and non-transmission seasons.

## Predictive Score for Dengue Infection with Complete Blood Count Parameters, Including the Monocyte Distribution Width: A Retrospective Single-Center Derivation and Validation Study.

**Poottasane N, Phornprasitsaeng P, Onthong Y, Sinthana T, Limvorapitak W.**
28-08-2023
*Am J Trop Med Hyg*.
https://pubmed.ncbi.nlm.nih.gov/37640293/

Early detection of dengue virus infection will lead to proper management and reduction in morbidity/mortality. Monocyte distribution width (MDW) was recently approved for use in the early detection of sepsis. Because monocytes are involved in the innate immune system against viral infection, we sought to determine changes in MDW to develop and validate a new predictive score for dengue viral infection. This study included patients who presented with symptoms or signs related to dengue infection and who had a complete blood count and dengue investigation performed during September 2019 to May 2020. The proportion of dengue infection was 29.5% in the current study. The MDW was significantly higher in dengue infection (median, 29.7 versus 24.2; $P < 0.001$). We then randomly separated patients into training and validation cohorts. Independent predictive factors of dengue infection were white blood cells < 4 × 109/L (score 1), platelets < 100 × 109/L (score 1), and MDW > 24 (score 1). Clinical features were not significantly predictive of dengue infection. The areas under the receiver operating characteristic curve (95% CI) of the prognostic score were 0.839 (0.779-0.899) in the training cohort and 0.742 (0.674-0.811) in the validation cohort. With a cutoff score ≥ 1, the sensitivity and specificity of the scores were 92.2% and 40.8% in the training cohort and 88.9% and 44.1% in the validation cohort, respectively. We concluded that MDW increases with dengue infection and MDW could easily be incorporated in the predictive scores for dengue infection.

## Isothermal amplification technology (IAT) for rapid diagnosis of Rickettsioses: scope, overview, existing evidence, and the way forward.

**Dixit R, Gopalan N, Behera SK.**

Nov-2023
*Diagn Microbiol Infect Dis*.
https://pubmed.ncbi.nlm.nih.gov/37625171/

## A predictive score for severity in patients with confirmed dengue fever in a tertiary care hospital in Kerala, India.

**Haridas S, M GP, Bhaskaran R.**
03-10-2023
*Trans R Soc Trop Med Hyg*.
https://pubmed.ncbi.nlm.nih.gov/37625166/

Background: The study aimed to identify predictors of severe dengue during the 2017 epidemic and to develop and validate a simple predictive score for severity.

Methods: A retrospective analytical study was conducted using clinical and laboratory data from adult dengue patients with a confirmed microbiological diagnosis. The study included patients who presented to a tertiary care centre in Kerala, India, during the febrile phase (≤4 d) between June 2017 and February 2019. Using appropriate statistical tests, we derived predictors of severe disease and computed a risk score model. Results: Of the 153 patients (mean age 50±17 y; 64% males), 31 (20%) had severe dengue and 4 (3%) died. Petechial lesions, hypoalbuminemia (<3.5 g/dl), elevated alanine aminotransferase (>40 IU/l) and urea >40 IU/l were significant predictors. Our scoring system (cut-off: 2) showed excellent performance, with an area under the receiver operating characteristics curve of 0.9741, sensitivity of 100%, specificity of 96% and accuracy of 98%. The risk score was secondarily validated on 48 patients hospitalized from March 2019 to June 2019. Conclusion: Our scoring system is easy to implement and will help primary healthcare practitioners in promptly identifying severe dengue cases upon hospital presentation.

## Praemonitus praemunitus: can we forecast and prepare for future viral disease outbreaks?

**Sessions Z, Bobrowski T, Martin HJ, Beasley JT, Kothari A, Phares T, Li M, Alves VM, Scotti MT, Moorman NJ, Baric R, Tropsha A, Muratov EN.**
05-09-2023
*FEMS Microbiol Rev*.
https://pubmed.ncbi.nlm.nih.gov/37596064/

Understanding the origins of past and present viral epidemics is critical in preparing for future outbreaks. Many viruses, including SARS-CoV-2, have led to significant consequences not only due to their virulence, but also because we were unprepared for their emergence. We need to learn from large amounts of data accumulated from well-studied, past pandemics and employ modern informatics and therapeutic development technologies to forecast future pandemics and help minimize their potential impacts. While acknowledging the complexity and difficulties associated with establishing reliable outbreak predictions, herein we provide a perspective on the regions of the world that are most likely to be impacted by future outbreaks. We specifically focus on viruses with epidemic potential, namely SARS-CoV-2, MERS-CoV, DENV, ZIKV, MAYV, LASV, noroviruses, influenza, Nipah virus, hantaviruses, Oropouche virus, MARV, and Ebola virus, which all require attention from both the public and scientific community to avoid societal catastrophes like COVID-19. Based on our literature review, data analysis, and outbreak simulations, we posit that these future viral epidemics are unavoidable, but that their societal impacts can be minimized by strategic investment into basic virology research, epidemiological studies of neglected viral diseases, and antiviral drug discovery.

## Investigation of the impact of AXL, TLR3, and STAT2 in congenital Zika syndrome through genetic polymorphisms and protein-protein interaction network analyses.

**Gomes JA, Sgarioni E, Boquett JA, Kowalski TW, Fraga LR, Terças-Trettel ACP, da Silva JH, Ribeiro BFR, Galera MF, de Oliveira TM, Carvalho de Andrade MDF, Carvalho IF, Schüler-Faccini L, Vianna FSL.**
01-10-2023
*Birth Defects Res*.
https://pubmed.ncbi.nlm.nih.gov/37526179/

Introduction: Zika virus (ZIKV) is a human teratogen that causes congenital Zika syndrome (CZS). AXL, TLR3, and STAT2 are proteins involved in the ZIKV's entry into cells (AXL) and host's immune response (TLR3 and STAT2). In this study, we evaluated the role of genetic polymorphisms in these three genes as risk factors to CZS, and highlighted which proteins that interact with them could be important for ZIKV infection and teratogenesis. Materials and methods: We evaluate eighty-eight children exposed to ZIKV during the pregnancy, 40 with CZS and 48 without congenital anomalies. The evaluated polymorphisms in AXL (rs1051008), TLR3 (rs3775291), and STAT2 (rs2066811) were genotyped using TaqMan® Genotyping Assays. A protein-protein interaction network was created in STRING database and analyzed in Cytoscape software. Results: We did not find any statistical significant association among the polymorphisms and the occurrence of CZS. Through the analyses of the network composed by AXL, TLR3, STAT2 and their interactions targets, we found that EGFR and SRC could be important proteins for the ZIKV infection and its teratogenesis. Conclusion: In summary, our results demonstrated that the evaluated polymorphisms do not seem to represent risk factors for CZS; however, EGFR and SRC appear to be important proteins that should be investigated in future studies.

## Untargeted-based metabolomics analysis and in vitro/in silico antiviral activity of extracts from Phyllanthus brasiliensis (Aubl.) Poir.

**Carvalho ARV, Reis JDE, Gomes PWP, Ferraz AC, Mardegan HA, Menegatto MBDS, Souza Lima RL, de Sarges MRV, Pamplona SDGSR, Jeunon Gontijo KS, de Magalhães JC, da Silva MN, Magalhães CLB, Silva CYYE.**
Oct-2023
*Phytochem Anal*.
https://pubmed.ncbi.nlm.nih.gov/37403427/

## Safety and immunogenicity of a purified inactivated Zika virus vaccine candidate in adults primed with a Japanese encephalitis virus or yellow fever virus vaccine in the USA: a phase 1, randomised, double-blind, placebo-controlled clinical trial.

**Koren MA, Lin L, Eckels KH, De La Barrera R, Dussupt V, Donofrio G, Sondergaard EL, Mills KT, Robb ML, Lee C, Adedeji O, Keiser PB, Curley JM, Copeland NK, Crowell TA, Hutter JN, Hamer MJ, Valencia-Ruiz A, Darden J, Peel S, Amare MF, Mebrahtu T, Costanzo M, Krebs SJ, Gromowski GD, Jarman RG, Thomas SJ, Michael NL, Modjarrad K.**
Oct-2023
*Lancet Infect Dis*.
https://pubmed.ncbi.nlm.nih.gov/37390836/

Background: Zika virus infection is a threat to at-risk populations, causing major birth defects and serious neurological complications. Development of a safe and efficacious Zika virus vaccine is, therefore, a global health priority. Assessment of heterologous flavivirus vaccination is important given co-circulation of Japanese encephalitis virus and yellow fever virus with Zika virus. We investigated the effect of priming flavivirus naive participants with a licensed flavivirus vaccine on the safety and immunogenicity of a purified inactivated Zika vaccine (ZPIV). Methods: This phase 1, placebo-controlled, double-blind trial was done at the Walter Reed Army Institute of Research Clinical Trials Center in Silver Spring, MD, USA. Eligible participants were healthy adults aged 18-49 years, with no detectable evidence of previous flavivirus exposure (by infection or vaccination), as measured by a microneutralisation assay. Individuals with serological evidence of HIV, hepatitis B, or hepatitis C infection were excluded, as were pregnant or breastfeeding women. Participants were recruited sequentially into one of three groups (1:1:1) to receive no primer, two doses of intramuscular Japanese encephalitis virus vaccine (IXIARO), or a single dose of subcutaneous yellow fever virus vaccine (YF-VAX). Within each group, participants were randomly assigned (4:1) to receive intramuscular ZPIV or placebo. Priming vaccinations were given 72-96 days before ZPIV. ZPIV was administered either two or three times, at days 0, 28, and 196-234. The primary outcome was occurrence of solicited systemic and local adverse events along with serious adverse events and adverse events of special interest. These data were analysed in all participants receiving at least one dose of ZPIV or placebo. Secondary outcomes included measurement of neutralizing antibody responses following ZPIV vaccination in all volunteers with available post-vaccination data. This trial is registered at ClinicalTrials.gov, NCT02963909. Findings: Between Nov 7, 2016, and Oct 30, 2018, 134 participants were assessed for eligibility. 21 did not meet inclusion criteria, 29 met exclusion criteria, and ten declined to participate. 75 participants were recruited and randomly assigned. 35 (47%) of 75 participants were male and 40 (53%) were female. 25 (33%) of 75 participants identified as Black or African American and 42 (56%) identified as White. These proportions and other baseline characteristics were similar between groups. There were no statistically significant differences in age, gender, race, or BMI between those who did and did not opt into the third dose. All participants received the planned priming IXIARO and YF-VAX vaccinations, but one participant who received YF-VAX dropped out before receipt of the first dose of ZPIV. 50 participants received a third dose of ZPIV or placebo, including 14 flavivirus-naive people, 17 people primed with Japanese encephalitis virus vaccine, and 19 participants primed with yellow fever vaccine. Vaccinations were well tolerated across groups. Pain at the injection site was the only adverse event reported more frequently in participants who received ZPIV than in those who received placebo (39 [65%] of 60 participants, 95% CI 51·6-76·9 who received ZPIV vs three [21·4%] of 14 who received placebo; 4·7-50·8; p=0·006). No patients had an adverse event of special interest or serious adverse event related to study treatment. At day 57, the flavivirus-naive volunteers had an 88% (63·6-98·5, 15 of 17) seroconversion rate (neutralising antibody titre ≥1:10) and geometric mean neutralising antibody titre (GMT) against Zika virus of 100·8 (39·7-255·7). In the Japanese encephalitis vaccine-primed group, the day 57 seroconversion rate was 31·6% (95% CI 12·6-56·6, six of 19) and GMT was 11·8 (6·1-22·8). Participants primed with YF-VAX had a seroconversion rate of 25% (95% CI 8·7-49·1, five of 20) and GMT of 6·6 (5·2-8·4). Humoral immune responses rose substantially following a third dose of ZPIV, with seroconversion rates of 100% (69·2-100; ten of ten), 92·9% (66·1-99·8; 13 of 14), and 60% (32·2-83·7, nine of 15) and GMTs of 511·5 (177·6-1473·6), 174·2 (51·6-587·6), and 79 (19·0-326·8) in the flavivirus naive, Japanese encephalitis vaccine-primed, and yellow fever vaccine-primed groups, respectively. Interpretation: We found ZPIV to be well tolerated in flavivirus naive and primed adults but that immunogenicity varied significantly according to antecedent flavivirus vaccination status. Immune bias towards the flavivirus antigen of initial exposure and the timing of vaccination may have impacted responses. A third ZPIV dose overcame much, but not all, of the discrepancy in immunogenicity. The results of this phase 1 clinical trial have implications for further evaluation of ZPIV's immunisation schedule and use of concomitant vaccinations. Funding: Department of Defense, Defense Health Agency; National Institute of Allergy and Infectious Diseases; and Division of Microbiology and Infectious Disease.

## Quantifying Mosquito Attraction Behavior Using Olfactometry.

**Castillo JS, Bellantuono AJ, DeGennaro M.**
03-10-2023
*Cold Spring Harb Protoc*.
https://pubmed.ncbi.nlm.nih.gov/37024240/

## Quantifying Mosquito Attraction Using a Uniport Olfactometer.

**Castillo JS, Bellantuono AJ, DeGennaro M.**
03-10-2023
*Cold Spring Harb Protoc*.
https://pubmed.ncbi.nlm.nih.gov/37019611/

## Dengue virus and its recent outbreaks: current scenario and counteracting strategies.

**Sah R, Siddiq A, Padhi BK, Mohanty A, Rabaan AA, Chandran D, Chakraborty C, Dhama K.**
01-09-2023
*Int J Surg*.
https://pubmed.ncbi.nlm.nih.gov/36906765/

## Zika virus spreads through infection of lymph node-resident macrophages.

**Reynoso GV, Gordon DN, Kalia A, Aguilar CC, Malo CS, Aleshnick M, Dowd KA, Cherry CR, Shannon JP, Vrba SM, Holmes AC, Alippe Y, Maciejewski S, Asano K, Diamond MS, Pierson TC, Hickman HD.**
28-02-2023
*Cell Rep*.
https://pubmed.ncbi.nlm.nih.gov/36795561/

To disseminate through the body, Zika virus (ZIKV) is thought to exploit the mobility of myeloid cells, in particular monocytes and dendritic cells. However, the timing and mechanisms underlying shuttling of the virus by immune cells remains unclear. To understand the early steps in ZIKV transit from the skin, at different time points, we spatially mapped ZIKV infection in lymph nodes (LNs), an intermediary site en route to the blood. Contrary to prevailing hypotheses, migratory immune cells are not required for the virus to reach the LNs or blood. Instead, ZIKV rapidly infects a subset of sessile $CD169^+$ macrophages in the LNs, which release the virus to infect downstream LNs. Infection of $CD169^+$ macrophages alone is sufficient to initiate viremia. Overall, our experiments indicate that macrophages that reside in the LNs contribute to initial ZIKV spread. These studies enhance our understanding of ZIKV dissemination and identify another anatomical site for potential antiviral intervention.

## Serological Evidence of Zika virus Circulation with Dengue and Chikungunya Infections in Sri Lanka from 2017.

**Abeygoonawardena H, Wijesinghe N, Navaratne V, Balasuriya A, Nguyen TTN, Moi ML, De Silva AD.**
30-08-2023
*J Glob Infect Dis*.
https://pubmed.ncbi.nlm.nih.gov/37800085/

## Changing Clinical Profile and Predictors of Mortality in Patients of Acute Febrile Encephalopathy from North India.

**Ary KA, Singh H, Suri V, Sharma K, Biswal M, Singh MP, Ahuja CK, Kharbanda P, Sharma N, Bhalla A.**
11-08-2023
*J Glob Infect Dis*.
https://pubmed.ncbi.nlm.nih.gov/37800084/

Introduction: Acute encephalitis syndrome (AES) or acute febrile encephalopathy is a clinical condition characterized by altered mental status occurring after or along with a short febrile illness. In developing countries, infections are the predominant cause of AES. Prominent infections known to cause AES include viruses (such as herpes simplex virus [HSV], Japanese Encephalitis [JE] virus, dengue, enteroviruses [EVs]), bacteria, fungus, and parasites. In the present study, we aim to analyze the etiology, clinical features, and predictors of mortality in patients presenting with acute febrile encephalopathy or acute encephalitic syndrome. The present study was a prospective observational study conducted at Post Graduate Institute of Medical Education and Research a tertiary care center in Chandigarh, India. Methods: A total of 105 patients with ≥18 years of age with fever (body temperature >101° F for duration ≤14 days) and altered sensorium (Glasgow coma scale [GCS] score ≤10) lasting for more than 24 h, either accompanying the fever or following it were enrolled. Demographic and clinical details were recorded on pro forma. Cerebrospinal fluid (CSF) analysis was performed for all the enrolled patients at admission for cytology, CSF glucose to blood glucose ratio, protein levels, gram stain and culture sensitivity, adenosine deaminase levels, polymerase chain reaction for HSV/EV/mycobacterium tuberculosis (TB) and immunoglobulin M Enzyme-linked immune assay for JE. Computed tomography of the brain was done in all patients while magnetic resonance imaging (MRI) of the brain was carried out in 75 patients. Results: Among the 105 patients, tubercular meningitis was seen in 27 (25.7%) patients followed by acute pyogenic meningitis in 18 (17.1%) patients. Probable viral encephalitis was present in 12 (11.4%) cases. Septic encephalopathy ($n$ = 10) and scrub typhus encephalitis ($n$ = 8), HSV encephalitis ($n$ = 6), dengue encephalitis ($n$ = 4), leptospirosis ($n$ = 3) were the other infections causing acute febrile encephalitis in our study. In addition to fever and altered sensorium common symptoms observed were headache (52.4%), vomiting (35.2%), and seizures (29.5%). The factors predicting increased mortality were female gender, fever of more than 38°C at admission, GCS <7, MRI showing disease-related findings like altered signal intensity bilateral medial temporal and insular area in herpes simplex encephalitis, etc., changes, and the group of patients where a definite diagnosis could not be established during the hospital stay. Conclusions: Tubercular meningitis/central nervous system TB is the predominant cause of acute febrile encephalopathy in developing countries. Scrub and dengue encephalitis are emerging as an important cause of acute febrile encephalopathy and occur predominantly in postmonsoon seasons. Acute febrile encephalopathy remains an important cause of mortality in patients presenting to Emergency Department (ER). The strongest predictors of mortality are low GCS and undiagnosed cases of AES.

## Brazil at the Center of Chikungunya Outbreaks.

**Amaral JK, Taylor PC, Schoen RT.**
12-07-2023
*J Glob Infect Dis*.
https://pubmed.ncbi.nlm.nih.gov/37800080/

## Facilitators and barriers to engaging communities in health service research

## on dengue control in Indo-Pacific region: a systematic review.

**Naing C, Htet NH, Tung WS, Aung HH, Whittaker MA.**
05-10-2023
*BMC Public Health*.
https://pubmed.ncbi.nlm.nih.gov/37798703/

Background: Dengue is a public health problem in the Indo-Pacific countries. There are concerns over the facilitators and barriers to community engagement in health service research aimed at dengue control. The objective of his study was to identify and synthesize facilitators and barriers to community engagement in health service research aimed at dengue control. Methodology: The Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) checklist was used to perform this review. Health-related databases including PubMed, Ovid, and Google Scholar were searched for relevant studies. A consolidated framework with five domains was developed after undertaking a six-phase reflective thematic assessment of the data. Results: Thirteen studies were identified, spanning eight low-and middle-income countries of the Indo-Pacific region including Cambodia, India, Indonesia, Myanmar, Philippines, Sri Lanka, Thailand, and Vietnam. The studies in this review covered the period from 2002 to 2021. A broad range of study designs and objectives were revealed across these 13 studies. An array of communities such as the local government, project-related health staff, local health services staff, community leaders, local communities/residences/general public, heads of households, community health volunteers, school teachers, and schoolchildren participated in these dengue related studies. The five Consolidated Framework for Implementation Research (CFIR) domains of 'intervention characteristics', 'inner setting', 'outer setting',' individual characteristics', and 'program implementations' were used to identify and describe barriers and facilitators. Conclusions: The findings indicate a range of barriers and facilitators to community engagement in dengue control in the selected LMIC in the Indo-Pacific countries. Future health services research on dengue control approaches should be carefully planned, methodologically constructed, aligned with community engagement principles, and involve considerable community participation at all stages of the research.

## Zika virus diversity in mice is maintained during early vertical transmission from placenta to fetus, but reduced in fetal bodies and brains at late stages of infection.

**Evans AB, Winkler CW, Anzick SL, Ricklefs SM, Sturdevant DE, Peterson KE.**
05-10-2023
*PLoS Negl Trop Dis*.
https://pubmed.ncbi.nlm.nih.gov/37796973/

Since emerging in French Polynesia and Brazil in the 2010s, Zika virus (ZIKV) has been associated with fetal congenital disease. Previous studies have compared ancestral and epidemic ZIKV strains to identify strain differences that may contribute to vertical transmission and fetal disease. However, within-host diversity in ZIKV populations during vertical transmission has not been well studied. Here, we used the established anti-interferon treated Rag1-/- mouse model of ZIKV vertical transmission to compare genomic variation within ZIKV populations in matched placentas, fetal bodies, and fetal brains via RNASeq. At early stages of vertical transmission, the ZIKV populations in the matched placentas and fetal bodies were similar. Most ZIKV single nucleotide variants were present in both tissues, indicating little to no restriction in transmission of ZIKV variants from placenta to fetus. In contrast, at later stages of fetal infection there was a sharp reduction in ZIKV diversity in fetal bodies and fetal brains. All fetal brain ZIKV populations were comprised of one of two haplotypes, containing either a single variant or three variants together, as largely homogenous populations. In most cases, the dominant haplotype present in the fetal brain was also the dominant haplotype present in the matched fetal body. However, in two of ten fetal brains the dominant ZIKV haplotype was undetectable or present at low frequencies in the matched placenta and fetal body ZIKV populations, suggesting evidence of a strict selective bottleneck and possible selection for certain variants during neuroinvasion of ZIKV into fetal brains.

## Synergistic correlation between host angiogenin and dengue virus replication.

**Madhry D, Malvankar S, Phadnis S, Srivastava RK, Bhattacharyya S, Verma B.**
Jan-2023
*RNA Biol*.
https://pubmed.ncbi.nlm.nih.gov/37796112/

## Transcriptome-based analysis of human peripheral blood reveals regulators of immune response in different viral infections.

**Ivanov SM, Tarasova OA, Poroikov VV.**
19-09-2023
*Front Immunol.*
https://pubmed.ncbi.nlm.nih.gov/37795081/

Introduction: There are difficulties in creating direct antiviral drugs for all viruses, including new, suddenly arising infections, such as COVID-19. Therefore, pathogenesis-directed therapy is often necessary to treat severe viral infections and comorbidities associated with them. Despite significant differences in the etiopathogenesis of viral diseases, in general, they are associated with significant dysfunction of the immune system. Study of common mechanisms of immune dysfunction caused by different viral infections can help develop novel therapeutic strategies to combat infections and associated comorbidities. Methods: To identify common mechanisms of immune functions disruption during infection by nine different viruses (cytomegalovirus, Ebstein-Barr virus, human T-cell leukemia virus type 1, Hepatitis B and C viruses, human immunodeficiency virus, Dengue virus, SARS-CoV, and SARS-CoV-2), we analyzed the corresponding transcription profiles from peripheral blood mononuclear cells (PBMC) using the originally developed pipeline that include

transcriptome data collection, processing, normalization, analysis and search for master regulators of several viral infections. The ten datasets containing transcription data from patients infected by nine viruses and healthy people were obtained from Gene Expression Omnibus. The analysis of the data was performed by Genome Enhancer pipeline. Results: We revealed common pathways, cellular processes, and master regulators for studied viral infections. We found that all nine viral infections cause immune activation, exhaustion, cell proliferation disruption, and increased susceptibility to apoptosis. Using network analysis, we identified PBMC receptors, representing proteins at the top of signaling pathways that may be responsible for the observed transcriptional changes and maintain the current functional state of cells. Discussion: The identified relationships between some of them and virus-induced alteration of immune functions are new and have not been found earlier, e.g., receptors for autocrine motility factor, insulin, prolactin, angiotensin II, and immunoglobulin epsilon. Modulation of the identified receptors can be investigated as one of therapeutic strategies for the treatment of severe viral infections.

## Prevalence of sleep disorders in children with Congenital Zika Syndrome.

**Tavares CSS, Marques RS, Santos VS, Santos HP, Reis MCDS, Martins-Filho PR.**
05-10-2023
*J Trop Pediatr.*
https://pubmed.ncbi.nlm.nih.gov/37794754/

Studies have reported that children with Congenital Zika Syndrome (CZS) experience changes in their sleep patterns, which can result in mood disturbances, behavioral issues and delays in growth and development. This systematic review synthesized the available evidence on the prevalence of sleep disorders in children with CZS. Eligible studies were those with an observational design that reported sleep disorders in children with CZS using validated questionnaires, polysomnography/electroencephalographic recording or parent/caregiver reports. Searches were conducted in PubMed, Web of Science, SCOPUS and Embase, as well as a gray literature search using Google Scholar. The Freeman-Tukey double-arcsine transformation with a random-effects model was used to estimate the pooled prevalence of sleep disorders with a 95% confidence interval (CI). Five studies were included and data from 340 Brazilian children with CZS were analyzed. The overall prevalence of sleep disorders was 27.4% (95% CI 16.7-39.4), without differences among studies using validated questionnaires (29.4%, 95% CI 21.4-37.8) or report from parents and caregivers (27.4%, 95% CI 11.5-47.0). Sleep disorders are prevalent in children with CZS, impacting their development and quality of life. It is critical to examine the quality of sleep in these children to develop appropriate interventions that can mitigate these issues.

## Aedes albopictus salivary adenosine deaminase is an immunomodulatory factor facilitating dengue virus replication.

**Mu X, Lin Z, Sun Y, Chen L, Lv Q, Ji C, Kuang X, Li W, Shang Z, Cheng J, Nie Y, Li Z, Wu J.**
04-10-2023
*Sci Rep.*
https://pubmed.ncbi.nlm.nih.gov/37794048/

## First report on evaluation of commercial eugenol and piperine against Aedes aegypti L (Diptera: Culicidae) larvae: Mortality, detoxifying enzyme, and histopathological changes in the midgut.

**Subahar R, Huang A, Wijaya RS, Nur LSE, Susanto L, Firmansyah NE, Yulhasri Y, El Bayani GF, Dwira S.**
02-10-2023
*Parasitol Int.*
https://pubmed.ncbi.nlm.nih.gov/37793471/

## Priming with Japanese encephalitis virus or yellow fever virus vaccination led to the recognition of multiple flaviviruses without boosting antibody responses induced by an inactivated Zika virus vaccine.

**Li Y, Merbah M, Wollen-Roberts S, Beckman B, Mdluli T, Curtis DJ, Currier JR, Mendez-Rivera L, Dussupt V, Krebs SJ, De La Barrera R, Michael NL, Paquin-Proulx D, Eller MA, Koren MA, Modjarrad K, Rolland M.**
02-10-2023
*EBioMedicine.*
https://pubmed.ncbi.nlm.nih.gov/37793212/

Background: Complex patterns of cross-reactivity exist between flaviviruses, yet there is no precise understanding of how sequential exposures due to flavivirus infections or vaccinations impact subsequent antibody responses. Methods: We investigated whether B cell priming from Japanese encephalitis virus (JEV) or yellow fever virus (YFV) vaccination impacted binding and functional antibody responses to flaviviruses following vaccination with a Zika virus (ZIKV) purified inactivated virus (ZPIV) vaccine. Binding antibody responses and Fc gamma receptor engagement against 23 flavivirus antigens were characterized along with neutralization titres and Fc effector responses in 75 participants at six time points. Findings: We found no evidence that priming with JEV or YFV vaccines improved the magnitude of ZPIV induced antibody responses to ZIKV. Binding antibodies and Fc gamma receptor engagement to ZIKV antigens did not differ significantly across groups, while antibody-dependent cellular phagocytosis (ADCP) and neutralizing responses were higher in the naïve group than in the JEV and YFV primed groups following the second ZPIV immunization ($p \leq 0.02$). After a third dose of ZPIV, ADCP responses remained higher in the naïve group than in the primed groups. However, priming affected the quality of the response following ZPIV vaccination, as primed individuals recognized a broader array of flavivirus antigens than individuals in the naïve group. Interpretation: While a priming vaccination to either JEV or YFV did not boost ZIKV-specific responses upon ZIKV vaccination, the qualitatively different responses elicited in the primed groups highlight the complexity in the cross-

reactive antibody responses to flaviviruses. Funding: This work was supported by a cooperative agreement between The Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc., and the U.S. Department of the Army [W81XWH-18-2-0040]. The work was also funded in part by the National Institute of Allergy and Infectious Diseases (NIAID) R01AI155983 to SJK and KM.

## The Drosophila melanogaster prophenoloxidase system participates in immunity against zika virus infection.

**Tafesh-Edwards G, Eleftherianos I.**
04-10-2023
*Eur J Immunol*.
https://pubmed.ncbi.nlm.nih.gov/37793051/

## Inflammation, fibrosis and E1 glycoprotein persistence in joint tissue of patients with post-Chikungunya chronic articular disease.

**Brito MSAG, Marchi MS, Perin MY, Côsso IDS, Bumlai RUM, Silva Júnior WVD, Prado AYM, Cruz TCDD, Avila ETP, Damazo AS, Slhessarenko RD.**
22-09-2023
*Rev Soc Bras Med Trop*.
https://pubmed.ncbi.nlm.nih.gov/37792834/

## Epidemiology and burden of dengue fever in the United States: a systematic review.

**Chen LH, Marti C, Perez CD, Jackson BM, Simon AM, Lu M.**
04-10-2023
*J Travel Med*.
https://pubmed.ncbi.nlm.nih.gov/37792822/

Background: Dengue is currently a global concern. The range of dengue vectors is expanding with climate change, yet US studies on dengue epidemiology and burden are limited. This systematic review sought to characterize the epidemiology and disease burden of dengue within the US. Methods: Studies evaluating travel-related and endemic dengue in US states and territories were identified and qualitatively summarized. Commentaries and studies on ex-US cases were excluded. MEDLINE, Embase, Cochrane Library, Latin American and Caribbean Center of Health Sciences Information, Centre for Reviews and Dissemination, and Clinicaltrials.gov were searched through January 2022. Results: 116 studies were included. In US states, dengue incidence was generally low with spikes occurring in recent years in 2013-2016 (0.17-0.31 cases/100,000) and peaking in 2019 (0.35 cases/100,000). Most cases (94%, n=7,895, 2010-2021) were travel related. Dengue was more common in Puerto Rico (cumulative average: 200 cases/100,000, 1980-2015); in 2010-2021, 99.9% of cases were locally acquired. There were <50 severe cases in US states (2010-2017); fatal cases were even rarer. Severe cases in Puerto Rico peaked in 1998 (n=173) and 2021 (n=76). Besides lower income, risk factors in US States included having birds in residence, suggesting unspecified environmental characteristics favorable to dengue vectors. Commonly reported symptoms included fever, headache, and rash; median disease duration was 3.5-11 days. Hospitalization rates increased following 2009 World Health Organization disease classification changes (pre-2009: 0%-54%; post-2009: 14%-75%); median length of stay was 2.7-8 days (Puerto Rico) and 2-3 days (US states). Hospitalization costs/case (2010 USD) were $14,350 (US states), $1,764-$5,497 (Puerto Rico), and $4,207 (US Virgin Islands). In Puerto Rico, average days missed were 0.2-5.3 (work) and 2.5 (school). Conclusions: Though dengue risk is ongoing, treatments are limited, and the economic burden of dengue is high. There is an urgent need for additional preventive and therapeutic interventions.

## [Association between schooling and mortality rate from dengue in Brazil].

**Guimarães LM, Cunha GMD, Leite IDC, Moreira RI, Carneiro ELNDC.**
25-09-2023
*Cad Saude Publica.*
https://pubmed.ncbi.nlm.nih.gov/37792819/

Dengue may be associated with individual level variables, such as schooling, increasing the risk of illness. The objective of this study is to analyze the disparities in dengue mortality among the least and the most educated in Brazil, from 2010 to 2018. This is a retrospective ecological study of the differences in the mortality rate due to dengue between the less and the more educated people in Brazil, according to the mortality rates due to general dengue, by age, sex, and Federative Unit (UF). A bootstrap and multiple imputation procedure for the variable schooling was implemented to consider the multilevel structure of the data from each UF over the years. For each aggregate bank generated, a multilevel Poisson model was adjusted. The improvement in the education level of the Brazilian population did not reflect on the decrease in mortality from dengue. There was an increase in the mortality rate from dengue in Brazil and an increase in the difference in mortality rates between less and more educated. Regardless of the imputation process, the results showed higher mortality rates from dengue among the less educated. Low schooling affected younger people more pronouncedly.

## Prevalence of malaria and dengue co-infections among febrile patients during dengue transmission season in Kassala, eastern Sudan.

**Alsedig K, Eldigail MH, Elduma AH, Elaagip A, Altahir O, Siam HA, Ali Y, Abdallah T.**
04-10-2023
*PLoS Negl Trop Dis*.
https://pubmed.ncbi.nlm.nih.gov/37792705/

## Signal Amplification for Cell-Free Biosensors, an Analog-to-Digital Converter.

**Franco RAL, Brenner G, Zocca VFB, de Paiva GB, Lima RN, Rech EL, Amaral DT, Lins MRCR, Pedrolli DB.**
04-10-2023
*ACS Synth Biol*.

https://pubmed.ncbi.nlm.nih.gov/37792474/

Toehold switches are biosensors useful for the detection of endogenous and environmental RNAs. They have been successfully engineered to detect virus RNAs in cell-free gene expression reactions. Their inherent sequence programmability makes engineering a fast and predictable process. Despite improvements in the design, toehold switches suffer from leaky translation in the OFF state, which compromises the fold change and sensitivity of the biosensor. To address this, we constructed and tested signal amplification circuits for three toehold switches triggered by Dengue and SARS-CoV-2 RNAs and an artificial RNA. The serine integrase circuit efficiently contained leakage, boosted the expression fold change from OFF to ON, and decreased the detection limit of the switches by 3-4 orders of magnitude. Ultimately, the integrase circuit converted the analog switches' signals into digital-like output. The circuit is broadly useful for biosensors and eliminates the hard work of designing and testing multiple switches to find the best possible performer.

## Countering Dengue infection in Bangladesh in the backdrop of current outbreak.

**Kumar S, Pattnaik R, Subhadra S, Soumyaranjan Sahu P.**
20-09-2023
*New Microbes New Infect*.
https://pubmed.ncbi.nlm.nih.gov/37790901/

## Evaluation of a new dengue 3 controlled human infection model for use in the evaluation of candidate dengue vaccines.

**Pierce KK, Whitehead SS, Diehl SA, Naro G, Carmolli MC, He H, Tibery CM, Sabundayo BP, Kirkpatrick BD, Durbin AP.**
13-6-2023
*medRxiv.*
https://pubmed.ncbi.nlm.nih.gov/37790382/

All four serotypes of dengue virus (DENV) cause the full spectrum of disease. Therefore, vaccines must protect against all serotypes. To evaluate candidate vaccines, a human challenge model of dengue serotype 3 (rDEN30Δ30) was developed. All challenge virus recipients safely met the primary endpoint of viremia and secondary endpoints of rash and seroconversion to DENV-3.

## The Inflammasome Pathway is Activated by Dengue Virus Non-structural Protein 1 and is Protective During Dengue Virus Infection.

**Wong MP, Juan EYW, Chelluri SS, Wang P, Pahmeier F, Castillo-Rojas B, Blanc SF, Biering SB, Vance RE, Harris E.**
21-09-2023
*bioRxiv.*
https://pubmed.ncbi.nlm.nih.gov/37790301/

Dengue virus (DENV) is a medically important flavivirus causing an estimated 50-100 million dengue cases annually, some of whom progress to severe disease. DENV non-structural protein 1 (NS1) is secreted from infected cells and has been implicated as a major driver of dengue pathogenesis by inducing endothelial barrier dysfunction. However, less is known about how DENV NS1 interacts with immune cells and what role these interactions play. Here we report that DENV NS1 can trigger activation of inflammasomes, a family of cytosolic innate immune sensors that respond to infectious and noxious stimuli, in mouse and human macrophages. DENV NS1 induces the release of IL-1β in a caspase-1 dependent manner. Additionally, we find that DENV NS1-induced inflammasome activation is independent of the NLRP3, Pyrin, and AIM2 inflammasome pathways, but requires CD14. Intriguingly, DENV NS1-induced inflammasome activation does not induce pyroptosis and rapid cell death; instead, macrophages maintain cellular viability while releasing IL-1β. Lastly, we show that caspase-1/11-deficient, but not NLRP3-deficient, mice are more susceptible to lethal DENV infection. Together, these results indicate that the inflammasome pathway acts as a sensor of DENV NS1 and plays a protective role during infection.

## Strengthening surveillance, disease detection, and outbreak response through Guinea-Bissau's Frontline Field Epidemiology Training Program: a cross-sectional descriptive study.

**Camará M, da Costa FP, Chambe G, Betunde A, Cardoso P, Johnson K, Rullan-Oliver P, Lopez A.**
19-07-2023
*Pan Afr Med J*.
https://pubmed.ncbi.nlm.nih.gov/37790146/

## Development of a novel lectin-based gold nanoparticle point-of-care immunoassay for rapid diagnosis of patients with severe Dengue infection.

**Paul M, Saha B, Mukhopadhyay S.**
04-10-2023
*J Immunoassay Immunochem.*
https://pubmed.ncbi.nlm.nih.gov/37789768/

Rapid diagnosis of patients with severe Dengue infection can be useful for the efficient clinical management of cases caused by the Dengue virus. Lateral Flow Immunoassay (LFIA) have been broadly used for rapid Dengue diagnosis, because of their quick readouts with the human eye, simplicity of use, and affordability. Despite the availability of several commercial Dengue point-of-care assays, none has shown to be successful in discriminating between severe and nonsevere forms of Dengue infection. In the current study, for the first time, a novel lectin-based point-of-care assay for the early detection of patients with severe Dengue infection with gold-adorned sheets as detection labels is being reported. In this assay, Dengue severity was diagnosed by detecting the glycosylation profile of vitronectin, a known Dengue severity marker. Two lectins were employed namely DSA (*Datura stramonium*) and MAA (*Maackia amurensis*) that can recognize specific glycans like galactose Gal-(1-4) GlcNAc and sialic acid in an (α2-3) linkage, which displayed high sensitivity and high specificity, i.e. 90% and 85% for DSA and 90.91% and 95% for MAA. The new assay has a

detection limit of 5 µg $µl^{-1}$ and enables the quick (30 min) and sensitive detection of severe Dengue cases. The reported point-of-care immunoassay exhibits considerable promise for early identification of patients with Dengue severity.

## Laboratory scale evaluation of the feasibility of locally found bladderworts as biological agents to control dengue vector, Aedes aegypti in Sri Lanka.

**Gunathilaka N, Perera R, Amerasinghe D, Udayanga L.**
04-10-2023
*BMC Plant Biol*.
https://pubmed.ncbi.nlm.nih.gov/37789290/

## Linear epitope mapping in the E and NS1 proteins of dengue and Zika viruses: Prospection of peptides for vaccines and diagnostics.

**Aquino VH, Fumagalli MJ, Silva A, de Moura Negrini BV, Rojas A, Guillen Y, Bernal C, Figueiredo LTM.**
Oct-2023
*PLoS One*.
https://pubmed.ncbi.nlm.nih.gov/37788262/

The arrival of the Zika virus (ZIKV) in dengue virus (DENV)-endemic areas has posed challenges for both differential diagnosis and vaccine development. Peptides have shown promise in addressing these issues. The aim of this study was to identify the linear epitope profile recognized by serum samples from dengue and Zika patients in the E and NS1 proteins of DENV and ZIKV. This cross-sectional study included individuals of all ages with laboratory-confirmed DENV and ZIKV infections, who were selected through convenience sampling. The serum samples from dengue and Zika patients detected epitopes evenly distributed across the viral proteins in a peptide microarray platform. However, several epitopes were located within "epitope hotspots", characterized by clusters of peptides recognized in more than 30% of the sub-arrays analyzed using individual or pooled serum samples. The serum samples from dengue and Zika patients showed a high level of cross-reactivity with peptides in the DENV and ZIKV proteins. Analysis using an additional peptide microarray platform, which contained peptides selected based on the results of the initial screening, revealed that two DENV and one ZIKV peptide, highly specific to their related viruses, were located within the epitope hotspots; however, they presented low detection rates (32.5, 35.0, and 28.6%, respectively). In addition, two DENV peptides detected at similarly high rates by both dengue and Zika patients were also found within the epitope hotspots. These hotspots contain several immunodominant epitopes that are recognized by a larger number of individuals when compared to 15-amino acid (aa) sequence peptides. Thus, epitope hotspots may have greater potential to serve as antigens in diagnostic tests and vaccine development than peptides composed of only 15 amino acids.

## Does prior exposure to larvicides influence dengue virus susceptibility in Aedes aegypti (Diptera: Culicidae)?

**Aldridge RL, Alto BW, Roxanne Connelly C, Okech B, Siegfried B, Eastmond BH, Alomar AA, Linthicum KJ.**
03-10-2023
*J Med Entomol.*
https://pubmed.ncbi.nlm.nih.gov/37788073/

Control of mosquito vector populations is primarily intended to reduce the transmission of pathogens they transmit. Use of chemical controls, such as larvicides, can have unforeseen consequences on adult traits if not applied properly. The consequences of under application of larvicides are little studied, specifically the impacts on pathogen infection and transmission by the vectors that survive exposure to larvicides. We compared vector susceptibility of Aedes aegypti (L.) for dengue virus, serotype 1 (DENV-1) previously exposed as larvae to an LC50 of different classes of insecticides as formulated larvicides. Larval exposure to insect growth regulators (methoprene and pyriproxyfen) significantly increased susceptibility to infection of DENV-1 in Ae. aegypti adults but did not alter disseminated infection or transmission. Larval exposure to temephos, spinosad, and Bti did not increase infection, disseminated infection, or transmission of DENV-1. Our findings describe a previously under observed phenomenon, the latent effects of select larvicides on mosquito vector susceptibility for arboviruses. These data suggest that there are unintended consequences of sublethal exposure to select larvicides that can influence susceptibility of Ae. aegypti to DENV infection, and indicates the need for further investigation of sublethal effects of insecticides on other aspects of mosquito biology, especially those parameters relevant to a mosquitoes ability to transmit arboviruses (life span, biting behavior, extrinsic incubation period).

## Brugada syndrome unmasked by dengue fever.

**Sivanandam LK, Basani HBR, Sanker V, Roshan S S, Hunjul M, Gupta U.**
30-09-2023
*Clin Case Rep*.
https://pubmed.ncbi.nlm.nih.gov/37786459/

## Eugenol isolated from supercritical fluid extract of Ocimum sanctum: a potent inhibitor of DENV-2.

**Kaushik S, Kaushik S, Dar L, Yadav JP.**
02-10-2023
*AMB Express.*
https://pubmed.ncbi.nlm.nih.gov/37783874/

## Time-series analysis of transcriptomic changes due to permethrin exposure reveals that Aedes aegypti undergoes detoxification metabolism over 24 h.

**Mack LK, Attardo GM.**
02-10-2023
*Sci Rep*.
https://pubmed.ncbi.nlm.nih.gov/37783800/

## 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.**
02-10-2023
*PLoS Negl Trop Dis*.
https://pubmed.ncbi.nlm.nih.gov/37782672/

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 wMel 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 wMel on mosquito gene transcription is multifactorial. Importantly, because Wolbachia limits, but does not completely prevent, replication of ZIKV and other viruses in coinfected 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.

## Convalescent Rash of Dengue.

**Ong EP, Ho FV.**
05-10-2023
*N Engl J Med*.
https://pubmed.ncbi.nlm.nih.gov/37782021/

## Mucocutaneous manifestations of chikungunya fever: an update.

**Vinay K, Thind A, Mehta H, Bishnoi A.**
02-10-2023
*Int J Dermatol.*
https://pubmed.ncbi.nlm.nih.gov/37781980/

Chikungunya is a viral disease transmitted by female Aedes mosquitoes that has been increasingly reported in many parts of the world across the geographical borders. In addition to fever and joint pain, mucocutaneous manifestations of chikungunya have been reported in 40-75% of infected patients. Dermatological manifestations of chikungunya are often under-recognized and misdiagnosed as clinicians are not sensitized or educated regarding these. The early-onset cutaneous manifestations of chikungunya fever, occurring within 1 month of the fever, include maculopapular rashes, vesiculobullous eruptions, Steven-Johnson syndrome/toxic epidermal necrolysis-like eruptions, flagellate lesions, scrotal dermatitis, oro-genital ulcers, and exacerbation of preexisting dermatoses like psoriasis. Hyperpigmentation, lichenoid eruptions, diffuse hair fall, and exacerbation of acne usually occur as a late manifestation. Diagnosis of these mucocutaneous manifestations can be challenging as they often resemble other common dermatoses. This review article elaborates on various mucocutaneous manifestations of chikungunya fever, based on literature review and authors' clinical experience.

## Guillain-Barré Syndrome Following the mRNA COVID-19 Vaccination: Comment.

**Mungmunpuntipantip R, Wiwanitkit V.**
30-12-2023
*Acta Neurol Taiwan*.
https://pubmed.ncbi.nlm.nih.gov/37781729/

## Zika virus modulates mitochondrial dynamics, mitophagy, and mitochondria-derived vesicles to facilitate viral replication in trophoblast cells.

**Lee JK, Shin OS.**
14-09-2023
*Front Immunol*.
https://pubmed.ncbi.nlm.nih.gov/37781396/

Zika virus (ZIKV) remains a global public health threat with the potential risk of a future outbreak. Since viral infections are known to exploit mitochondria-mediated cellular processes, we investigated the effects of ZIKV infection in trophoblast cells in terms of the different mitochondrial quality control pathways that govern mitochondrial integrity and function. Here we demonstrate that ZIKV (PRVABC59) infection of JEG-3 trophoblast cells manipulates mitochondrial dynamics, mitophagy, and formation of mitochondria-derived vesicles (MDVs). Specifically, ZIKV nonstructural protein 4A (NS4A) translocates to the mitochondria, triggers mitochondrial fission and mitophagy, and suppresses mitochondrial associated antiviral protein (MAVS)-mediated type I interferon (IFN) response. Furthermore, proteomics profiling of small extracellular vesicles (sEVs) revealed an enrichment of mitochondrial proteins in sEVs secreted by ZIKV-infected JEG-3 cells, suggesting that MDV formation may also be another mitochondrial quality control mechanism manipulated during placental ZIKV

infection. Altogether, our findings highlight the different mitochondrial quality control mechanisms manipulated by ZIKV during infection of placental cells as host immune evasion mechanisms utilized by ZIKV at the placenta to suppress the host antiviral response and facilitate viral infection.

### Utility of CDC DENV1-4 real time PCR assay and trioplex assay for the diagnosis of dengue in patients with acute febrile illness.

**Sarkar S, Bora I, Gupta P, Sapkal G, Shethi S, Kaur K, Ratho RK.**
Sept-2023
*Virusdisease*.
https://pubmed.ncbi.nlm.nih.gov/37780908/

Nucleic acid amplification tests (NAATs) have revolutionized reliable detection of dengue virus (DENV) during acute phase of infection. The study evaluated performance of CDC DENV-1-4 real-time assay, trioplex RT-PCR and heminested conventional RT-PCR assay in the diagnosis of DENV. The three NAATs were performed on 107 consecutive samples collected from patients suspected of DENV infection during acute phase of illness. Their performance was compared against composite reference standard, consisting of DENV NS1 antigen ELISA and DENV IgM ELISA. 88/107 study samples were positive by DENV ELISA, either NS1Ag (80), IgM (3) or both (5). The overall sensitivity of CDC DENV-1-4 RT-PCR assay, trioplex RT-PCR assay and conventional multiplex RT-PCR was 68.18%, 54.55% and 38.64%, respectively in diagnosing dengue during acute phase, with an area under the curve of 0.841, 0.773 and 0.693 respectively when compared against composite reference standard. The sensitivity was 82.93%, 73.17% and 51.22%, respectively within three days of illness and 60%, 42.86% and 28.57%, respectively between 4 and 5th day of illness. All the three molecular assays had 100% specificity. Maximum concordance values of 86.9% were recorded among CDC DENV-1-4 rRT-PCR assay and trioplex assay with kappa value of 0.74, suggestive of substantial agreement. CDC DENV-1-4 rRT-PCR assay can be used as a reliable and accurate test for diagnosis of DENV during acute phase of illness.

### Therapeutic Potential of Antiviral Peptides against the NS2B/NS3 Protease of Zika Virus.

**Hossain MS, Shovon MTI, Hasan MR, Hakim FT, Hasan MM, Esha SA, Tasnim S, Nazir MS, Akhter F, Ali MA, Halim MA.**
13-09-2023
*ACS Omega*.
https://pubmed.ncbi.nlm.nih.gov/37779969/

### Molecular surveillance of dengue virus in field-collected Aedes mosquitoes from Bhopal, central India: evidence of circulation of a new lineage of serotype 2.

**Sarma DK, Rathod L, Mishra S, Das D, Agarwal A, Sharma G, Singh TA, Kumawat M, Singh S, Verma V, Kumar M, Shubham S, Tiwari RR, Prakash A.**
14-09-2023
*Front Microbiol.*
https://pubmed.ncbi.nlm.nih.gov/37779723

## Dracunculose

### Mechanisms of metabolic adaptation in the duckweed Lemna gibba: an integrated metabolic, transcriptomic and flux analysis.

**Shi H, Ernst E, Heinzel N, McCorkle S, Rolletschek H, Borisjuk L, Ortleb S, Martienssen R, Shanklin J, Schwender J.**
03-10-2023
*BMC Plant Biol*.
https://pubmed.ncbi.nlm.nih.gov/37789269/

### Functional analysis of a dirigent protein AtsDIR23 in Acorustatarinowii.

**Guo Z, Xu W, Wei D, Zheng S, Liu L, Cai Y.**
23-09-2023
*J Plant Physiol*.
https://pubmed.ncbi.nlm.nih.gov/37774564/

Acorus tatarinowii (A. tatarinowii) is a medicinal plant of the Araceae family. Currently, pharmacology focuses on the study of volatile oils, but there are few reports of another important secondary metabolite, lignan. Dirigent protein is thought to play an important role in plant secondary metabolism and responds to a variety of biotic and abiotic stresses. However, the DIR gene family of A. tatarinowii has not been systematically analyzed, and it is unknown whether it affects lignan synthesis. In this study, a total of 27 AtsDIRs were identified by comprehensive analysis of the genome of the medicinal plant A. tatarinowii, and the candidate gene AtsDIR23 that may be involved in lignan synthesis was screened through bioinformatics and transcriptome analysis. It is worth noting that AtsDIR23 is significantly expressed in rhizomes and is a member of the DIR-a subfamily. Subsequently, subcellular localization revealed that AtsDIR23 was localized in chloroplasts. The functional verification of AtsDIR23 b y the transient transformation of A. tatarinowii and the stable transformation of Arabidopsis thaliana showed that the content of lignans in overexpressed plants increased. Co-expression analysis screening revealed the MYB transcription factor (AtsMYB91) that is highly correlated with AtsDIR23 expression, while yeast one-hybrid assays and double luciferase experiments showed that AtsMYB91 negatively regulated the expression of AtsDIR23 b y binding to the AtsDIR23 promoter. In conclusion, AtsDIR23 can promote the accumulation of lignans, which provides a reference for further research on the regulation of lignans by DIR genes.

## Echinococcose

### Tumor suppressor p73 induces apoptosis of murine peritoneal cell after exposure to hydatid cyst antigens; a possibly

## survival mechanism of cystic echinococcosis in vivo mice model.

**Ahmadpour E, Spotin A, Moghimi A, Shahrivar F, Jadidi-Niaragh F, Hajizadeh F, Mehrani S, Mazhab-Jafari K.**
05-10-2023
*PLoS One*.
https://pubmed.ncbi.nlm.nih.gov/37796859/

Cystic echinococcosis (CE) is a life-threatening helminthic disease caused by the Echinococcus granulosus sensulato complex. Previous evidence indicates that the host's innate immune responses against CE can combat and regulate the growth rate and mortality of hydatid cyst in the host's internal organs. However, the survival mechanisms of CE are not yet fully elucidated in the human body. In the present study, the apoptotic effects of fertile and infertile hydatid fluid (HF) were tested on murine peritoneal cells in vivo mice model. Mice were divided into five groups including; control group, fertile HF-treated peritoneal cells, infertile HF-treated peritoneal cells, protoscolices (PSCs)-treated peritoneal cells and HF+PSCs-treated peritoneal cells group. Mice groups were intraperitoneally inoculated with PBS, HF, and/or PSCs. Afterwards, peritoneal cells were isolated and mRNA expression of STAT3, caspase-3, p73 and Smac genes were evaluated by quantitative Real-time PCR. After 48 hours of exposure, the protein levels of Smac and STAT3 was determined by western blotting technique. After 6 hours of exposure, Caspase-3 activity was also measured by fluorometric assay. The intracellular reactive oxygen species (ROS) production was examined in all groups. The mRNA expression levels of p73, caspase-3 and also Caspase-3 activity in HF+PSCs-treated peritoneal cells were higher than in the test and control groups ($Pv<0.05$), while the mRNA expression level of anti-apoptotic STAT3 and Smac genes in HF+PSC-treated peritoneal cells were lower than in the other groups ($Pv<0.05$). As well, the level of intracellular ROS in the fertile HCF-treated peritoneal cells, infertile HCF-treated peritoneal cells, PSC-treated peritoneal cells and HF+PSC-treated peritoneal cells groups were significantly higher than in the control group ($Pv<0.05$).Current findings indicates that oxidative stress and p73 can trigger the apoptosis of murine peritoneal cells through modulator of HF-treated PSCs that is likely one of the hydatid cyst survival mechanisms in vivo mice model.

## Expression of Tim-3/galectin-9 pathway and CD8+T cells and related factors in patients with cystic echinococcosis.

**Zhao H, Ma Y, Tian F, Li B, Xiao N, Mo X, Aibibula M, Min H, Cai X, Zhang T, Ma X.**
02-10-2023
*Exp Parasitol*.
https://pubmed.ncbi.nlm.nih.gov/37793539/

## Management of a pancreatic tail hydatid cyst: a case report.

**Hasnaouia A, Trigui R, Heni S, Kammoun H, Sassi I.**
14-07-2023
*Pan Afr Med J*.
https://pubmed.ncbi.nlm.nih.gov/37790154/

The case report describes a 73-year-old woman, with a history of diabetes, who presented with left hypochondrium pain. Interrogation revealed a long-term history of living with Echinococcus granulosus endemic area, associated to close contact with sheep and dogs. Upon physical examination, a painless mass of the left hypochondrium, fixed to the deep plane. Abdominal ultrasonography (USG) showed a 9 cm encapsulated mass in contact with the tail of the pancreas. Further investigation was carried out by performing an abdominal computed tomography (CT) scan showing: large cystic mass with a partially calcified thickened wall, containing multiple vesicles, measuring 11.5 cm, located at the tail of the pancreas. The patient was put under Albendazole for a week and then operated on. During laparotomy, a hydatid cyst was located in the tail of the pancreas. Conservative treatment was done sparing the healthy pancreatic parenchyma and avoiding major surgery for a diabetic patient.

## Hydatid cyst of the liver invading the inferior vena cava.

**Laasri K, Zhim M, Naggar A, El Aoufir O, Laamrani FZ, Jroundi L.**
28-09-2023
*Radiol Case Rep*.
https://pubmed.ncbi.nlm.nih.gov/37789919/

Hydatid disease is a parasitic infestation due to the development of Echinococcus granulosus in the organism. This disease is particularly frequent in Morocco where echinococcosis is endemic. The liver is the most common organ to be affected by hydatidosis, and several complications have been described. Vascular complications secondary to hepatic echinococcosis such as fistulization or rupture of hydatid liver cysts to the inferior vena cava (IVC) are an extremely rare and life-threatening condition. This report aims to describe a case of invasion of the IVC by a hydatid cyst of the liver resulting in portal hypertension in a 60-year-old female patient. The diagnosis was established in the preoperative phase by a CT scan. IVC invasion remains an infrequent complication that should be routinely looked for in patients with hydatid disease of the liver, and few cases have been reported in the literature to date.

## Giant muscle hydatid in lower extremity: a rare case with neurological symptoms as the first manifestation.

**Jia Q, Wu S, Guo J, Alimujiang A, Zheng H, Zhang J, Wang Y, Xie Z, Ma C.**
02-10-2023
*BMC Infect Dis*.
https://pubmed.ncbi.nlm.nih.gov/37784034/

Background: Human hydatid disease typically occurs in organs such as the liver and kidney. Primary solitary intramuscular hydatid disease, however, is rare. Case presentation: We report a case of a giant muscle hydatid in the lower extremity, with neurological symptoms as the first manifestation. The symptoms specifically manifested as intermittent pain in the right lower extremity and numbness in the sole of the right foot. However, there

were no obvious abnormalities detected in electromyography and lumbar MRI. Subsequent ultrasonography and calf MRI showed that the patient had cystic lesions in the calf. The patient was initially diagnosed with a muscle hydatid cyst. Treatment involved complete surgical excision of the lesion, and the diagnosis of a hydatid cyst was confirmed through macroscopic and microscopic histopathological examination after the mass was excised. The patient was given oral albendazole, and no recurrence was observed during the 12 months of follow-up. Conclusions: This case underscores the need to consider hydatid disease when diagnosing soft tissue masses in muscles, particularly in endemic areas. Patients may initially present with atypical symptoms like peripheral nerve issues.

### Gray wolves as sentinels for the presence of Echinococcus spp. and other gastrointestinal parasites in France.

**Umhang G, Duchamp C, Boucher JM, Caillot C, Legras L, Demerson JM, Lucas J, Gauthier D, Boué F.**
20-09-2023
*Int J Parasitol Parasites Wildl.*
https://pubmed.ncbi.nlm.nih.gov/37780970/

### Two Cases of Disseminated Alveolar Echinococcosis: The Diagnosis, Management, and Differential Considerations for Liver Lesions.

**Hirano K, Maruki Y, Yamashige D, Kobayashi O, Shiotsuka M, Morizane C, Imamura T, Hiraoka N, Okusaka T.**
29-09-2023
*Intern Med*.
https://pubmed.ncbi.nlm.nih.gov/37779063/

Alveolar echinococcosis (AE), caused by Echinococcus multilocularis, is an aggressive and potentially critical infestation that primarily affects the liver and can metastasize to any part of the body. We herein report two cases of echinococcosis, which could be differentiated from malignancy on imaging studies, with infections of the liver and mediastinal lymph nodes, and also associated with systemic disseminated lesions. AE is a very invasive infectious disease, and in order to detect such lesions at an early stage when they are still resectable, it is necessary to understand the characteristic imaging findings and determine the patient's current medical history.

### First cases of alveolar echinococcosis in dogs in Poland.

**Jańczak D, Skibiński F, Borkowski A, Jerchewicz M, Włodarz K, Klimiuk P, Sapierzyński RA, Gawor J.**
28-09-2023
*Ann Agric Environ Med*.
https://pubmed.ncbi.nlm.nih.gov/37772535/

## Filariose lymphatique

### Battle of the milky way: Lymphatic targeted drug delivery for pathogen eradication.

**Taheri A, Bremmell KE, Joyce P, Prestidge CA.**
03-10-2023
*J Control Release*.
https://pubmed.ncbi.nlm.nih.gov/37797891/

### Determinants of podoconiosis among residents of Machakle District East Gojjam Zone Amhara Region Ethiopia.

**Tefera T, Bogale KA, Tegegn Y, Azene AG, Mulatu K, Wassie GT.**
05-10-2023
*PLoS Negl Trop Dis*.
https://pubmed.ncbi.nlm.nih.gov/37797041/

Background: Podoconiosis (endemic non-filarial elephantiasis) is a chronic disease characterized by the development of persistent swelling of plantar foot initially; which progresses to the dorsal foot and lower leg slowly or in a number of acute episodes to reach the knee. About 4 million people are said to be affected by the disease worldwide and it is deemed a serious public health problem in at least 10 African countries including Ethiopia. Therefore this study aimed to identify the determinants of podoconiosis among residence in Machakel district. Method: Unmatched case control study design was conducted at Machakel district from August 30 to September 30, 2022. The sample size calculated using Epi-info software yielded 211 controls and 106 cases (317 study participants). Simple random sampling technique was used to select the cases using registration books of the district. Data were entered to Epi info version 7 and exported to SPSS version 22 for statistical analysis. Binary logistic regression was used to identify explanatory variables. Result: A total of 312 study participants (104 cases and 208 controls) were included giving a response rate of 98.42%. Bare foot (AOR, 5.83 [95% CI: 2.34-14.50]), female sex (AOR, 4.25 [95% CI: 2.22-8.14]), family history of podoconiosis (AOR 3.01(95% CI: 1.41-6.42) and age group 41-60 (AOR 5.05(95% CI: 2.35-10.83), and 61-80 AOR 15.74 95% CI: (5.56-44.55) were determinants of Podoconiosis. Conclusion and recommendation: Barefoot, sex, family history of podoconiosis and age were determinants of Podoconiosis. District health office should encourage at risk populations especially older people and individuals with family history of podoconiosis about shoe wearing practice all the time and not to expose their skin and feet.

### Lymphatic filariasis in Zambia: A scoping review protocol.

**Shirley H, Orriols A, Hogan D, Chimfwembe K, Balya A, Sibbuku K, Lardizabal J, Tillotson S, Coombs PE, Wamai R.**
04-10-2023
*PLoS One.*
https://pubmed.ncbi.nlm.nih.gov/37792737/

**Background:** Zambia is among the countries making major progress in limiting cases of the neglected tropical disease lymphatic filariasis on the path to reaching global elimination targets. For this trend to continue, it is essential for strategies and policies targeting the disease in Zambia to be based on the most recent and relevant literature. The scope of research on lymphatic filariasis in the Zambian context is currently poorly understood. Therefore, this study describes a scoping review protocol which will be used to analyze the body of literature on lymphatic filariasis in Zambia. **Methods:** The scoping review protocol was developed following the PRISMA reporting guidelines for Scoping Reviews (PRISMA-ScR) and the JBI Scoping Review Methodology Group's guidance on conducting scoping reviews. In consultation with a research librarian, these guidelines will be applied to a literature search of articles from peer-reviewed journals, or government and international regulatory bodies using PubMed, Embase, Web of Science, Cochrane CENTRAL, WHO ICTRP, Pan African Clinical Trials Registry, and ClinicalTrials.gov. Each record will be screened at the abstract and full-text level by two independent reviewers, and results reported via summary statistics. **Discussion:** Understanding the current state of research on lymphatic filariasis in Zambia will identify major knowledge and intervention gaps in this context, and serve as a source of information for surrounding countries in the region. As the disease prevalence drops, efforts for elimination will require carefully targeted strategies which can be informed from the literature identified in this protocol.

## Integrative Medicine and Self-Care In The Treatment of Lymphatic Filariasis Associated Lymphoedema: An effective strategy!

**Singal A, Bisherwal K.**
29-09-2023
*Br J Dermatol.*
https://pubmed.ncbi.nlm.nih.gov/37772973/

## Safety and tolerability of moxidectin and ivermectin combination treatments for lymphatic filariasis in Côte d'Ivoire: A randomized controlled superiority study.

**Bjerum CM, Koudou BG, Ouattara AF, Lew D, Goss CW, Gabo PT, King CL, Fischer PU, Weil GJ, Budge PJ.**
18-09-2023
*PLoS Negl Trop Dis*.
https://pubmed.ncbi.nlm.nih.gov/37721964/

**Background:** Moxidectin is a macrocyclic lactone registered for the treatment of human onchocerciasis. The drug has a good safety profile, large volume of distribution and a long elimination half-life. This paper reports tolerability data from the first use of moxidectin in persons with Wuchereria bancrofti infection. **Methods:** In this randomized, open-label, masked-observer superiority trial, adults with Wuchereria bancrofti microfilaremia in Côte d'Ivoire were randomized to 1 of 4 treatment arms: ivermectin + albendazole (IA), moxidectin + albendazole (MoxA), ivermectin + diethylcarbamazine (DEC) + albendazole (IDA), or moxidectin + DEC + albendazole (MoxDA). As part of a larger efficacy trial, all participants were closely monitored for 7 days after treatment. **Results:** One hundred sixty-four individuals were treated, and monitored for treatment emergent adverse events (TEAE). Eighty-seven participants (53%) experienced one or more mild (grade 1) or moderate (grade 2) TEAE. Four participants had transient Grade 3 hematuria after treatment (3 after IDA and 1 after IA). There were no serious adverse events. There were no significant differences in frequency or types of TEAE between treatment groups (IA = 22/41 (53%), MoxA = 24/40 (60%), IDA = 18/41 (44%), MoxDA = 15/42 (36%), p = 0.530). Fifty-nine participants (36%) had multiple TEAE, and 8.5% had a one or more grade 2 (moderate) TEAE. Grade 2 TEAE were more frequent after triple drug treatments (IDA, 14.6%; MoxDA, 9.5%) than after two-drug treatments (IA, 7.3%; MoxA, 2.5%). There was no difference in TEAEs based on baseline Mf counts (OR 0.69 (0.33, 1.43), p-value 0.319). **Conclusion:** All treatment regimens were well tolerated. We observed no difference in safety parameters between regimens that contained ivermectin or moxidectin. **Trial registration:** Clinicaltrials.gov, NCT04410406.

## Integrated Prevalence Assessment of Wuchereria bancrofti and Onchocerca volvulus in Three Co-Endemic Districts of Gambella Region, Ethiopia.

**Hassen M, Mohammed A, Endeshaw T, Seid T, Samuel F, Asmare T, Birhanu H, Bekele F, Yayeh A, Seife F, Tamiru M, Meribo K, Tadesse Z, Griswold E, Katabarwa M, Richards F, Noland GS.**
11-09-2023
*Am J Trop Med Hyg*.
https://pubmed.ncbi.nlm.nih.gov/37696513/

## Programmed cell death pathways as targets for developing antifilarial drugs: Lessons from the recent findings.

**Das NC, Chakraborty P, Nandy S, Dey A, Malik T, Mukherjee S.**
Oct-2023
*J Cell Mol Med.*
https://pubmed.ncbi.nlm.nih.gov/37605891/

More than half a century has passed since the introduction of the National Filariasis Control Program; however, as of 2023, lymphatic filariasis (LF) still prevails globally, particularly in the tropical and subtropical regions, posing a substantial challenge to the objective of worldwide elimination. LF is affecting human beings and its economically important livestock leading to a crucial contributor to morbidities and disabilities. The current scenario has been blowing up alarms of attention to develop potent therapeutics and strategies having efficiency against the adult stage of filarial nematodes. In this context, the exploration of a suitable drug target that ensures lethality to macro and microfilariae is now our first goal to achieve. Apoptosis has been the potential target across all three stages of filarial nematodes viz. oocytes, microfilariae (mf) and adults resulting in filarial death after receiving the signal from the reactive oxygen species (ROS)

and executed through intrinsic and extrinsic pathways. Hence, it is considered a leading target for developing antifilarial drugs. Herein, we have shown the efficacy of several natural and synthetic compounds/nanoformulations in triggering the apoptotic death of filarial parasites with little or no toxicity to the host body system.

# Gale

### The most effective systemic treatment in dogs with sarcoptic mange: a critically appraised topic.

**Dumitrache MO, Cadiergues MC.**
05-10-2023
*BMC Vet Res*.
https://pubmed.ncbi.nlm.nih.gov/37798627/

Background: Sarcoptic mange is a common, pruritic parasitic skin disease of dogs. Due to its highly contagious character, it represents a potential veterinary and public health risk. Because of clinical similarity with other diseases, cross-antigenicity, and low sensitivity of available diagnostic methods, therapeutical trial is frequently used to confirm the disease. Considering the variety of available acaricidal molecules as well as the need to use the most effective treatment, the present paper reviews evidence comparing different types of systemic treatment of canine scabies. Results: Analysis of the results showed that afoxolaner, fluralaner and sarolaner as well as several macrocyclic lactones such as selamectin, moxidectin and milbemycin oxime can lead to parasitological and clinical cure. Conclusion: The similarity in the clinical and parasitological efficacy of these substances enhances the need for comparative studies, which could allow the identification of the most efficacious product. Keywords: Dog; Sarcoptes scabiei var. canis; Sarcoptic mange; Systemic treatment; Treatment efficacy.

### Holy medicine. Patron saints of wounds due to animal bites.

**Polak A, Chomentowska E, Grzybowski A.**
29-09-2023
*Clin Dermatol.*
https://pubmed.ncbi.nlm.nih.gov/37778706/

### Scabies: the neglected tropical disease that is everywhere.

**Burki T.**
Oct-2023
*Lancet Infect Dis*.
https://pubmed.ncbi.nlm.nih.gov/37776887/

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

### Assessment of Intestinal Parasites and Its Associated Factors among Fruits and Vegetables Collected from Local Markets of Bule Hora Town, Southeast Ethiopia.

**Gemechu T, Bona J, Aliyo A, Dedecha W, Ashenafi G.**
21-09-2023
*J Trop Med*.
https://pubmed.ncbi.nlm.nih.gov/37781133/

# Leishmaniose

### Exploring the leishmanicidal potential of terpenoids: a comprehensive review on mechanisms of cell death.

**Rodrigues ACJ, Carloto ACM, Gonçalves MD, Concato VM, Detoni MB, Dos Santos YM, Cruz EMS, Madureira MB, Nunes AP, Pires MFMK, Santos NC, Marques REDS, Bidoia DL, Borges Figueiredo F, Pavanelli WR.**
19-09-2023
*Front Cell Infect Microbiol*.
https://pubmed.ncbi.nlm.nih.gov/37799331/

Leishmaniasis is a neglected tropical disease with a wide spectrum of clinical manifestations, ranging from visceral to cutaneous, with millions of new cases and thousands of deaths reported each year. The species of *Leishmania* and the immune response of the host determine the severity of the disease. Leishmaniasis remains challenging to diagnose and treat, and there is no vaccine available. Several studies have been conducted on the use of herbal medicines for the treatment of leishmaniasis. Natural products can provide an inexhaustible source of chemical diversity with therapeutic potential. Terpenes are a class of natural products derived from a single isoprene unit, a five-carbon compound that forms the basic structure of isoprenoids. This review focuses on the most important and recent advances in the treatment of parasites of the genus *Leishmania* with different subclasses of terpenes. Several mechanisms have been proposed in the literature, including increased oxidative stress, immunomodulatory role, and induction of different types of parasite cell death. However, this information needs to be brought together to provide an overview of how these compounds can be used as therapeutic tools for drug development and as a successful adjuvant strategy against *Leishmania* sp.

### In vitro susceptibility to miltefosine of amphotericin B-resistant Leishmania (Mundinia) martiniquensis.

**Mano C, Kongkaew A, Tippawangkosol P, Junkum A, Siriyasatien P, Jariyapan N.**
05-10-2023
*Parasitol Res.*

https://pubmed.ncbi.nlm.nih.gov/37796293/

## A blinded, randomized and controlled multicenter clinical trial to assess the efficacy and safety of Leisguard® as an immunotherapeutic treatment for healthy Leishmania infantum-seropositive dogs.

**Baxarias M, Donato G, Mateu C, Salichs M, Homedes J, Miró G, Pennisi MG, Solano-Gallego L.**
04-10-2023
*Parasit Vectors.*
https://pubmed.ncbi.nlm.nih.gov/37799331/

Background: Domperidone (Leisguard®) is an immunomodulatory drug used as a preventive measure in healthy dogs. However, no studies have been published in healthy Leishmania infantum-seropositive dogs. The aim of this study was to evaluate the clinical efficacy and safety of domperidone as immunotherapy in Leishmania-seropositive healthy dogs. Methods: Sixty-seven dogs were treated with domperidone at 0.5 mg/kg and 44 dogs received placebo, once daily for 4 consecutive weeks. Monthly treatments were repeated every 4 months until the end of the 1-year follow-up period. Veterinary examinations were performed on days 0, 30, 120, 150, 240, 270 and 360. Samples of blood and urine were collected on days 0, 120, 240 and 360 for routine laboratory tests and quantitative in-house ELISA for the detection of L. infantum-specific antibodies. Furthermore, Leishmania real-time PCR and IFN-γ ELISA were performed at day 0 and the end of the study. Dogs that developed disease were withdrawn from the study and classified as sick dogs. Adverse drug reactions were reported. Results: Thirty dogs developed disease during the follow-up period: 13/67 (19.4%) in the group treated with domperidone and 17/44 (38.6%) in the placebo-treated group (P = 0.03). Low-seropositive dogs treated with domperidone (4/40, 9.1%) were significantly less likely to develop disease compared to low-seropositive dogs treated with placebo (7/24, 29.2%; P = 0.04), while no differences were found between domperidone (9/23, 39.1%) and placebo (10/20, 50%) in medium- to high-seropositive dogs. At the end of the study, a higher proportion of Leishmania PCR-positive dogs was observed in the placebo-treated group (16/33, 48.5%) compared to the domperidone group (13/51, 25.5%; P = 0.04). Furthermore, low-seropositive dogs treated with domperidone with an increase of IFN-γ concentration presented a higher increase than those treated with placebo at the end of the study. Four dogs treated with domperidone presented self-limiting diarrhea. Conclusions: Healthy dogs with low L. infantum antibody levels treated with domperidone were less likely to develop disease compared to placebo-treated dogs. Furthermore, domperidone presented a good safety profile.

## Parasitic infections in hematopoietic stem cell transplant recipients.

**Haque E, Muhsen IN, Rasheed W, Fakih RE, Aljurf M.**
04-10-2023
*Transpl Infect Dis*.
https://pubmed.ncbi.nlm.nih.gov/37793057/

Introduction: Hematopoietic stem cell transplantation (HSCT) is a vital treatment for various hematological disorders. However, HSCT recipients face increased risks of infectious complications due to immunosuppression. Parasitic infections are a significant concern in this vulnerable population and can lead to substantial morbidity and mortality. This review examines parasitic infections in HSCT recipients, focusing on major infections affecting different organ systems, including intestinal parasites (Giardia spp., Entamoeba histolytica, and Cryptosporidium spp.), hematologic parasites (Plasmodium spp. and Babesia spp.), and tissue/visceral parasites (Toxoplasma gondii, Leishmania spp., and Trypanosoma cruzi). Methods: A systematic search of relevant literature was conducted and included studies up to August 2023. Databases included PubMed, Google Scholar, were queried using specific keywords related to parasitic infections in HSCT patients. The epidemiology, risk factors, clinical presentation, diagnostic methods, and treatment approaches for each infection were evaluated. Results and conclusion: Knowing the epidemiology, risk factors, and clinical presentations are crucial for timely intervention and successful management. By emphasizing early detection, effective therapies, and the unique challenges posed by each of these infections, this review highlights the importance of tailored strategies for HSCT recipients. Future research can further refine management protocols to enhance care and outcomes for these patients.

## Natural infection of Lutzomyia longipalpis (Lutz & Neiva, 1912) by Leishmania infantum in a municipality with a high incidence of visceral leishmaniasis in the Brazilian Midwest.

**Neitzke-Abreu HC, Andrade GMC, Almeida PS, Ribeiro GC, Ribeiro TA, Barrios DM, Pussi KF, Andrade Filho JD, Dutra-Rêgo F, Ovallos FG.**
22-09-2023
*Rev Soc Bras Med Trop*.
https://pubmed.ncbi.nlm.nih.gov/37792832/

## A non-replicative antibiotic resistance-free DNA vaccine delivered by the intranasal route protects against canine leishmaniasis.

**Alonso A, Alcolea PJ, Larraga J, Peris MP, Esteban A, Cortés A, Ruiz-García S, Castillo JA, Larraga V.**
18-09-2023
*Front Immunol.*
https://pubmed.ncbi.nlm.nih.gov/37790927/

*Leishmania infantum* is the etiological agent of zoonotic visceral leishmaniasis (ZVL). The disease is endemic in Central and South America, Central and South East Asia, and the Mediterranean basin. Dogs are the main reservoir, with an estimated prevalence of approximately 2.5 million dogs in Southern Europe. Current treatments cause side effects, disease recurrence, and drug resistance. Therefore, the development of vaccines against canine

leishmaniasis is necessary. We have generated a DNA vaccine based on the non-replicative antibiotic resistance marker-free plasmid vector pPAL that contains the encoding gene for the *L. infantum* activated protein kinase C receptor analog (LACK). Homologous pPAL-LACK prime-boost intranasal administration confers efficacious protection in Beagle dogs with a reduction of clinical signs and a statistically significant reduction of the parasite burden in the bone marrow of more than 90% of dogs after experimental infection with highly infective promastigotes. This DNA vaccine elicits a robust cellular immune response skewed towards the Th1 profile.

## Unveiling drug-tolerant and persister-like cells in Leishmania braziliensis lines derived from patients with cutaneous leishmaniasis.

**Jara M, Arevalo J, Llanos-Cuentas A, den Broeck FV, Domagalska MA, Dujardin JC.**
18-09-2023
*Front Cell Infect Microbiol.*
https://pubmed.ncbi.nlm.nih.gov/37790908/

## Leishmania PNUTS discriminates between PP1 catalytic subunits through a RVxF-ΦΦ-F motif and polymorphisms in the PP1 C-tail and catalytic domain.

**Zhang Y, Sabatini R.**
20-09-2023
*bioRxiv.*
https://pubmed.ncbi.nlm.nih.gov/37790576/

PP1 phosphatases lack substrate specificity and associate with specific regulatory subunits to achieve selectivity. Among the eight PP1 isotypes in Leishmania, PP1-8e associates with the regulatory protein PNUTS along with the structural factors JBP3 and Wdr82 in the PJW/PP1 complex that modulates RNA polymerase II (Pol II) phosphorylation and transcription termination. Little is known regarding interactions involved in PJW/PP1 complex formation, including how PP1-8e is the selective isotype associated with PNUTS. Here, we show that PNUTS uses an established RVxF-ΦΦ-F motif to bind the PP1 catalytic domain with similar interfacial interactions as mammalian PP1- PNUTS and non-canonical motifs. These atypical interactions involve residues within the PP1-8e catalytic domain and N- and C-terminus for isoform specific regulator binding. This work advances our understanding of PP1 isoform selectivity and reveals key roles of PP1 residues in regulator binding. We also explore the role of PNUTS as a scaffold protein for the complex by identifying the C-terminal region involved in binding JBP3 and Wdr82, and impact of PNUTS on the stability of complex components and function in Pol II transcription *in vivo* . Taken together, these studies provide a potential mechanism where multiple motifs within PNUTS are used combinatorially to tune binding affinity to PP1, and the C-termini for independent binding of JBP3 and Wdr82, in the Leishmania PJW/PP1 complex. Overall, our data provide insights in the formation of the PJW/PP1 complex involved in regulating Pol II transcription in divergent protozoans where little is understood.

## Zingiber officinale rhizome extracts mediated ni nanoparticles and its promising biomedical and environmental applications.

**Abdullah, Hussain T, Faisal S, Rizwan M, Almostafa MM, Younis NS, Yahya G.**
03-10-2023
*BMC Complement Med Ther*.
https://pubmed.ncbi.nlm.nih.gov/37789322/

## Repurposing of conformationally-restricted cyclopentane-based AKT-inhibitors leads to discovery of potential and more selective antileishmanial agents than miltefosine.

**Hassan AHE, Alam MM, Phan TN, Baek KH, Lee H, Cho SB, Lee CH, Kim YJ, No JH, Lee YS.**
27-09-2023
*Bioorg Chem.*
https://pubmed.ncbi.nlm.nih.gov/37783099/

Conformational restriction was addressed towards the development of more selective and effective antileishmanial agents than currently used drugs for treatment of Leishmania donovani; the causative parasite of the fatal visceral leishmaniasis. Five types of cyclopentane-based conformationally restricted miltefosine analogs that were previously explored in literature as anticancer AKT-inhibitors were reprepared and repurposed as antileishmanial agents. Amongst, positions-1 and 2 cis-conformationally-restricted compound 1a and positions-2 and 3 trans-conformationally-restricted compound 3b were highly potent eliciting sub-micromolar $IC_{50}$ values for inhibition of infection and inhibition of parasite number compared with the currently used miltefosine drug that showed low micromolar $IC_{50}$ values for inhibition of infection and inhibition of parasite number. Compounds 1a and 3b eradicated the parasite without triggering host cells cytotoxicity over more than one log concentration interval which is a superior performance compared to miltefosine. In silico studies suggested that conformational restriction conserved the conformer capable of binding LdAKT-like kinase while it might be possible that it excludes other conformers mediating undesirable effects and/or toxicity of miltefosine. Together, this study presents compounds 1a and 3b as antileishmanial agents with superior performance over the currently used miltefosine drug.

## Vaccinomics-based next-generation multi-epitope chimeric vaccine models prediction against Leishmania tropica - a hierarchical subtractive proteomics and immunoinformatics approach.

**Aiman S, Ahmad A, Khan AA, Alanazi AM, Samad A, Ali SL, Li C, Ren Z, Khan A, Khattak S.**
15-09-2023
*Front Immunol.*
https://pubmed.ncbi.nlm.nih.gov/37781384/

*Leishmania tropica* is a vector-borne parasitic protozoa that is the leading cause of leishmaniasis throughout the

global tropics and subtropics. *L. tropica* is a multidrug-resistant parasite with a diverse set of serological, biochemical, and genomic features. There are currently no particular vaccines available to combat leishmaniasis. The present study prioritized potential vaccine candidate proteins of *L. tropica* using subtractive proteomics and vaccinomics approaches. These vaccine candidate proteins were downstream analyzed to predict B- and T-cell epitopes based on high antigenicity, non-allergenic, and non-toxic characteristics. The top-ranked overlapping MHC-I, MHC-II, and linear B-cell epitopes were prioritized for model vaccine designing. The lead epitopes were linked together by suitable linker sequences to design multi-epitope constructs. Immunogenic adjuvant sequences were incorporated at the N-terminus of the model vaccine constructs to enhance their immunological potential. Among different combinations of constructs, four vaccine designs were selected based on their physicochemical and immunological features. The tertiary structure models of the designed vaccine constructs were predicted and verified. The molecular docking and molecular dynamic (MD) simulation analyses indicated that the vaccine design V1 demonstrated robust and stable molecular interactions with toll-like receptor 4 (TLR4). The top-ranked vaccine construct model-IV demonstrated significant expressive capability in the *E. coli* expression system during *in-silico* restriction cloning analysis. The results of the present study are intriguing; nevertheless, experimental bioassays are required to validate the efficacy of the predicted model chimeric vaccine.

## Lymphocytic hypophysitis in dogs infected with Leishmania spp.

**Frigerio ED, Guizelini CC, Jussiani GG, Março KS, de Melo GD, Watanabe TTN, Machado GF.**
14-09-2023
*Front Vet Sci*.
https://pubmed.ncbi.nlm.nih.gov/37781278/

## Adjuvantation of whole-killed Leishmania vaccine with anti-CD200 and anti-CD300a antibodies potentiates its efficacy and provides protection against wild-type parasites.

**Singh R, Anand A, Mahapatra B, Saini S, Singh A, Singh S, Kumar V, Das P, Singh S, Singh RK.**
29-09-2023
*Mol Immunol.*
https://pubmed.ncbi.nlm.nih.gov/37778149/

## Biostimulated-sesame sprout extracts as potential agents against Leishmania mexicana.

**Garduño-Félix KG, Rochín-Medina JJ, Murua-López CC, López-Moreno HS, Ramírez K.**
04-10-2023
*Lett Appl Microbiol.*
https://pubmed.ncbi.nlm.nih.gov/37777833/

Leishmania mexicana is one of the causal agents of cutaneous leishmaniasis. Current antileishmanial chemotherapeutics have demonstrated adverse side effects; thus, alternative treatments are needed. In this study, we performed in silico and in vitro analyses of the leishmanicidal potential of the most abundant phenolic compounds identified in black sesame sprouts biostimulated with Bacillus clausii. The molecular docking analysis showed strong interactions (binding free energies between -6.5 and -9.5 kcal/mol) of sesaminol 2-O-triglucoside, pinoresinol dihexoside, isoverbascoside, and apigenin with the arginase, leishmanolysin, cysteine peptidase B, and pyruvate kinase leishmanial enzymes. Furthermore, almost all phenolic compounds interacted with the active site residues of L. mexicana enzymes. In vitro, the B. clausii-biostimulated sprout phenolic extracts and apigenin inhibited the growth of promastigotes with IC50 values of 0.08 mg gallic acid equivalent/mL and 6.42 µM (0.0017 mg/mL), respectively. Additionally, in the macrophage infection model, cells treated with B. clausii-biostimulated sprout phenolic extracts and infected with L. mexicana exhibited significantly ($P < 0.05$) reduced nitric oxide production and decreased parasite burden. Altogether, our study provides important data related to high efficacy and less toxic natural antileishmanial candidates against promastigotes of L. mexicana.

## SHIP1 inhibition via 3-alpha-amino-cholestane enhances protection against Leishmania infection.

**Chowdhury BP, Das S, Bodhale N, Prakash Pandey S, Sudan R, Srivastava N, Chisholm JD, Kerr WG, Majumdar S, Saha B.**
27-09-2023
*Cytokine.*
https://pubmed.ncbi.nlm.nih.gov/37776719/

## Interaction between Cfd1 and Nbp35 proteins involved in cytosolic FeS cluster assembly machinery deciphers a stable complexation in Leishmania donovani.

**Gupta P, Mansoori R, Priydarshni P, Behera S, Zaidi A, Nehar S, Sahoo GC, Pandey K, Ali V.**
27-10-2023
*Int J Biol Macromol*.
https://pubmed.ncbi.nlm.nih.gov/37774824/

Leishmania donovani is the causative unicellular parasite for visceral leishmaniasis (VL); and FeS proteins are likely to be very essential for their survival and viability. Cytosolic FeS cluster assembly (CIA) machinery is one of the four systems for the biosynthesis and transfer of FeS clusters among eukaryotes; Cfd1 and Nbp35 are the scaffold components for cytosolic FeS cluster biogenesis. We investigated the role of CIA machinery components and purified Cfd1 and Nbp35 proteins of L. donovani. We also investigated the interactive nature between LdCfd1 and LdNbp35 proteins by in silico analysis, in vitro co-purification, pull down assays along with in vivo immuno-precipitation; which inferred that both LdCfd1 and LdNbp35 proteins are interacting with each other. Thus, our collective data revealed the interaction between these two proteins which forms a stable complex that can be attributed to the cellular process of FeS clusters

biogenesis, and transfer to target apo-proteins of L. donovani. The expression of Cfd1 and Nbp35 proteins in Amp B resistant parasites is up-regulated leading to increased amount of FeS proteins. Hence, it favors increased tolerance towards ROS level, which helps parasites survival under drug pressure contributing in Amphotericin B resistance.

## Miltefosine repositioning: A review of potential alternative antifungal therapy.

**Spadari CC, Borba-Santos LP, Rozental S, Ishida K.**
20-09-2023
*J Mycol Med*.
https://pubmed.ncbi.nlm.nih.gov/37774486/

## Trichophoromyia auraensis: evidence for cryptic species and first record in the state of Maranhão, Brazil.

**Rodrigues BL, Brilhante AF, de Souza Pinto I, Galati EAB.**
29-09-2023
*Parasitol Res*.
https://pubmed.ncbi.nlm.nih.gov/37773460/

## Investigation of the Potential Targets behind the Promising and Highly Selective Antileishmanial Action of Synthetic Flavonoid Derivatives.

**Lourenço EMG, da Silva F, das Neves AR, Bonfá IS, Ferreira AMT, Menezes ACG, da Silva MEC, Dos Santos JT, Martines MAU, Perdomo RT, Toffoli-Kadri MC, G Barbosa E, Saba S, Beatriz A, Rafique J, de Arruda CCP, de Lima DP.**
29-09-2023
*ACS Infect Dis*.
https://pubmed.ncbi.nlm.nih.gov/37772925/

## Disruption of the inositol phosphorylceramide synthase gene affects Trypanosoma cruzi differentiation and infection capacity.

**Dos Santos NSA, Estevez-Castro CF, Macedo JP, Chame DF, Castro-Gomes T, Santos-Cardoso M, Burle-Caldas GA, Covington CN, Steel PG, Smith TK, Denny PW, Teixeira SMR.**
20-09-2023
*PLoS Negl Trop Dis*.
https://pubmed.ncbi.nlm.nih.gov/37729272/

Sphingolipids (SLs) are essential components of all eukaryotic cellular membranes. In fungi, plants and many protozoa, the primary SL is inositol-phosphorylceramide (IPC). Trypanosoma cruzi is a protozoan parasite that causes Chagas disease (CD), a chronic illness for which no vaccines or effective treatments are available. IPC synthase (IPCS) has been considered an ideal target enzyme for drug development because phosphoinositol-containing SL is absent in mammalian cells and the enzyme activity has been described in all parasite forms of T. cruzi. Furthermore, IPCS is an integral membrane protein conserved amongst other kinetoplastids, including Leishmania major, for which specific inhibitors have been identified. Using a CRISPR-Cas9 protocol, we generated T. cruzi knockout (KO) mutants in which both alleles of the IPCS gene were disrupted. We demonstrated that the lack of IPCS activity does not affect epimastigote proliferation or its susceptibility to compounds that have been identified as inhibitors of the L. major IPCS. However, disruption of the T. cruzi IPCS gene negatively affected epimastigote differentiation into metacyclic trypomastigotes as well as proliferation of intracellular amastigotes and differentiation of amastigotes into tissue culture-derived trypomastigotes. In accordance with previous studies suggesting that IPC is a membrane component essential for parasite survival in the mammalian host, we showed that T. cruzi IPCS null mutants are unable to establish an infection in vivo, even in immune deficient mice.

## Prostaglandin E2 contributes to L. braziliensis survival and therapeutic failure in cutaneous leishmaniasis.

**Nascimento MT, Viana DL, Peixoto FC, Arruda SM, Carvalho EM, Carvalho LP.**
Déc-2023
*Emerg Microbes Infect*.
https://pubmed.ncbi.nlm.nih.gov/37729084/

## Increased Risk of American Tegumentary Leishmaniasis in an Urban and Rural Area of Caratinga, Brazil between 2016 and 2021.

**Neves RL, Ker FTO, Dutra-Rêgo F, Rugani JMN, Andrade Filho JD, Soares RP, Gontijo CMF.**
28-08-2023
*Am J Trop Med Hyg*.
https://pubmed.ncbi.nlm.nih.gov/37640295/

We used spatial analysis tools to examine the epidemiological situation and spatial distribution of American tegumentary leishmaniasis in the municipality of Caratinga between 2016 and 2021. In addition, potential sandfly vectors were captured. All information used in this study was retrieved from public health archives and confirmed in the state health services databases. All cases were analyzed using Geographic Information Systems software. In addition, sandfly collections and molecular detection of Leishmania were carried out in areas with the highest number of cases. During the analyzed period, American tegumentary leishmaniasis (ATL) cases increased and remained high in the last years. The hotspots included urban areas of Caratinga city and the districts of Patrocínio of Caratinga and Sapucaia. The species Nyssomyia whitmani, Nyssomyia intermedia, and Migonemyia migonei were the most abundant species and the ITS1-polymerase chain reaction technique detected Leishmania DNA in these species. On the basis of our analyses, the urbanization of ATL in Caratinga has taken place in recent years. Because of the increase in the number of human cases and the presence of vectors, it is recommended that health authorities focus on control measures in hotspots.

## Complete assembly, annotation of virulence genes and CRISPR editing of the genome of Leishmania amazonensis PH8 strain.

**Goes WM, Brasil CRF, Reis-Cunha JL, Coqueiro-Dos-Santos A, Grazielle-Silva V, de Souza Reis J, Souto TC, Laranjeira-Silva MF, Bartholomeu DC, Fernandes AP, Teixeira SMR.**
Spet-2023
*Genomics.*
https://pubmed.ncbi.nlm.nih.gov/37263313/

We report the sequencing and assembly of the PH8 strain of Leishmania amazonensis one of the etiological agents of leishmaniasis. After combining data from long Pacbio reads, short Illumina reads and synteny with the Leishmania mexicana genome, the sequence of 34 chromosomes with 8317 annotated genes was generated. Multigene families encoding three virulence factors, A2, amastins and the GP63 metalloproteases, were identified and compared to their annotation in other Leishmania species. As they have been recently recognized as virulence factors essential for disease establishment and progression of the infection, we also identified 14 genes encoding proteins involved in parasite iron and heme metabolism and compared to genes from other Trypanosomatids. To follow these studies with a genetic approach to address the role of virulence factors, we tested two CRISPR-Cas9 protocols to generate L. amazonensis knockout cell lines, using the Miltefosine transporter gene as a proof of concept.

## Computational multi-target approach to target essential enzymes of Leishmania donovani using comparative molecular dynamic simulations and MMPBSA analysis.

**Saha D, Nath Jha A.**
Oct-2023
*Phytochem Anal*.
https://pubmed.ncbi.nlm.nih.gov/36760044/

# Lèpre

## F-waves persistence in peripheral sensory syndromes.

**Lima FD, Martinez ARM, Schmitt GDS, França AFEDC, Velho PENF, Akita J, Garbino JA, Nucci A, França MC Jr.**
Sept-2023
*Arq Neuropsiquiatr.*
https://pubmed.ncbi.nlm.nih.gov/37793400/

Background: The distinction between sensory neuronopathies (SN), which is by definition purely sensory, and sensory polyneuropathies (SP) and sensory multineuropathies (SM) is important for etiologic investigation and prognosis estimation. However, this task is often challenging in clinical practice. We hypothesize that F-wave assessment might be helpful, since it is able to detect subtle signs of motor involvement, which are found in SP and SM, but not in SN. Objective: The aim of the present study was to determine whether F-waves are useful to distinguish SN from SP and SM. Methods: We selected 21 patients with SP (12 diabetes mellitus, 4 transthyretin familial amyloid polyneuropathy, 4 others), 22 with SM (22 leprosy), and 26 with SN (13 immune-mediated, 10 idiopathic, 3 others) according to clinical-electrophysiological-etiological criteria. For every subject, we collected data on height and performed 20 supramaximal distal stimuli in median, ulnar, peroneal, and tibial nerves, bilaterally, to record F-waves. Latencies (minimum and mean) and persistences were compared across groups using the Kruskal-Wallis and Bonferroni tests. *P*-values < 0.05 were considered significant. Results: All groups were age, gender, and height-matched. Overall, there were no significant between-group differences regarding F-wave latencies. In contrast, F-wave persistence was able to stratify the groups. Peroneal F-wave persistence was higher, bilaterally, in the SN group compared to SM and SP ($p < 0.05$). In addition, F-waves persistence of the ulnar and tibial nerves was also helpful to separate SN from SP ($p < 0.05$). Conclusion: F-wave persistence of the peroneal nerves might be an additional and useful diagnostic tool to differentiate peripheral sensory syndromes.

## Are leprosy and Hansen's disease identical?

**Guo J, Dong X.**
Oct-2023
*Nature.*
https://pubmed.ncbi.nlm.nih.gov/37789244/

## Evaluating the impact of a pre-recorded online video on doctor's knowledge and attitude towards leprosy in Sabah and Labuan - a quasi experimental study.

**Teoh XY, Voo SYM, Sulaiman N.**
Sept-2023
*Med J Malaysia*.
https://pubmed.ncbi.nlm.nih.gov/37775482/

Introduction: Global actions have been implemented worldwide to eliminate leprosy. However, under-recognition and stigmatisation continue to be the challenges. In Sabah, the grade two disability rate was 0.15/100,000 population in 2019, implicating a significant delay in diagnosis. This study aimed to assess the knowledge and attitude towards leprosy and the impact of lecture intervention among doctors in Sabah and Labuan, Malaysia. Materials and methods: This study consists of two parts. First, a cross-sectional study on the knowledge of and attitude towards leprosy using an online quesitonnaire was conducted among doctors working in the primary care clinics and hospitals in Sabah and Labuan. Subsequently, the participants were asked to watched an online prerecorded video lecture on leprosy and to answered the same questionnaire. Results: Of the 310 participants, one fifth (20.6%) had good knowledge and 36.5% had positive attitude towards leprosy. Being a specialist (adjusted odds ratio [aOR] 4.55, 95% confidence interval [CI] 2.17-9.57, $p < 0.001$), managed ≥ 5 leprosy cases (aOR 3.37, 95% CI 1.52-7.47, $p = 0.003$), and involved in educational activities related to leprosy within last year

(aOR 4.7, 95% CI 1.69-13.04, p < 0.001) were the significant predictors of good knowledge. Working in tertiary care was significantly associated with good attitude towards leprosy (OR 2.19, 95% CI 1.22-3.94, p = 0.025). There was a significant improvement in participants' knowledge post-intervention (87.0% participants post-lecture vs 20.6% participants pre-lecture with good knowledge, p < 0.001). Conclusion: The proportion of doctors in Sabah and Labuan with good knowledge and attitude towards leprosy was low. Knowledge of leprosy improved significantly postintervention. This highlights the need for educational and training programmes to improve doctors' knowledge of leprosy.

## Vision-related quality of life among released from treatment cases of leprosy evaluated with NEI-VFQ-25: a cross-sectional study.

**Irawati Y, Andayani G, Rahayu T, Zakiyah H, Kurniawardhani DR, Paramita C, Bani AP, Daniel H, Susiyanti M, Lestari YD, Friska D, Menaldi SL, Harini M.**
02-10-2023
*BMC Ophthalmol.*
https://pubmed.ncbi.nlm.nih.gov/37784121/

Background: People with leprosy who have been declared Release From Treatment (RFT) are often not aware of the leprosy sequelae possibility which can decrease their quality of life. This could be because they have been adapting for a long time hence they do not feel the need to see physicians. This study seeks to compare the results of Vision-Related Quality of Life (VR-QoL) among RFT persons based on the National Eye Institute Visual Functioning Questionnaire-25 (NEI-VFQ-25) and WHO grading disability based on physical examination. Methods: A cross-sectional study of 325 RFT subjects from leprosy communities (Singkawang, West Kalimantan and Tangerang, Banten) was conducted between 2018 and 2019. We used the NEI-VFQ-25 questionnaire that had been validated and translated into Indonesian and distributed to the leprosy population. Relationships and comparisons among variables were evaluated using Kruskal-Wallis and Mann-Whitney tests. Results: There were three main results: The median composite score of VR-QoL for WHO grade 0, 1, and 2 disabilities has decreased by 13%, 25.5%, and 30% of the maximum value, respectively. Of the total, eleven subscales were statistically significant between WHO grading disability and VR-QoL based on the NEI-VFQ-25 (p < 0.05). The comparison between grade 0 and grade 2 disability in all subscales was statistically significant (p < 0.05). Conclusions: The grade of disability is related to their VR-QoL assessment using the NEI-VFQ-25 questionnaire. Thus, it can be used as an initial screening in primary healthcare settings to increase awareness of disability before a thorough physical examination.

## Specialized active leprosy search strategies in an endemic area of the Brazilian Amazon identifies a hypermutated Mycobacterium leprae strain causing primary drug resistance.

**Bouth RC, Gobbo AR, Barreto JG, do Carmo Pinto PD, Bittencourt MS, Frade MAC, Nascimento AC, Bandeira SS, da Costa PF, Conde GAB, Avanzi C, Ribeiro-Dos-Santos Â, Spencer JS, da Silva MB, Salgado CG.**
13-09-2023
*Front Med (Lausanne).*
https://pubmed.ncbi.nlm.nih.gov/37780551/

## Holy medicine. Patron saints of wounds due to animal bites.

**Polak A, Chomentowska E, Grzybowski A.**
29-09-2023
*Clin Dermatol.*
https://pubmed.ncbi.nlm.nih.gov/37778706/

## Leprosy - neglected tropical disease in Pygmies inhabiting Central African Republic.

**Bylicka-Szczepanowska E, Podlasin RB, Korzeniewski K.**
28-09-2023
*Ann Agric Environ Med*.
https://pubmed.ncbi.nlm.nih.gov/37772537/

Leprosy is a neglected tropical disease that is still present worldwide despite efforts aimed at elimination of the disease. The BaAka Pygmy community inhabiting rural areas in the Central African Republic is one of the most leprosy-vulnerable populations. The aim of the study was to assess the prevalence of leprosy in the BaAka Pygmy population. People living in the Dzanga Sangha protected area were regularly visited by a mobile clinic in 2019/2020. The diagnosis was based on the clinical manifestation of the disease. Deformations of skin and extremities were assessed. In a 12-month period 26 cases of leprosy were diagnosed and 25 patients received treatment. 24 of those patients were BaAka Pygmies, 10 were women, 7 were children under 15 years old and 8 were diagnosed with grade 2 disability. Presented data shows that leprosy in Dzanga Sangha region is not well controlled due to the high transmission rate. Efforts to diagnose and report new leprosy cases should be intensified.

## Bilateral Thickened Transverse Cervical Nerve in a Leprosy Patient.

**Prabha N, Khare S, Yadav H.**
29-09-2023
*Skinmed.*
https://pubmed.ncbi.nlm.nih.gov/37771020/

## Systemic treatments in Parthenium dermatitis: A systematic review and meta-analysis.

**Akham R, Bhatia R, Das A, Bhadoria AS, Pathak M, Hazarika N.**
Nov-2023
*Contact Dermatitis.*
https://pubmed.ncbi.nlm.nih.gov/37634936/

# Morsures de serpent

## Barriers to the hospital treatment among Bede snake charmers in Bangladesh with special reference to venomous snakebite.

**Yoshimura K, Hossain M, Tojo B, Tieu P, Trinh NN, Huy NT, Sato M, Moji K.**
02-10-2023
*PLoS Negl Trop Dis*.
https://pubmed.ncbi.nlm.nih.gov/37782628/

Snakebite envenoming is a potentially life-threatening global public health issue with Bangladesh having one of the highest rates of snakebite cases. The Bede, a nomadic ethnic group in Bangladesh, traditionally engages in snake-related business such as snake charming. The Bede relies on their own ethnomedicinal practitioners for snakebite treatment while there is a lack of concrete evidence on the effectiveness of such ethnomedicinal treatment. To identify the barriers to the utilization of biomedical treatment for snakebite we conducted interviews with 38 Bede snake charmers, who have experienced snakebite, and six family members of those who died of snakebite. Our results show that four critical barriers, Accessibility, Affordability, Availability, and Acceptability (4As), prevented some of the Bede from seeking biomedical treatment. Moreover, we found that a few Bede died of a snakebite every year. There are survivors of snakebite who were able to receive biomedical treatment by overcoming all of the 4As. Our results provide insights into the current state of snakebite treatment in Bangladesh and can inform the development of more effective and accessible treatment options for those affected. Partnership between the public sector and the Bede community has the potential to make a significant impact in reducing snakebite morbidity and mortality in Bangladesh.

## Severity of a Vipera palaestinae envenomation objective findings associated with a complicated hospitalization course following a Vipera palaestinae bite.

**Koter N, Gat T, Furth M, Sadeh R, Galante O, Tomer O, Klein S, Muszkat M, Fuchs L, Nachshon A.**
29-09-2023
*Toxicon.*
https://pubmed.ncbi.nlm.nih.gov/37778739/

## Holy medicine. Patron saints of wounds due to animal bites.

**Polak A, Chomentowska E, Grzybowski A.**
29-09-2023
*Clin Dermatol.*
https://pubmed.ncbi.nlm.nih.gov/37778706/

The cult (system of religious beliefs and rituals) of saints in Western Europe appeared in the 3rd century AD and gained momentum from the 4th to the 6th centuries. Its importance for the European society in the Late Antiquity and the early Middle Ages was undeniable; the holy medicine was the only hope for the sick people because the number of physicians was insufficient and usually physicians were helpless in the face of most the ailments that plagued society at that time. The number of saints had increased over the years, and people sought medical help from them through prayer and other religious practices. Some saints "specialized" in the treatment of various wounds, including skin diseases. Our research revealed a large number of saints who were patrons of wounds and skin. They can be collected in three groups: patron saints against snake bites and dog bites; patron saints of the treatment of wounds, ulcers, burns, and frostbite; and patron saints against spreadable diseases such as ergotism, leprosy, and scabies. A large number of saints who were patrons against snake bites and dog bites shows the relevance and importance of the problem. In our research, we tried to find out whether the cult of saints led to the development of hospitals for the treatment of skin diseases like ergotism in the hospital of Brother St. Anthony, or only in miracles of healing emphasized the power of faith in the cure of diseases.

## miRNAs derived from cobra venom exosomes contribute to the cobra envenomation.

**Liao T, Gan M, Qiu Y, Lei Y, Chen Q, Wang X, Yang Y, Chen L, Zhao Y, Niu L, Wang Y, Zhang S, Zhu L, Shen L.**
30-09-2023
*J Nanobiotechnology.*
https://pubmed.ncbi.nlm.nih.gov/37777744/

Currently, there is an increasing amount of evidence indicating that exosomes and the miRNAs they contain are crucial players in various biological processes. However, the role of exosomes and miRNAs in snake venom during the envenomation process remains largely unknown. In this study, fresh venom from Naja atra of different ages (2-month-old, 1-year-old, and 5-year-old) was collected, and exosomes were isolated through ultracentrifugation. The study found that exosomes with inactivated proteins and enzymes can still cause symptoms similar to cobra envenomation, indicating that substances other than proteins and enzymes in exosomes may also play an essential role in cobra envenomation. Furthermore, the expression profiles of isolated exosome miRNAs were analyzed. The study showed that a large number of miRNAs were co-expressed and abundant in cobra venom exosomes (CV-exosomes) of different ages, including miR-2904, which had high expression abundance and specific sequences. The specific miR-2094 derived from CV-exosomes (CV-exo-miR-2904) was overexpressed both in vitro and in vivo. As a result, CV-exo-miR-2904 induced symptoms similar to cobra envenomation in mice and caused liver damage, demonstrating that it plays a crucial role in cobra envenomation. These results reveal that CV-exosomes and the miRNAs they contain play a significant regulatory role in cobra envenomation. Our findings provide new insights for the treatment of cobra bites and the development of snake venom-based medicines.

## Novel Toxicodynamic Model of Subcutaneous Envenomation to Characterize Snake Venom

### Coagulopathies and Assess the Efficacy of Site-Directed Inorganic Antivenoms.

**Nielsen VG.**
11-09-2023
*Int J Mol Sci.*
https://pubmed.ncbi.nlm.nih.gov/37762243/

### Polyvalent Snake Antivenoms: Production Strategy and Their Therapeutic Benefits.

**Ratanabanangkoon K.**
24-08-2023
*Toxins (Basel).*
https://pubmed.ncbi.nlm.nih.gov/37755943/

## Mycétome

### Case report: Mycetoma caused by Gordonia soli.

**França JCB, Carneiro BH, Cognialli RCR, Queiroz-Telles F.**
22-09-2023
*Rev Soc Bras Med Trop*.
https://pubmed.ncbi.nlm.nih.gov/37792837/

### Specific and sensitive loop-mediated isothermal amplification (LAMP) method for Madurella strains, eumycetoma filamentous fungi causative agent.

**Yoshioka I, Mori Y, Fahal AH, Siddig EE, Kaneko S, Yaguchi T.**
18-09-2023
*PLoS Negl Trop Dis*.
https://pubmed.ncbi.nlm.nih.gov/37721946/

Background: Filamentous fungi of the genus Madurella are the primary causative agents of mycetoma, a disease observed in tropical and subtropical regions. Since early diagnostics based on a morphological approach are difficult and have many shortcomings, a molecular diagnostic method suitable for rural settings is required. In this study, we developed the loop-mediated isothermal amplification (LAMP) method to present a foundational technique of the diagnosis of Madurella spp. (M. mycetomatis, M. pseudomycetomatis, M. tropicana, and M. fahalii), the common causative organisms of eumycetoma. Principal findings: We successfully designed a primer pair targeting the rDNAs of three Madurella spp. excluding M. fahalii, and detected up to 100 fg of genomic DNA extracted from isolates of M. mycetomatis and 1 pg of M. pseudomycetomatis and M. tropicana, within one hour. Second, a primer pair specific to M. mycetomatis, the most common causative species, or M. fahalii, a drug-resistant species, was constructed, and the detection limit of both primer pairs was 1 pg. The designed primers accurately distinguished 16 strains of the genus Madurella from various fungal species known to cause mycetomas.

Conclusion: In summary, we established the first model of a LAMP detection method that rapidly and sensitively detects and identifies Madurella isolates for clinical diagnostics. Moreover, the combined designed primer sets could identify mycetoma-causing strains simultaneously.

### Positron emission tomography and computed tomography imaging in primary cutaneous nocardiosis with osteomyelitis clinically mimicking soft tissue sarcoma.

**Okamoto M, Yamamoto T, Sugiyama S, Sunada M, Yamane M, Tanaka R, Endo H, Yaguchi T, Aoyama Y.**
Oct-2023
*J Dermatol.*
https://pubmed.ncbi.nlm.nih.gov/37183522/

## Onchocercose

### Integrated Prevalence Assessment of Wuchereria bancrofti and Onchocerca volvulus in Three Co-Endemic Districts of Gambella Region, Ethiopia.

**Hassen M, Mohammed A, Endeshaw T, Seid T, Samuel F, Asmare T, Birhanu H, Bekele F, Yayeh A, Seife F, Tamiru M, Meribo K, Tadesse Z, Griswold E, Katabarwa M, Richards F, Noland GS.**
11-09-2023
*Am J Trop Med Hyg*.
https://pubmed.ncbi.nlm.nih.gov/37696513/

### Sociodemographics, Clinical Factors, and Biological Factors Associated with Loiasis in Endemic Onchocerciasis Areas in Southern Gabon.

**Moutongo Mouandza R, Mourou JR, Moutombi Ditombi B, Roger Sibi Matotou H, Ekomi B, Bouyou-Akotet MK, Mawili-Mboumba DP.**
20-06-2023
*Am J Trop Med Hyg*.
https://pubmed.ncbi.nlm.nih.gov/37339766/

To implement the appropriate strategies for scale-up interventions to eliminate onchocerciasis without severe adverse events, clinical and biological factors associated with loiasis were analyzed in onchocerciasis-endemic areas. Blood was collected from volunteers after examination by a physician. Detection of microfilariae and measurement of Ov16 IgG4 were performed using direct microscopic examination of blood and onchocerciasis rapid test detection, respectively. Areas with sporadic, hypoendemic, and hyperendemic onchocerciasis endemicity were found. Participants with microfilaremia were considered microfilaremic, and those without microfilaremia were seen as amicrofilaremic. Of the 471 study participants, 40.5% (n = 191) had microfilariae. Among them, Mansonella spp. was the most common (78.2%, n = 147), followed by Loa loa (41.4%, n = 79). The association between the two species represented 18.3% (n = 35). The specific immunoglobulins of Onchocerca volvulus were detected in 24.2% of participants (n = 87/359). Overall prevalence of L. loa was 16.8%. Hypermicrofilaremia was found in 3% (N = 14), and one

participant had more than 30,000 microfilaremiae per milliliter. The frequency of L. loa did not vary according to the level of onchocerciasis transmission. Pruritus was the most common clinical sign (60.5%, n = 285) reported, mainly in microfilaremic participants (72.2%, n = 138/191). The prevalence of L. loa microfilaria in the study population was below the threshold at risk for the occurrence of serious side effects due to ivermectin. Clinical manifestations frequently observed could be exacerbated by microfilaremia in areas where onchocerciasis transmission is high.

# Pian

## Prospecting for yaws in the Mbaïki Health District in the Central African Republic.

**Piamale G, Bohy-Ngombet RGZ, Doyama-Woza RH, Fandema E, Pamatika CM, Dombeti CJ, Diemer HSC, Longo JD, Gresenguet G.**
12-07-2023
*Pan Afr Med J*.
https://pubmed.ncbi.nlm.nih.gov/37790147/

Introduction: yaws is endemic in the Central African Republic. The last cases of yaws notified by CAR to WHO date back to 2012. The objective of this study was to measure the prevalence of yaws in the health district of Mbaïki and to describe its clinical and epidemiological characteristics. Methods: this is a descriptive cross-sectional study, conducted from April 10 to 18, 2020 in the Mbaïki health district. Yaws cases were sought in 570 households in the 38 selected villages of the district. Any consenting individual over the age of one year with yaws-like skin lesions was a suspected case of yaws and included in the study. Blood was taken from suspected cases for serological testing (TDR, RPR and TPHA). Any suspected case of yaws with positive RPR and TPHA was considered a confirmed case. Results: a total of 1967 people were examined, of whom 113 were considered suspected cases of yaws. All suspected cases were RPR-positive, 41 TPHA-positive and 13 RDT-positive. Forty-one cases of yaws were confirmed in 18 (47.37%) villages. The prevalence of yaws in the Mbaïki health district was 2.08%. Among the cases, 38.94% were children aged 1 to 14. The sex ratio was 1.69. Lesions clinically suggestive of yaws were papilloma-like in 77.00% of cases, followed by micropapules (8.00%) and ulcerations (5.00%). Conclusion: eight of the nine communes in the Mbaïki health district are yaws-endemic. This result suggests the need to implement the Morges strategy in the Mbaïki health district.

# Rage

## Rabies control in Nepal: a missed opportunity.

**Acharya KP, Kwon R, Cho SH, Yon DK.**
20-09-2023
*Front Vet Sci*.
https://pubmed.ncbi.nlm.nih.gov/37799411/

## Evolution and divergence of the genetic lineage Desmodus rotundus/Artibeus lituratus of rabies virus in São Paulo State.

**de Souza DN, Oliveira RN, Asprino PF, Bettoni F, Macedo CI, Achkar SM, Fahl WO, Brandão PE, Castilho JG.**
06-10-2023
*Arch Virol*.
https://pubmed.ncbi.nlm.nih.gov/37798456/

## Dispersion and diversification of Lyssavirus rabies transmitted from haematophagous bats Desmodus rotundus: a phylogeographycal study.

**de Carvalho Ruthner Batista HB, Vieira LFP, Kawai JGC, de Oliveira Fahl W, Barboza CM, Achkar S, de Novaes Oliveira R, Brandão PE, Carnieli Junior P.**
05-10-2023
*Virus Genes*.
https://pubmed.ncbi.nlm.nih.gov/37796410/

## Barriers and opportunities for improving dog bite prevention and dog management practices in northern Indigenous communities.

**Daigle L, Ravel A, Lévesque F, Mokoush KN, Rondenay Y, Simon A, Aenishaenslin C.**
19-09-2023
*Front Vet Sci*.
https://pubmed.ncbi.nlm.nih.gov/37795013/

Globally, people living in northern Indigenous communities are at higher risk of dog bites than the rest of the population living in North America, with annual incidence ranging from 0.61 to 59.6/10,000 inhabitants. Considering that rabies is endemic in wild canid populations in certain regions of the Arctic, the prevention of dog bites and the management of dog populations are of crucial importance for public health in these contexts. Most northern communities lack access to veterinary services, mainly due to their remote geographical location and to limited financial resources. Currently, northern Indigenous communities are using different approaches and strategies to prevent dog bites and manage dog populations, but the effectiveness of these approaches sometimes lacks evidence, and their low acceptability may affect their implementation. This study aims to describe (1) the current access and uses of veterinary services, and (2) the perceived barriers and opportunities related to dog population management practices currently implemented, or that could be implemented, in a Naskapi community and an Innu community located in northern Quebec (Canada). Quantitative data were collected through a survey to inhabitants on veterinary services ($n$ = 122). Qualitative data were collected using individual interviews to inhabitants and health professionals to describe how dog population management measures were perceived, and to identify barriers and opportunities related to their implementation ($n$ = 37). Descriptive and inferential analysis (quantitative data) and thematic analysis (qualitative data) were performed. Results show that the two main measures implemented at the time of

the study - dog culling and short-duration veterinary clinics - were not perceived as fully acceptable and sustainable. Reinforcing access to veterinary services and other dog-related services, such as shelters and training programs on dogs, was identified as a need to improve dog bites prevention and dog population management in remote Indigenous communities. The implementation of animal health measures should be decided by concerned Indigenous communities to follow decolonial practices. It includes ensuring informed consent of dog owners, improving communication before, during and after interventions, separating veterinary services from rehoming and, most importantly giving back to Indigenous communities the complete leadership over animal health in their communities.

## Bio-clickable, small extracellular vesicles-COCKTAIL therapy for ischemic stroke.

**Haroon K, Ruan H, Zheng H, Wu S, Liu Z, Shi X, Tang Y, Yang GY, Zhang Z.**
02-10-2023
*J Control Release.*
https://pubmed.ncbi.nlm.nih.gov/37793483/

## Optimized lipopolymers with curcumin to enhance AZD5582 and GDC0152 activity and downregulate inhibitors of apoptosis proteins in glioblastoma multiforme.

**Kuo YC, Yen MH, De S, Rajesh R, Tai CK.**
28-09-2023
*Biomater Adv.*
https://pubmed.ncbi.nlm.nih.gov/37793310/

## Parallel pathways carrying direction and orientation selective retinal signals to layer 4 of mouse visual cortex.

**Wang H, Dey O, Lagos WN, Behnam N, Callaway EM, Stafford BK.**
18-09-2023
*bioRxiv.*
https://pubmed.ncbi.nlm.nih.gov/37786698/

Parallel functional and anatomical visual pathways from the retina to primary visual cortex (V1) via the lateral geniculate nucleus (LGN) are common to many mammalian species, including mice, carnivores and primates. However, the much larger number of retinal ganglion cell (RGC) types that project to the LGN, as well as the more limited lamination of both the LGN and the thalamocortical-recipient layer 4 (L4) in mice, leaves considerable uncertainty about which visual features present in both retina and V1 might be inherited from parallel pathways versus extracted by V1 circuits in the mouse visual system. Here, we explored the relationships between functional properties of L4 V1 neurons and their RGC inputs by taking advantage of two Cre-expressing mouse lines - Nr5a1-Cre and Scnn1a-Tg3-Cre - that each label functionally and anatomically distinct populations of L4 neurons. Visual tuning properties of L4 V1 neurons were evaluated using Cre-dependent expression of GCaMP6s followed by 2-photon calcium imaging. RGCs providing input to these neurons (via LGN) were labeled and characterized using Cre-dependent trans-synaptic retrograde labeling with G-deleted rabies virus. We find significant differences in the tuning of Nr5a1-Cre versus Scnn1a-Tg3-Cre neurons for direction, orientation, spatial frequency, temporal frequency, and speed. Strikingly, a subset of the RGCs had tuning properties that matched the direction and orientation tuning properties of the L4 V1 neurons to which they provided input. Altogether, these results suggest that direction and orientation tuning of V1 neurons may be at least partly inherited from parallel pathways originating in the retina.

## Immunogenicity and Antigenicity of the Ectodomain of Rabies Virus Glycoprotein Stably Expressed in HEK293T Cells.

**Li Q, Yan R, Bai N, Tan Z, Yu Q, Su H, Wei X, Li A, Chen X, Li Z, He Y, Li H, Li X, Mao Y.**
15-08-2023
*Int J Med Sci.*
https://pubmed.ncbi.nlm.nih.gov/37786447/

Rabies continues to be a huge threat to public health. The rabies virus envelope glycoprotein (RABV G) is a major rabies virus antigen and contains neutralizing epitopes, which are primary candidates for subunit vaccines and diagnostic antigens. However, the production and purification of rRABV G while retaining its antigenic and immunogenic remains to be a challenge. Here, we aimed to establish a platform for rRABV G production and purification, and determine the immunogenicity and antigenicity of rRABV G. The cDNA fragment encoding the soluble form of RABV G was synthesized and cloned into a lentiviral expressing vector. Recombinant lentiviral vector LV-CMV-RABV G-eGFP was packaged, titered, and then transduced into HEK 293T cells. The cell culture supernatant was purified using nickel affinity chromatography and subsequently confirmed through Western Blot analysis and indirect enzyme-linked immunosorbent assay (ELISA). The ELISA utilized human sera obtained from individuals who had been vaccinated with the human commercial Purified Vero Cells Rabies Vaccine (PVRV). Notably, we observed a neutralizing antibody response in immunized pigs rather than in mice. This discrepancy could potentially be attributed to factors such as the instability of the rRABV G protein, variations in host responses, and variances in the adjuvant used. Taking all these findings into account, the rRABV G protein generated in this study exhibits promise as a potential vaccine candidate for the prevention of rabies.

## Case Report: Survival from Clinical Rabies in a Young Child from Maharashtra, India, 2022.

**Ullas PT, Balachandran C, Pathak N, Manikrao YP, Rathod S, Pavitrakar DV, Bondre VP, Abraham P.**
02-10-2023
*Am J Trop Med Hyg*.
https://pubmed.ncbi.nlm.nih.gov/37783454/

## A multifaceted architectural framework of the mouse claustrum complex.

**Grimstvedt JS, Shelton AM, Hoerder-Suabedissen A, Oliver DK, Berndtsson CH, Blankvoort S, Nair RR, Packer AM, Witter MP, Kentros CG.**
02-10-2023
*J Comp Neurol.*
https://pubmed.ncbi.nlm.nih.gov/37782702/

Accurate anatomical characterizations are necessary to investigate neural circuitry on a fine scale, but for the rodent claustrum complex (CLCX), this has yet to be fully accomplished. The CLCX is generally considered to comprise two major subdivisions, the claustrum (CL) and the dorsal endopiriform nucleus (DEn), but regional boundaries to these areas are debated. To address this, we conducted a multifaceted analysis of fiber- and cytoarchitecture, genetic marker expression, and connectivity using mice of both sexes, to create a comprehensive guide for identifying and delineating borders to CLCX, including an online reference atlas. Our data indicated four distinct subregions within CLCX, subdividing both CL and DEn into two. Additionally, we conducted brain-wide tracing of inputs to CLCX using a transgenic mouse line. Immunohistochemical staining against myelin basic protein (MBP), parvalbumin (PV), and calbindin (CB) revealed intricate fiber-architectural patterns enabling precise delineations of CLCX and its subregions. Myelinated fibers were abundant dorsally in CL but absent ventrally, whereas PV expressing fibers occupied the entire CL. CB staining revealed a central gap within CL, also visible anterior to the striatum. The Nr2f2, Npsr1, and Cplx3 genes expressed specifically within different subregions of the CLCX, and Rprm helped delineate the CL-insular border. Furthermore, cells in CL projecting to the retrosplenial cortex were located within the myelin sparse area. By combining own experimental data with digitally available datasets of gene expression and input connectivity, we could demonstrate that the proposed delineation scheme allows anchoring of datasets from different origins to a common reference framework.

## Pharmacokinetic study and preliminary evaluation of safety and efficacy of the recombinant human monoclonal antibodies against rabies virus (rhRIG) in Chinese healthy population: A randomized, single-blinded, placebo-controlled phase Ia clinical trial.

**Chen X, Duan J, Li Y, Zhao Q, Zhao Y, Yu L, Li X, Wang H.**
29-09-2023
*Travel Med Infect Dis*.
https://pubmed.ncbi.nlm.nih.gov/37778451/

# Schistosomiase

## Alterations in gut microbiome and metabolite profile of patients with Schistosoma japonicum infection.

**Zhou C, Li J, Guo C, Zhou Z, Yang Z, Zhang Y, Jiang J, Cai Y, Zhou J, Xia M, Ming Y.**
05-10-2023
*Parasit Vectors.*
https://pubmed.ncbi.nlm.nih.gov/37798771

Background: Schistosoma infection is a significant public health issue, affecting over 200 million individuals and threatening 700 million people worldwide. The species prevalent in China is Schistosoma japonicum. Recent studies showed that both gut microbiota and metabolome are closely related to schistosomiasis caused by S. japonicum, but clinical study is limited and the underlying mechanism is largely unclear. This study aimed to explore alterations as well as function of gut microbiota and metabolite profile in the patients with S. japonicum infection. Methods: This study included 20 patients diagnosed with chronic schistosomiasis caused by S. japonicum, eight patients with advanced schistosomiasis caused by S. japonicum and 13 healthy volunteers. The fresh feces of these participators, clinical examination results and basic information were collected. 16S ribosomal RNA gene sequencing was used to investigate gut microbiota, while ultraperformance liquid chromatography-mass spectrometry (UHPLC-MS) was applied to explore the metabolome of patients in different stages of schistosomiasis. Results: The study found that gut microbiota and metabolites were altered in patients with different stages of S. japonicum infection. Compared with healthy control group, the gut microbial diversity in patients with chronic S. japonicum infection was decreased significantly. However, the diversity of gut microbiota in patients with chronic schistosomiasis was similar to that in patients with advanced schistosomiasis. Compared with uninfected people, patients with schistosomiasis showed decreased Firmicutes and increased Proteobacteria. As disease progressed, Firmicutes was further reduced in patients with advanced S. japonicum infection, while Proteobacteria was further increased. In addition, the most altered metabolites in patients with S. japonicum infection were lipids and lipid-like molecules as well as organo-heterocyclic compounds, correlated with the clinical manifestations and disease progress of schistosomiasis caused by S. japonicum. Conclusions: This study suggested that the gut microbiota and metabolome altered in patients in different stages of schistosomiasis, which was correlated with progression of schistosomiasis caused by S. japonicum. This inter-omics analysis may shed light on a better understanding of the mechanisms of the progression of S. japonicum infection and contribute to identifying new potential targets for the diagnosis and prognosis of S. japonicum infection. However, a large sample size of validation in clinic is needed, and further study is required to investigate the underlying mechanism.

## A case of pericardial schistosomiasis and non-Hodgkin high grade B-cell lymphoma.

**Boyd MJ, Mendelson M, Dlamini SK, Wasserman S, Fakier G, Roberts R, Papavarnavas NS.**
29-09-2023
*S Afr J Infect Dis*.
https://pubmed.ncbi.nlm.nih.gov/37795202/

## Macrophage-mediated trogocytosis contributes to destroying human schistosomes in a non-susceptible rodent host, Microtus fortis.

**Shen J, Zhao S, Peng M, Li Y, Zhang L, Li X, Hu Y, Wu M, Xiang S, Wu X, Liu J, Zhang B, Chen Z, Lin D, Liu H, Tang W, Chen J, Sun X, Liao Q, Hide G, Zhou Z, Lun ZR, Wu Z.**
05-10-2023
*Cell Discov.*
https://pubmed.ncbi.nlm.nih.gov/37794085/

Schistosoma parasites, causing schistosomiasis, exhibit typical host specificity in host preference. Many mammals, including humans, are susceptible to infection, while the widely distributed rodent, Microtus fortis, exhibits natural anti-schistosome characteristics. The mechanisms of host susceptibility remain poorly understood. Comparison of schistosome infection in M. fortis with the infection in laboratory mice (highly sensitive to infection) offers a good model system to investigate these mechanisms and to gain an insight into host specificity. In this study, we showed that large numbers of leukocytes attach to the surface of human schistosomes in M. fortis but not in mice. Single-cell RNA-sequencing analyses revealed that macrophages might be involved in the cell adhesion, and we further demonstrated that M. fortis macrophages could be mediated to attach and kill schistosomula with dependence on Complement component 3 (C3) and Complement receptor 3 (CR3). Importantly, we provided direct evidence that M. fortis macrophages could destroy schistosomula by trogocytosis, a previously undescribed mode for killing helminths. This process was regulated by $Ca^{2+}$/NFAT signaling. These findings not only elucidate a novel anti-schistosome mechanism in M. fortis but also provide a better understanding of host parasite interactions, host specificity and the potential generation of novel strategies for schistosomiasis control.

## Target-based discovery of a broad spectrum flukicide.

**Sprague DJ, Park SK, Gramberg S, Bauer L, Rohr CM, Chulkov EG, Smith E, Scampavia L, Spicer TP, Haeberlein S, Marchant JS.**
22-09-2023
*bioRxiv*.
https://pubmed.ncbi.nlm.nih.gov/37790347/

Diseases caused by parasitic flatworms impart a considerable healthcare burden worldwide. Many of these diseases - for example, the parasitic blood fluke infection, schistosomiasis - are treated with the drug praziquantel (PZQ). However, PZQ is ineffective against disease caused by liver flukes from the genus *Fasciola* . This is due to a single amino acid change within the target of PZQ, a transient receptor potential ion channel (TRPM $_{PZQ}$ ), in *Fasciola* species. Here we identify benzamidoquinazolinone analogs that are active against *Fasciola* TRPM $_{PZQ}$ . Structure-activity studies define an optimized ligand (BZQ) that caused protracted paralysis and damage to the protective tegument of these liver flukes. BZQ also retained activity against *Schistosoma mansoni* comparable to PZQ and was active against TRPM $_{PZQ}$ orthologs in all profiled species of parasitic fluke. This broad spectrum activity was manifest as BZQ adopts a pose within the binding pocket of TRPM $_{PZQ}$ dependent on a ubiquitously conserved residue. BZQ therefore acts as a universal activator of trematode TRPM $_{PZQ}$ and a first-in-class, broad spectrum flukicide.

## Excretory/Secretory Products from Schistosoma japonicum Eggs Alleviate Ovalbumin-Induced Allergic Airway Inflammation.

**Li Z, Wang X, Zhang W, Yang W, Xu B, Hu W.**
03-10-2023
*PLoS Negl Trop Dis*.
https://pubmed.ncbi.nlm.nih.gov/37788409/

## Chronic intestinal schistosomiasis caused by co-infection with Schistosoma intercalatum and Schistosoma mansoni.

**Kołodziej P, Szostakowska B, Lass A, Sulima M, Sikorska K, Kocki J, Krupski W, Starownik D, Bojar P, Szumiło J, Kasztelan-Szczerbińska B, Cichoż-Lach H, Bogucki J, Szymańska M, Fota-Markowska H, Bogucka-Kocka A.**
29-09-2023
*Lancet Infect Dis.*
https://pubmed.ncbi.nlm.nih.gov/37783223/

## Assigning function to active site residues of Schistosoma mansoni thioredoxin/glutathione reductase from analysis of transient state reductive half-reactions with variant forms of the enzyme.

**Smith MM, Moran GR.**
13-09-2023
*Front Mol Biosci.*
https://pubmed.ncbi.nlm.nih.gov/37780207/

Thioredoxin/glutathione reductase (TGR) from the platyhelminthic parasitic worms has recently been identified as a drug target for the treatment of schistosomiasis. Schistosomes lack catalase, and so are heavily reliant on the regeneration of reduced thioredoxin (Trx) and glutathione (GSH) to reduce peroxiredoxins that ameliorate oxidative damage from hydrogen peroxide generated by the host immune response. This study focuses on the characterization of the catalytic mechanism of *Schistosoma mansoni* TGR (SmTGR). Variant forms of SmTGR were studied to assign the function of residues that participate in the electron distribution chain within the enzyme. Using anaerobic transient state spectrophotometric methods, redox changes for the FAD and NADPH were observed and the function of specific residues was defined from observation of charge transfer absorption transitions that are indicative of specific complexations and redox states. The C159S variant prevented distribution of electrons beyond the flavin and as such did not accumulate thiolate-FAD charge transfer absorption. The lack of this absorption facilitated observation of a new charge transfer absorption consistent with proximity of NADPH and FAD. The C159S variant was used to confine electrons from NADPH at the flavin, and it was shown that NADPH and FAD exchange

hydride in both directions and come to an equilibrium that yields only fractional FAD reduction, suggesting that both have similar reduction potentials. Mutation of U597 to serine resulted in sustained thiolate-FAD charge transfer absorption and loss of the ability to reduce Trx, indicating that the C596-U597 disulfide functions in the catalytic sequence to receive electrons from the C154 C159 pair and distribute them to Trx. No kinetic evidence for a loss or change in function associated with the distal C28-C31 disulfide was observed when the C31S variant reductive half-reaction was observed. The Y296A variant was shown to slow the rate of but increase extent of reduction of the flavin, and the dissociation of $NADP^+$. The H571 residue was confirmed to be the residue responsible for the deprotonation of the C159 thiol, increasing its reactivity and generating the prominent thiolate-FAD charge transfer absorption that accumulates with oxidation of the flavin.

## Evaluation of isotype-based serology for diagnosis of Schistosoma mansoni infection in individuals living in endemic areas with low parasite burden.

**Magalhães FDC, Moreira JMP, de Rezende MC, Favero V, Graeff-Teixeira C, Coelho PMZ, Carneiro M, Geiger SM, Negrão-Corrêa D.**
28-09-2023
*Acta Trop.*
https://pubmed.ncbi.nlm.nih.gov/37774894/

Intestinal schistosomiasis is a chronic and debilitating disease that affects public health systems worldwide. Control interventions to reduce morbidity primarily involve the diagnosis and treatment of infected individuals. However, the recommended Kato-Katz (KK) parasitological method shows low sensitivity in individuals with low parasite loads and is not useful for monitoring elimination of parasite transmission at later stages. In the current study, we evaluated the accuracy of serum reactivity levels of different immunoglobulin isotypes in an enzyme-linked immunosorbent assay (ELISA), utilizing Schistosoma mansoni crude extracts, with the aim to improve the diagnosis of infected individuals with low parasite loads. The serum reactivity of IgM and IgG subclass antibodies (IgG1, IgG3, and IgG4) against soluble adult worm and egg antigen preparations was evaluated in residents from a schistosomiasis-endemic area in northern Minas Gerais, Brazil. The parasitological status of the study population was determined through fecal examination with multiple parasitological tests to create a consolidated reference standard (CRS) plus a fecal DNA detection test (q-PCR). Twelve months after praziquantel treatment, a second serum sample was obtained from the population for reexamination. A two-graph receiver operating characteristic curve (TG-ROC) analysis was performed using the serum reactivity of non-infected endemic controls and egg-positive individuals, and the cut-off value was established based on the intersection point of the sensibility and specificity curves in TG-ROC analyses. The diagnostic accuracy of each serological test was evaluated in relation to the parasitological CRS and to the combination of CRS plus qPCR results. The data revealed that serum reactivity of IgM and IgG3 against S. mansoni antigens did not allow identification of infected individuals from the endemic area. In contrast, serum IgG1 and IgG4-reactivity against schistosome antigens could distinguish between infected and non-infected individuals, with AUC values ranging between 0.728-0.925. The reactivity of IgG4 anti-soluble egg antigen - SEA (sensitivity 79 %, specificity 69 %, kappa = 0.49) had the best diagnostic accuracy, showing positive reactivity in more than 75 % of the infected individuals who eliminated less than 12 eggs per gram of feces. Moreover, serum IgG4 reactivity against SEA and against soluble worm antigen preparation (SWAP) was significantly reduced in the serum of infected individuals after 12 months of confirmed parasitological cure and in the absence of re-infection. These results reinforce that the described IgG4 anti-SEA ELISA assay is a sensitive alternative for the diagnosis of active intestinal schistosomiasis in individuals from endemic areas, including in those with a very low parasite load.

## Mining host candidate regulators of schistosomiasis-induced liver fibrosis in response to artesunate therapy through transcriptomics approach.

**Yuan Y, Lv X, Wu Y, Weng Y, Dai F, Ding H, Chen R, Zheng B, Zhao W, Tong Q, Ding J, Lou D, Lai Y, Chu X, Zhao L, Lu S, Kong Q.**
19-09-2023
*PLoS Negl Trop Dis*.
https://pubmed.ncbi.nlm.nih.gov/37773953/

Background: Artesunate (ART) has been reported to have an antifibrotic effect in various organs. The underlying mechanism has not been systematically elucidated. We aimed to clarify the effect of ART on liver fibrosis induced by Schistosoma japonicum (S. japonicum) in an experimentally infected rodent model and the potential underlying mechanisms. Methods: The effect of ART on hepatic stellate cells (HSCs) was assessed using CCK-8 and Annexin V-FITC/PI staining assays. The experimental model of liver fibrosis was established in the Mongolian gerbil model infected with S. japonicum cercariae and then treated with 20 mg/kg or 40 mg/kg ART. The hydroxyproline (Hyp) content, malondialdehyde (MDA) content, superoxide dismutase (SOD) and glutathione peroxidase (GPX) activities in liver tissue were measured and histopathological changes of liver tissues were observed. Whole-transcriptome RNA sequencing (RNA-seq) of the liver tissues was performed. Differentially expressed genes (DEGs) were identified using bioinformatic analysis and verified by quantitative PCR (qPCR) and western blot assay. Results: ART significantly inhibited the proliferation and induce the apoptosis of HSCs in a dose-dependent manner. In vivo, Hyp content decreased significantly in the ART-H group compared to the model (MOD) group and GPX activity was significantly higher in the ART-H group than in the MOD group. Besides, ART treatment significantly reduced collagen production ($p < 0.05$). A total of 158 DEGs and 44 differentially expressed miRNAs related to ART-induced anti-schistosomiasis liver fibrosis were identified. The qPCR and western blot results of selected DEGs were consistent with the sequencing results. These DEGs were implicated in key pathways such as immune and inflammatory response,

integrin-mediated signaling and toll-like receptor signaling pathways. Conclusion: ART is effective against liver fibrosis using Mongolian gerbil model induced by S. japonicum infection. We identified host candidate regulators of schistosomiasis-induced liver fibrosis in response to ART through transcriptomics approach.

### Update on the Geographic Distribution of the Intermediate Host Snails of Schistosoma mansoni on St. Lucia: A Step Toward Confirming the Interruption of Transmission of Human Schistosomiasis.

**Mukaratirwa S, Laidemitt MR, Hewitt R, Sengupta ME, Marchi S, Polius C, Belmar S, Scholte RGC, Perez F, Stensgaard AS, Vennervald BJ, Willingham AL, Loker ES.**
14-08-2023
*Am J Trop Med Hyg*.
https://pubmed.ncbi.nlm.nih.gov/37580035/

### Prevalence of Schistosoma mansoni, soil-transmitted helminths and intestinal protozoa in orphans and street children in Mwanza city, Northern Tanzania.

**Franz A, Fuss A, Mazigo HD, Ruganuza D, Müller A.**
Oct-2023
*Infection*.
https://pubmed.ncbi.nlm.nih.gov/36805439/

## Trachome

### "Etiology of trichiasis/distichiasis and its management with CO2 laser ablation".

**Wang LA, Lai CC.**
03-10-2023
*Plast Reconstr Surg*.
https://pubmed.ncbi.nlm.nih.gov/37797242/

Background: Many techniques have been used to treat trichiasis/distichiasis, but none of them are consistently successful, without complications, or effective in different severities. Additionally, etiologic factors and their relationship with the severity or prognosis has not been identified in non-trachoma-endemic area. Methods: In this retrospective consecutive study, we enrolled patients with trichiasis or distichiasis who had undergone CO2 laser ablation in our tertiary medical center between November 2013 and May 2022. Surgical success was defined as no regrowth of misdirected eyelashes for at least 3 months postoperatively. We recorded the success rate within three months and one year after one treatment session, and within three treatment sessions. We also investigated the relationship between etiologic factors, severity, and the success rate. Results: We enrolled 216 eyelids of 137 patients (average age: 69.4 years, mean follow-up durations: 22.9 months). The major underlying causes of trichiasis/distichiasis were idiopathic (64.4%) and prior eyelid surgery (20.8%). More major trichiasis/distichiasis was observed among patients aged <60 years than that in patients aged ≥60 years (43% vs. 21%, p<0.01), and among patients with an underlying cause of prior eyelid surgery compared to patients with idiopathic etiology (42.2% vs. 23.0%, p<0.01). The success rates within three months and within one year after one treatment session, and within three treatment sessions were 87.5%, 76.2%, and 94.4%. Conclusions: Our study demonstrated idiopathic etiology and prior eyelid surgery are common causes of trichiasis/distichiasis. CO2 laser ablation is a safe, effective, and efficient treatment modality.

### Perceptions and acceptability of co-administered albendazole, ivermectin and azithromycin mass drug administration, among the health workforce and recipient communities in Ethiopia.

**McPherson S, Geleta D, Tafese G, Tafese T, Behaksira S, Solomon H, Oljira B, Miecha H, Gemechu L, Debebe K, Kebede B, Gebre T, Kebede F, Seife F, Tadesse F, Mammo B, Aseffa A, Solomon AW, Mabey DCW, Marks M, Gadisa E.**
02-10-2023
*PLoS Negl Trop Dis*.
https://pubmed.ncbi.nlm.nih.gov/37782675/

Several neglected tropical diseases (NTDs) employ mass drug administration (MDA) as part of their control or elimination strategies. This has historically required multiple distinct campaigns, each targeting one or more NTDs, representing a strain on both the recipient communities and the local health workforce implementing the distribution. We explored perceptions and attitudes surrounding combined MDA among these two groups of stakeholders. Our qualitative study was nested within a cluster randomized non-inferiority safety trial of combined ivermectin, albendazole and azithromycin MDA. Using semi-structured question guides, we conducted 16 key informant interviews with selected individuals involved in implementing MDA within the participating district. To better understand the perceptions of recipient communities, we also conducted four focus group discussions with key community groups. Individuals were selected from both the trial arm (integrated MDA) and the control arm (standard MDA) to provide a means of comparison and discussion. All interviews and focus group discussions were led by fluent Afaan oromo speakers. Interviewers transcribed and later translated all discussions into English. The study team synthesized and analyzed the results via a coding framework and software. Most respondents appreciated the time and effort saved via the co-administered MDA strategy but there were some misgivings amongst community beneficiaries surrounding pill burden. Both the implementing health work force members and beneficiaries reported refusals stemming from lack of understanding around the need for the new drug regimen as well as some mistrust of government officials among the youth. The house-to-house distribution method, adopted as a COVID-19 prevention strategy, was by far preferred by all beneficiaries over central-point MDA, and may have led to greater acceptability of co-administration. Our data demonstrate that a co-administration strategy for NTDs is acceptable to both communities and health staff.

### Iraq eliminates trachoma as a public health problem.

**Balakrishnan VS.**
Oct-2023
*Lancet Infect Dis*.
https://pubmed.ncbi.nlm.nih.gov/37776886/

### Impact of refresher training on the outcomes of trachomatous trichiasis surgery.

**Pak C, Hall N, Bekele DT, Kollmann KHM, Tadele T, Tekle-Haimanot R, Taye T, Qureshi B, Yalew W, Gower EW, Kempen JH.**
29-09-2023
*Br J Ophthalmol.*
https://pubmed.ncbi.nlm.nih.gov/37775258/

Background/aims: Trachomatous trichiasis (TT) is a severe consequence of chronic inflammation/conjunctival scarring resulting from trachoma, the leading infectious cause of blindness worldwide. Our prospective cohort study evaluated the effectiveness of refresher training (RT) for experienced surgeons (1-22 years) on the outcomes of upper lid (UL) TT surgery in rural Ethiopia. Methods: Patients undergoing UL TT surgery in at least one eye by a participating surgeon were included. Patients were split into two cohorts: patients enrolled prior to (C1) and after (C2) RT. RT consisted of a 1-week programme with practice on a HEAD START mannequin and supportive supervision in live surgery by expert trainers. Data were collected at preoperative enrolment, and at 6-month and 12-month follow-up visits. The primary outcome was development of postoperative TT (PTT). A series of multivariate generalised estimating equations were fit to model PTT involving potential covariates of interest. Results: A total of 261 eyes contributed by 173 patients were studied between 2017 and 2019. By 1-year postoperatively, 37/128 eyes (28.9%) in C1 and 22/133 eyes (16.5%) in C2 had developed PTT (p=0.03). Other than surgeon RT participation, no factors studied were associated with differences in PTT. Conclusion: Our results indicate a significant reduction in the risk of PTT after experienced surgeons' participation in RT as compared with eyes receiving surgery before RT. This observation suggests a significant potential benefit of the RT with HEAD START mannequin practice and supportive supervision during surgery, and suggests RT may be a valuable strategy to improve surgical outcomes.

## Trématodoses d'origine alimentaire (clonorchiase, opisthorchiase, fasciolase et paragonimose

### Target-based discovery of a broad spectrum flukicide.

**Sprague DJ, Park SK, Gramberg S, Bauer L, Rohr CM, Chulkov EG, Smith E, Scampavia L, Spicer TP, Haeberlein S, Marchant JS.**
22-09-2023
*bioRxiv.*
https://pubmed.ncbi.nlm.nih.gov/37790347/

Diseases caused by parasitic flatworms impart a considerable healthcare burden worldwide. Many of these diseases - for example, the parasitic blood fluke infection, schistosomiasis - are treated with the drug praziquantel (PZQ). However, PZQ is ineffective against disease caused by liver flukes from the genus *Fasciola* . This is due to a single amino acid change within the target of PZQ, a transient receptor potential ion channel (TRPM $_{PZQ}$ ), in *Fasciola* species. Here we identify benzamidoquinazolinone analogs that are active against *Fasciola* TRPM $_{PZQ}$ . Structure-activity studies define an optimized ligand (BZQ) that caused protracted paralysis and damage to the protective tegument of these liver flukes. BZQ also retained activity against *Schistosoma mansoni* comparable to PZQ and was active against TRPM $_{PZQ}$ orthologs in all profiled species of parasitic fluke. This broad spectrum activity was manifest as BZQ adopts a pose within the binding pocket of TRPM $_{PZQ}$ dependent on a ubiquitously conserved residue. BZQ therefore acts as a universal activator of trematode TRPM $_{PZQ}$ and a first-in-class, broad spectrum flukicide.

### Triclabendazole resistance in Fasciola hepatica: First report in sheep from the Santa Cruz province, Argentinian Patagonia.

**Larroza M, Aguilar M, Soler P, Mora J, Roa M, Cabrera R, Martinez Stanziola JP, Ceballos L, Alvarez LI.**
Oct-2023
*Vet Parasitol Reg Stud Reports*.
https://pubmed.ncbi.nlm.nih.gov/37783530/

### The use of cathepsin L1 (FhCL1) serological ELISA in sentinel screening for liver fluke on sheep farms.

**Corrales JL, McEvoy A, Lalor R, Cwiklinski K, Doyle S, Parkinson M, Keane OM, Dalton JP, Dorey AL.**
Oct-2023
*Vet Parasitol Reg Stud Reports*.
https://pubmed.ncbi.nlm.nih.gov/37783527/

### Emerging Human Fascioliasis: A Retrospective Study of Epidemiological Findings in Dali, Yunnan Province, China (2012-2021).

**Huang L, Li F, Su H, Luo J, Gu W.**
02-10-2023
*Med Sci Monit*.
https://pubmed.ncbi.nlm.nih.gov/37779277/

BACKGROUND Human fascioliasis is an emerging zoonotic disease caused by the trematodes, or flatworms, Fasciola hepatica and Fasciola gigantica, also known as liver flukes. This retrospective study aimed to report the epidemiological findings in 95 cases of human fascioliasis

in Dali, Yunnan Province, southwestern China, diagnosed between 2012 and 2021. MATERIAL AND METHODS The epidemiologic and clinical data of 95 patients diagnosed with human fascioliasis in Dali area from January 2012 to December 2021 were collected and retrospectively analyzed. The diagnosis of fascioliasis was based on the Chinese National Standard of Diagnosis of Fascioliasis (WS/T566-2017). RESULTS The mean age of patients was 38.54±15.68 years, and there were more female patients than male (61.05% vs 38.95%). The high-incidence seasons were identified as summer and autumn. The patients with human fascioliasis lived in pastoral areas or were infected F. gigantica by consuming contaminated vegetables or water containing metacercaria. Meanwhile, human fascioliasis was diagnosed by positive serologic tests (1: 640), and Fasciola eggs (144-180×73-96 μm) were detected in stool samples of 6 patients. The most common clinical features were abdominal pain (70.53%), accompanied by elevated eosinophils in 89.5% of these patients. Antiparasitic treatment with triclabendazole at 10 mg/kg/day for 2 days led to symptom relief in all patients. CONCLUSIONS The findings from this observational epidemiological study have highlighted the importance of recognizing, diagnosing, and managing fascioliasis, which is an emerging zoonosis associated with increased human proximity to plant-eating domestic and farmed animals.

### In vitro and in vivo studies on a group of chalcones find promising results as potential drugs against fascioliasis.

**Artía Z, Ferraro F, Sánchez C, Cerecetto H, Gil J, Pareja L, Alonzo MN, Freire T, Cabrera M, Corvo I.**
28-09-2023
*Exp Parasitol.*
https://pubmed.ncbi.nlm.nih.gov/37776969/

### Association of MICA Gene Polymorphism in Opisthorchis viverrini-Induced Periductal Fibrosis in Northeastern Thais.

**Myo Oo TZ, Saichua P, Phoksawat W, Sithithaworn P, Mairiang E, Sripa B, Leelayuwat C, Jumnaisong A.**
01-09-2023
*Asian Pac J Cancer Prev*.
https://pubmed.ncbi.nlm.nih.gov/37774074/

Objective: Chronic Opisthorchis viverrini (OV) infection is the cause of advanced periductal fibrosis (APF), subsequently leading to cholangiocarcinoma (CCA). Natural killer (NK) cells can kill hepatic stellate cells (HSCs), the initiating cells for fibrosis formation, by using the interaction between the natural killer group 2 member D (NKG2D) receptor and its ligand on the HSCs. This can inhibit the fibrosis formation. Major histocompatibility complex class I chain-related A (MICA) is the ligand of the NKG2D receptor and has highly polymorphic characteristics that are involved in NKG2D binding and NK cell activation. This study aimed to investigate the polymorphism of MICA in OV-induced fibrosis. Method: MICA typing was performed by polymerase chain reaction-sequence specific primer (PCR-SSP) and sequencing in two groups: OV infection without fibrosis (N = 99) and with fibrosis (N = 290). Result: Six alleles were identified and the MICA*010 allele had the highest frequency in both groups. The MICA*00201-02 allele was a protective factor for fibrosis (OR= 0.508, 95%CI= 0.34-0.76, Pc <0.05), while the MICA*019 allele was suggested to be a risk allele for fibrosis (OR=1.95, 95%CI=1.25-3.03, Pc<0.005). In addition, two motifs, glycine (G) at position 14 and glutamine (Q) at position 251, were negatively associated with fibrosis (G14: OR=0.508, 95%CI=0.34-0.76, Pc <0.05 and Q251: OR=0.586, 95%CI=0.41-0.84, Pc <0.05). Moreover, the distribution of the MICA-129 genotype also showed the protective genotype (Pc<0.05, OR=0.319, 95%CI= 0.12-0.54) for fibrosis. The MICA*00201-02 allele encoded all these motifs, and this suggested that it might lead to strong NK cell activation to kill HSCs, subsequently preventing fibrosis formation. Conclusion: This study described initial evidence suggesting that the polymorphism of the MICA gene might be a marker for OV-derived periductal fibrosis.

## Trypanosomes (trypanosomiase et maladie de Chagas)

### The transcriptome landscape of 3D-cultured placental trophoblasts reveals activation of TLR2 and TLR3/7 in response to low Trypanosoma cruzi parasite exposure.

**Silberstein E, Chung CC, Debrabant A.**
20-09-2023
*Front Microbiol.*
https://pubmed.ncbi.nlm.nih.gov/37799608/

### Signature of cardiac alterations in early and late chronic infections with Trypanosoma cruzi in mice.

**Arias-Argáez BC, Dzul-Huchim VM, Haro-Álvarez AP, Rosado-Vallado ME, Villanueva-Lizama L, Cruz-Chan JV, Dumonteil E.**
05-10-2023
*PLoS One*.
https://pubmed.ncbi.nlm.nih.gov/37797045/

Chagas disease by Trypanosoma cruzi (T. cruzi) infection is a leading cause of myocarditis worldwide. Chagas cardiomyopathy is presented with a wide variety of conduction abnormalities including arrhythmias, first- and second-degree atrioventricular blockade, left ventricular systolic dysfunction and some cases heart failure leading to the death. Currently, there are no effective treatments available against advanced Chagas disease. With the advance in the development of novel therapies, it is important to utilize an animal model that can effectively replicate the diverse stages of Chagas disease, including chronic asymptomatic and symptomatic infection, that are akin to those observed in humans. Therefore, to characterize the cardiac alterations during the evolution of the infection, we evaluated the progression of

cardiomyopathy caused by T. cruzi H1 infection in both BALB/c and ICR mouse models by performing electrocardiogram (ECG) studies in unanesthetized mice every month until 210 days post-infection (dpi). In the late chronic phase of infection, we also performed echocardiogram (ECHO) studies to further assess cardiac function. In conclusion, we demonstrated that ICR mice were more susceptible to cardiac alterations compared to BALB/c mice and both mouse strains are suitable experimental models to study chronic T. cruzi infection and novel treatments.

## Developmental dynamics of mitochondrial mRNA abundance and editing reveal roles for temperature and the differentiation-repressive kinase RDK1 in cytochrome oxidase subunit II mRNA editing.

**Smith JT Jr, Tylec B, Naguleswaran A, Roditi I, Read LK.**
05-10-2023
*mBio*.
https://pubmed.ncbi.nlm.nih.gov/37795988/

## Biomarkers for the diagnosis, treatment follow-up, and prediction of cardiac complications in Chagas disease in chronic phase: Recent advances.

**Morales-Velásquez M, Barón-Vera JP, Osorio-Pulgarín MI, Sánchez-Jiménez MM, Ospina-Villa JD.**
05-10-2023
*Parasite Immunol.*
https://pubmed.ncbi.nlm.nih.gov/37795913/

Chagas disease is caused by the Trypanosoma cruzi parasite and is transmitted by infected triatomine bugs. This infection affects approximately 8 million people in the Americas, and due to globalisation and displacement, it is becoming increasingly common to find infected patients worldwide. Diagnosis of the disease in its acute form is relatively simple, as the parasite can be detected in peripheral blood smears, and symptoms are visible. However, in its chronic condition, the parasite is almost undetectable, and indirect tests are necessary to determine the presence of antibodies in infected patients. It is important to note that a single test is not enough to confirm the disease in this phase, as a second serological test should confirm the diagnosis. If the results are contradictory, a third test should be performed to confirm or discard the disease. Unfortunately, laboratories may not have access to all necessary tests in many rural areas where the disease is more frequent. Rapid tests to diagnose this disease present problems, such as significant variations in sensitivity and specificity in different countries. Therefore, searching for new biomarkers that allow for optimal correlation is essential. In this work, we have searched scientific literature from the last 10 years for mentions of novel biomarkers for diagnosis, treatment follow-up, and prediction of cardiac complications in Chagas disease in its chronic phase.

## Parasitic infections in hematopoietic stem cell transplant recipients.

**Haque E, Muhsen IN, Rasheed W, Fakih RE, Aljurf M.**
04-10-2023
*Transpl Infect Dis*.
https://pubmed.ncbi.nlm.nih.gov/37793057/

Introduction: Hematopoietic stem cell transplantation (HSCT) is a vital treatment for various hematological disorders. However, HSCT recipients face increased risks of infectious complications due to immunosuppression. Parasitic infections are a significant concern in this vulnerable population and can lead to substantial morbidity and mortality. This review examines parasitic infections in HSCT recipients, focusing on major infections affecting different organ systems, including intestinal parasites (Giardia spp., Entamoeba histolytica, and Cryptosporidium spp.), hematologic parasites (Plasmodium spp. and Babesia spp.), and tissue/visceral parasites (Toxoplasma gondii, Leishmania spp., and Trypanosoma cruzi). Methods: A systematic search of relevant literature was conducted and included studies up to August 2023. Databases included PubMed, Google Scholar, were queried using specific keywords related to parasitic infections in HSCT patients. The epidemiology, risk factors, clinical presentation, diagnostic methods, and treatment approaches for each infection were evaluated. Results and conclusion: Knowing the epidemiology, risk factors, and clinical presentations are crucial for timely intervention and successful management. By emphasizing early detection, effective therapies, and the unique challenges posed by each of these infections, this review highlights the importance of tailored strategies for HSCT recipients. Future research can further refine management protocols to enhance care and outcomes for these patients.

## External quality assessment of the entomological identification of triatomines in the network of public laboratories in Rondônia, Brazil.

**Souza TO, Oliveira-Correia JPS, Lobato A, Rocha DDS, Galvão C.**
22-09-2023
*Rev Soc Bras Med Trop*.
https://pubmed.ncbi.nlm.nih.gov/37792830/

Background: An external quality assessment on the identification of triatomines within the laboratory network in the state of Rondônia. Methods: Seven laboratories participated in this evaluation. Each was provided with support materials and nine insects from the Hemiptera order for identification. Results: All samples were accurately identified at the species level. However, correct sex identification was achieved for only 79% of the samples. The most significant challenges were encountered in determining the sex of predators, phytophagous species, Rhodnius robustus, and Rhodnius pictipes. Conclusions: The identified shortcomings can inform enhancements in vector control programs for Chagas disease.

## Socio-environmental factors associated with the occurrence of triatomines (Hemiptera: Reduviidae) in an endemic

## municipality in northern Minas Gerais, Brazil.

**Gonçalves TDS, Ursine RL, Cardozo M, Matos RLFDR, de Souza RCM, Diotaiuti LG, Gorla DE, de Carvalho SFG, Vieira TM.**
04-10-2023
*Zoonoses Public Health*.
https://pubmed.ncbi.nlm.nih.gov/37792668/

## Evolutionary, structural and functional insights in nuclear organisation and nucleocytoplasmic transport in trypanosomes.

**Padilla-Mejia NE, Field MC.**
03-10-2023
*FEBS Lett*.
https://pubmed.ncbi.nlm.nih.gov/37789516/

## Live imaging of microglia during sleeping sickness reveals early and heterogeneous inflammatory responses.

**Uzcategui NL, Güçer S, Richter C, Speidel A, Zirdum E, Duszenko M, Garaschuk O, Figarella K.**
13-09-2023
*Front Immunol*.
https://pubmed.ncbi.nlm.nih.gov/37781403/

Introduction: Invasion of the central nervous system (CNS) is the most serious consequence of *Trypanosoma brucei* infection, which causes sleeping sickness. Recent experimental data have revealed some more insights into the disease during the meningoencephalitic stage. However, detailed cellular processes befalling the CNS during the disease are poorly understood. Methods: To further address this issue, we implanted a cranial window on the cortex of B6.129P2(Cg)-*Cx3cr1*$^{tm1Litt}$/J mice, infected them with *Trypanosoma brucei* expressing RFP via intraperitoneal injection, and monitored microglial cells and parasites longitudinally over 30 days using *in vivo* 2-photon imaging. We correlated the observed changes with histological analyses to evaluate the recruitment of peripheral immune cells. Results and discussion: We uncovered an early involvement of microglia that precedes invasion of the CNS by the parasite. We accomplished a detailed characterization of the progressive sequence of events that correlates with microglial morphological changes and microgliosis. Our findings unveiled a heterogeneous microglial response in places of initial homeostatic disruption near brain barriers and pointed out an exceptional capability of microglia to hamper parasite proliferation inside the brain. We also found early signs of inflammation in the meninges, which synchronize with the microglial response. Moreover, we observed a massive infiltration of peripheral immune cells into the parenchyma as a signature in the final disease stage. Overall, our study provides new insights into the host-pathogen immune interactions in the meningeal and parenchymal compartments of the neocortex.

## DNA segregation in mitochondria and beyond: insights from the trypanosomal tripartite attachment complex.

**Aeschlimann S, Stettler P, Schneider A.**
27-09-2023
*Trends Biochem Sci*.
https://pubmed.ncbi.nlm.nih.gov/37775421/

## Cafeteria diet-induced obesity remodels immune response in acute Trypanosoma cruzi infection.

**Goulart A, Anchieta NF, Sampaio PA, Brazão V, Silva JLD, Portapilla GB, Duarte A, Tezuca DY, Providello MV, Stabile AM, Prado JCD Júnior.**
15-09-2023
*Immunobiology*.
https://pubmed.ncbi.nlm.nih.gov/37774598/

Background: Obesity is a global problem associated with several conditions, including hypertension, diabetes, arthritis and cardiovascular diseases. With the increase in the prevalence of obesity in recent years, mostly in developing countries, it is important to study its impact on various diseases, including infectious illnesses, such as Chagas disease, caused by the protozoan Trypanosoma cruzi. Considering that a diet rich in salt, sugar, and fat is associated with obesity, this study aimed to evaluate the influence of cafeteria diet (CAF)-induced obesity on immune responses in T. cruzi-infected rats. Methods: Male Wistar Hannover rats were provided with water and food ad libitum (chow group). The CAF-fed groups received a normal rodent diet or CAF. The animals were intraperitoneally infected with $10^5$ trypomastigote forms of the Y strain of T. cruzi present in the whole blood from a previously infected mouse. Results: CAF-fed rats showed a significant increase in visceral adipose tissue weight compared to chow-fed rats. A significant reduction in $CD3^+$ $CD4^+$ helper splenic T cells was observed in obese-infected rats compared to non-obese-infected rats, as well as CD11b and macrophages. In addition, macrophages from obese animals displayed reduced RT1b levels compared to those from control animals. Moreover, INF-γ, an important factor in macrophage activation, was reduced in obese-infected rats compared with their counterparts. Conclusions: These results indicate that a CAF can impair the cell-mediated immune response against T. cruzi.

## Molecular targets for Chagas disease: validation, challenges and lead compounds for widely exploited targets.

**Laureano de Souza M, Lapierre TJWJD, Vitor de Lima Marques G, Ferraz WR, Penteado AB, Henrique Goulart Trossini G, Murta SMF, de Oliveira RB, de Oliveira Rezende C Jr, Ferreira RS.**
29-09-2023
*Expert Opin Ther Targets*.
https://pubmed.ncbi.nlm.nih.gov/37772733/

Introduction: Chagas disease (CD) imposes social and economic burdens, yet theavailable treatments have limited efficacy in the disease's chronic phase andcause serious adverse effects. To address this challenge, target-basedapproaches are a possible strategy to develop new, safe, and active treatments for both phases of the disease. Areas covered: This review delves into target-basedapproaches applied to CD drug discovery,

emphasizing the studies from the lastfive years. We highlight the proteins cruzain (CZ), trypanothionereductase (TR), sterol 14 α-demethylase (CPY51), iron superoxide dismutase(Fe-SOD), proteasome, cytochrome *b* (Cyt*b)*, and cleavage and polyadenylationspecificity factor 3 (CPSF3), chosen based on their biological andchemical validation as drug targets. For each, wediscuss its biological relevance and validation as a target, currently relatedchallenges, and the status of the most promising inhibitors. **Expert opinion:** Target-based approaches toward developing potentialCD therapeutics have yielded promising leads in recent years. We expect asignificant advance in this field in the next decade, fueled by the new optionsfor *Trypanosoma cruzi* genetic manipulation that arose in the pastdecade, combined with recent advances in computational chemistry and chemicalbiology.

## Genomic evidence of sex chromosome aneuploidy and infection-associated genotypes in the tsetse fly Glossina fuscipes, the major vector of African trypanosomiasis in Uganda.

**Saarman NP, Son JH, Zhao H, Cosme LV, Kong Y, Li M, Wang S, Weiss BL, Echodu R, Opiro R, Aksoy S, Caccone A.**

Oct-2023

*Infect Genet Evol*.

https://pubmed.ncbi.nlm.nih.gov/37709241/