



Réseau MTN Francophone

# Veille scientifique Maladies tropicales négligées

**Semaine 19**

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## DENGUE, CHIKUNGUNYA ET MALADIE A VIRUS ZIKA

### Clinicopathological alteration of symptoms with serotype among dengue infected pediatric patients.

Verma, P., Banerjee, S., Baskey, U., Dutta, S., Bakshi, S., Das, R., Samanta, S., Dutta, S., Sadhukhan, P.

16-05-2022

*J Med Virol*

<https://doi.org/10.1002/jmv.27862>

Dengue fever is a self-limiting, acute febrile illness caused by an arbovirus. This infection may be asymptomatic or symptomatic with its potential life-threatening form as DHF/DSS. Severe dengue cases occur typically in children due to overproduction of pro-inflammatory and anti-inflammatory cytokines (called cytokines storm) as well as increased microvascular permeability in them. This study aimed to find prevalent circulating dengue serotype and their clinicopathological association among pediatric patients admitted to tertiary care hospitals in Kolkata, India. Overall, 210 patients were approached and among them, 170 dengue suspected children admitted to three tertiary care hospitals were included in this study. Dengue samples were screened for the presence of NS1 antigen and dengue IgM antibodies by ELISA. Viral RNA was extracted from NS1 seropositive serum samples and subjected to molecular serotyping by semi-nested RT-PCR. All patients were followed up for clinical manifestations and biochemical parameters associated with dengue. Co-circulation of all four serotypes was observed and DENV2 was the major circulating strain. Physiological classification of associated clinical symptoms was done and represented as a percentage variable. A multivariate logistic regression approach was used for making a regression model including dengue-associated clinical symptoms with dengue positivity and negativity as dependent variables. Thrombocytopenia was observed in 69% of patients and the commonest bleeding manifestation was petechia. Liver function profiles of infected patients were observed during follow-up and represented using a box plot. A significant change in trends of dengue-associated clinical manifestations and differential expression of liver functional profile with different phase transitions of dengue fever was obtained in the study population. This article is protected by copyright. All rights reserved.

### Direct and indirect costs for hospitalized patients with dengue in Southern Sri Lanka.

Weerasinghe, N., Bodinayake, C., Wijayarathne, W., Devasiri, I., Dahanayake, N., Kurukulasooriya, M., Premamali, M., Sheng, T., Nicholson, B., Ubeysekera, H., de Silva, A., Østbye, T., Woods, C., Tillekeratne, L., Nagahawatte, A.

16-05-2022

*BMC Health Serv Res*

<https://doi.org/10.1186/s12913-022-08048-5>

**Background:** The Southern Province of Sri Lanka is endemic

with dengue, with frequent outbreaks and occurrence of severe disease. However, the economic burden of dengue is poorly quantified. Therefore, we conducted a cost analysis to assess the direct and indirect costs associated with hospitalized patients with dengue to households and to the public healthcare system. **Methods:** From June 2017-December 2018, we prospectively enrolled children and adults with acute dengue hospitalized at the largest, public tertiary-care (1800 bed) hospital in the Southern Province, Sri Lanka. We administered a structured questionnaire to obtain information regarding direct costs spent by households on medical visits, medications, laboratory testing, and travel for seeking care for the illness. Indirect costs lost by households were estimated by identifying the days of work lost by patients and caregivers and school days lost by children. Direct hospital costs were estimated using gross costing approach and adjusted by multiplying by annual inflation rates in Sri Lankan rupees and converted to US dollars. **Results:** A total of 1064 patients with laboratory-confirmed dengue were enrolled. The mean age (SD) was 35.9years (15.6) with male predominance (66.2%). The mean durations of hospitalization for adults and paediatric patients were 3.86 (SD=1.51) and 4 (SD=1.32) days, respectively. The per-capita direct cost borne by the healthcare system was 233.76 USD, and was approximately 14 times greater than the per-capita direct cost borne by households (16.29 USD, SD=14.02). The per-capita average number of loss of working days was 21.51 (SD=41.71), with mean per-capita loss of income due to loss of work being 303.99 USD (SD=569.77), accounting for over 70% of average monthly income. On average, 10.88days (SD=10.97) of school days were missed due to the dengue episode. School misses were expected to reduce future annual income of affected children by 0.44%. **Conclusions:** Dengue requiring hospitalization had a substantial economic burden on the public healthcare system in Sri Lanka and the affected households. These findings emphasize the importance of strengthening dengue control activities and improved use of hospital-based resources for care to reduce the economic impact of dengue in Sri Lanka.

### Island biogeography and human practices drive ecological connectivity in mosquito species richness in the Lakshadweep Archipelago.

P, M., D, R., G, S., K, A., K, S., A, S., P, R., V, S., Dasgupta, S., Krishnan, J., Ishtiaq, F.

16-05-2022

*Sci Rep*

<https://doi.org/10.1038/s41598-022-11898-y>

Mosquitoes are globally distributed and adapted to a broad range of environmental conditions. As obligatory hosts of many infectious pathogens, mosquito abundance and distribution are primarily determined by the presence and quality of larval habitats. To understand the dynamics and productivity of larval habitats in changing island environments, we conducted a four-month mosquito survey across ten inhabited islands in the Lakshadweep archipelago. Using fine-resolution larval habitat mapping, we recorded 7890

mosquitoes representing 13 species and 7 genera. Of these, four species comprised 95% of the total collections—*Aedes albopictus* (*Stegomyia*) was the dominant species followed by *Armigeres subalbatus*, *Culex quinquefasciatus* and *Malaya genurostris*. We found larval species richness was positively associated with the island area and mosquito larval richness (Chao1 estimator) was higher in artificial habitats than in natural habitats. Furthermore, mosquito species composition did not deteriorate with distance between islands. Mosquito abundance by species was associated with microclimatic variables—pH and temperature. We detected co-existence of multiple species at a micro-habitat level with no evidence of interactions like competition or predation. Our study analyzed and identified the most productive larval habitats—discarded plastic container and plastic drums contributing to high larval indices predicting dengue epidemic across the Lakshadweep islands. Our data highlight the need to devise vector control strategies by removal of human-induced plastic pollution (household waste) which is a critical driver of disease risk.

### A retrospective study of environmental predictors of dengue in Delhi from 2015 to 2018 using the generalized linear model.

Singh, P., Chaturvedi, H.

16-05-2022

*Sci Rep*

<https://doi.org/10.1038/s41598-022-12164-x>

Dengue fever is a mosquito-borne infection with a rising trend, expected to increase further with the rise in global temperature. The study aimed to use the environmental and dengue data 2015–2018 to examine the seasonal variation and establish a probabilistic model of environmental predictors of dengue using the generalized linear model (GLM). In Delhi, dengue cases started emerging in the monsoon season, peaked in the post-monsoon, and thereafter, declined in early winter. The annual trend of dengue cases declined, but the seasonal pattern remained alike (2015–18). The Spearman correlation coefficient of dengue was significantly high with the maximum and minimum temperature at 2 months lag, but it was negatively correlated with the difference of average minimum and maximum temperature at lag 1 and 2. The GLM estimated  $\beta$  coefficients of environmental predictors such as temperature difference, cumulative rainfall, relative humidity and maximum temperature were significant ( $p < 0.01$ ) at different lag (0 to 2), and maximum temperature at lag 2 was having the highest effect (IRR 1.198). The increasing temperature of two previous months and cumulative rainfall are the best predictors of dengue incidence. The vector control should be implemented at least 2 months ahead of disease transmission (August–November).

### Early childhood neurodevelopmental outcomes in children with prenatal Zika virus exposure: a cohort study in Puerto Rico.

Alvarado-Domenech, L., Rivera-Amill, V., Appleton, A., Rosario-Villafañe, V., Repollet-Carrer, I., Borges-Rodríguez, M., Pérez-

Rodríguez, N., Olivieri-Ramos, O., González, M., González-Montalvo, C., Muñiz-Forestier, W., Vargas-Lasalle, L., Pérez-Padilla, J., Paz-Bayley, G., Rodríguez-Rabassa, M.

13-05-2022

*J Pediatr*

<https://pubmed.ncbi.nlm.nih.gov/35577118>

**Objective:** To describe anthropometric, sensory, and neurodevelopmental outcomes of Zika virus exposed children from birth to 36 months. **Study design:** The cohort includes 114 children born to mothers with confirmed and probable ZIKV pregnancy infection, from 2016–2017. Children attending study visits from May 2017 through February 2020 underwent physical/neurologic, sensory examinations, and neurodevelopmental assessments with Bayley Scales of Infant and Toddler Development (BSID-III) and Ages and Stages Questionnaires (ASQ-3). **Results:** Three of 114 (2.6%) children had microcephaly ( $z$  score  $< -2$ ) at birth, 19 of 35 (54.3%) had posterior eye abnormalities in retinal image, and 11 of 109 (10.1%) had nonspecific findings on brain ultrasound. Three of 107 (2.8%) failed hearing screening at birth. Of those with follow up, 17 of 97 (17.5%) failed age-appropriate vision screening; BSID-III identified developmental delay in at least one domain in at least one-third of children, with higher prevalence in the language domain. ASQ-3 screen positive delay peaked around 24 or 36 months, some domains showing decrease at older ages. Correlations were observed among BSID-III and ASQ-3 scores, representing professional and parental perspectives at 24 and 36 months ( $r = 0.32$  to  $0.78$   $p < .05$ ). **Conclusion:** The presence of neurodevelopmental sequelae in early childhood suggests that identification of long-term impairment remains critical to attaining optimal child development. Long-term follow up highlights vulnerability in the language domain, which likely could be influenced by early intervention, promoting cognitive development and school readiness among exposed children.

### Somatic Hypermutation and Framework Mutations of Variable Region Contribute to Anti-Zika Virus-Specific Monoclonal Antibody Binding and Function.

Tsuji, I., Vang, F., Dominguez, D., Karwal, L., Sanjali, A., Livengood, J., Davidson, E., Fouch, M., Doranz, B., Das, S., Dean, H.

16-05-2022

*J Virol*

<https://doi.org/10.1128/jvi.00071-22>

Zika virus (ZIKV) is a global public health concern due to its ability to cause congenital Zika syndrome and lack of approved vaccine, therapeutic, or other control measures. We discovered eight novel rabbit monoclonal antibodies (MAbs) that bind to distinct ZIKV envelope protein epitopes. The majority of the MAbs were ZIKV specific and targeted the lateral ridge of the envelope (E) protein domain III, while the MAb with the highest neutralizing activity recognized a putative quaternary epitope spanning E protein domains I and III. One of the non-neutralizing MAbs specifically recognized ZIKV precursor membrane protein (prM). Somatic

hypermutation of immunoglobulin variable regions increases antibody affinity maturation and triggers antibody class switching. Negative correlations were observed between the somatic hypermutation rate of the immunoglobulin heavy-chain variable region and antibody binding parameters such as equilibrium dissociation constant, dissociation constant, and half-maximal effective concentration value of MAb binding to ZIKV virus-like particles. Complementarity-determining regions recognize the antigen epitopes and are scaffolded by canonical framework regions. Reversion of framework region amino acids to the rabbit germ line sequence decreased anti-ZIKV MAb binding activity of some MAbs. Thus, antibody affinity maturation, including somatic hypermutation and framework region mutations, contributed to the binding and function of these anti-ZIKV MAbs. **IMPORTANCE** ZIKV is a global health concern against which no vaccine or therapeutics are available. We characterized eight novel rabbit monoclonal antibodies recognizing ZIKV envelope and prM proteins and studied the relationship between somatic hypermutation of complementarity-determining regions, framework regions, mutations, antibody specificity, binding, and neutralizing activity. The results contribute to understanding structural features and somatic mutation pathways by which potent Zika virus-neutralizing antibodies can evolve, including the role of antibody framework regions.

### Investment, Q and epidemic diseases.

**Tut, D.**

11-05-2022

*Financ Res Lett*

<https://doi.org/10.1016/j.frl.2022.102943>

We study the effects of epidemic diseases on corporate investment. Epidemic diseases tend to be unanticipated and exogenous to firms' decisions. Using difference-in-difference estimation strategy and a firm-level exposure to an epidemic disease measure, we find that corporate investment declines significantly following the onset of an epidemic disease. We also show that the COVID-19 pandemic has the strongest negative impact on investment when compared to the other most recent epidemic diseases.

### COVID-19 lockdown and increased incidence of dengue: A note.

**Joob, B., Wiwanitkit, V.**

16-05-2022

*Trop Doct*

<https://doi.org/10.1177/00494755221099994>

COVID-19 is the important global problem. Lockdown is a general disease control measure against COVID-19. The aim of lockdown is the reduce incidence of COVID-19. From reappraisal on the available data from a tropical endemic country (1), the change of incidences of both COVID-19 and rotavirus infection incidence after lockdown can be seen.

### Ocular findings of congenital Zika virus infection with microcephaly.

**Costa, C., Freitas, D.**

15-05-2022

*Int Ophthalmol*

<https://doi.org/10.1007/s10792-022-02311-8>

**Purpose:** To describe ocular findings in infants with signs of congenital Zika virus syndrome (CZS) in Paraíba, Brazil, as well as to conduct a literature review and report correlations with published clinical cases. **Methods:** In the Paraíba sample, infants with microcephaly suggestive of CZS were classified as Z (confirmed), PZ (probable), or SZ (suspected) according to serological testing and/or clinical findings of CZS. The patients underwent a clinical eye examination, and the results were correlated with published clinical cases. **Results:** Ocular findings were present in 24 (42.9%) of 56 patients, consisting of gross retinal pigmentation in 11 (45.8%), macular chorioretinal atrophy in 11 (45.8%), optic nerve hypoplasia in 1 (4.2%), optic nerve pallor in 14 (58.3%), and increased cup-to-disk ratio in 2 (8.3%). The study revealed retina and optic nerve findings consistent with previous reports of ophthalmic involvement in CZS. However, external ocular changes observed in other studies were not detected. **Conclusion:** Ocular findings similar and consistent with the literature on CZS were observed with considerable frequency and severity, regardless of the patients' serological confirmation or classification. Infants with signs of CZS should undergo ocular examination.

### Highly potent multivalent VHH antibodies against Chikungunya isolated from an alpaca naïve phage display library.

**Li, Q., Zhang, F., Lu, Y., Hu, H., Wang, J., Guo, C., Deng, Q., Liao, C., Wu, Q., Hu, T., Chen, Z., Lu, J.**

14-05-2022

*J Nanobiotechnology*

<https://doi.org/10.1186/s12951-022-01417-6>

**Background:** Chikungunya virus (CHIKV) is a re-emerged mosquito-borne alphavirus that can cause musculoskeletal diseases, imposing a substantial threat to public health globally. High-affinity antibodies are need for diagnosis and treatment of CHIKV infections. As a potential diagnostic and therapeutic agent, the multivalent VHH antibodies is a promising toolkit in nanomedicine. Here, we developed potent multivalent VHH antibodies from an alpaca naïve phage display library targeting the E2 glycoprotein of the CHIKV virus. **Results:** In the present study, we generated 20 VHH antibodies using a naïve phage display library for binders to the CHIKV E2 glycoprotein. Of these, multivalent VHH antibodies Nb-2E8 and Nb-3C5 had specific high-affinity binding to E2 protein within the nanomolar range. The equilibrium dissociation constant (KD) was between 2.59-20.7 nM, which was 100-fold stronger than the monovalent antibodies' affinity. Moreover, epitope mapping showed that Nb-2E8 and Nb-3C5 recognized different linear epitopes located on the E2 glycoprotein domain C and A, respectively. A facile protocol of sandwich

ELISA was established using BiNb-2E8 as a capture antibody and HRP-conjugated BiNb-3C5 as a detection antibody. A good linear correlation was achieved between the OD<sub>450</sub> value and the E2 protein concentration in the 5-1000 ng/mL range ( $r=0.9864$ ,  $P<0.0001$ ), indicating its potential for quantitative detection of the E2 protein. **Conclusions:** Compared to monovalent antibodies, multivalent VHH antibodies Nb-2E8 and Nb-3C5 showed high affinity and are potential candidates for diagnostic applications to better detect CHIKV virions in sera.

### Dynamics of dengue and SARS-COV-2 co-infection in an endemic area of Colombia.

Acosta-Pérez, T., Rodríguez-Yáñez, T., Almanza-Hurtado, A., Martínez-Ávila, M., Dueñas-Castell, C.

15-05-2022

*Trop Dis Travel Med Vaccines*

<https://doi.org/10.1186/s40794-022-00169-3>

Since the COVID-19 outbreak, millions of people have been infected with SARS-CoV-2 around the world. An area of epidemiological relevance is Latin America, tropical regions, due to the distribution of endemic diseases such as chikungunya, dengue (DENV), malaria, Zika virus, where febrile disease abounds. The early signs and symptoms of DENV and COVID-19 could be similar, making it a risk that patients may be wrongly diagnosed early during the disease. The problem increases since COVID-19 infection can lead to false positives in DENV screening tests. We present two cases of acute undifferentiated febrile syndrome that were diagnosed with SARS-CoV-2 and DENV co-infection, confirmed by ELISA and RT-PCR for both viral pathogens. The occurrence of simultaneous or overlapped infections can alter the usual clinical course, severity, or outcome of each infection. Therefore, epidemiological surveillance and intensified preparation for those scenarios must be considered, as well as further studies should be done to address cases of co-infection promptly to avoid major complications and fatal outcomes during the current pandemic. Other endemic tropical diseases should not be neglected.

### Household clustering supports a novel chemoprophylaxis trial design for a mosquito-borne viral disease.

Watson, H., Duong, V., Ly, S., Mandron, M., Siqueira, A., Ribeiro, G.

11-05-2022

*Int J Infect Dis*

<https://pubmed.ncbi.nlm.nih.gov/35568359>

Infections due to chikungunya and other mosquito-borne viruses, such as dengue and Zika, represent an area of significant unmet medical need. There are currently no approved medicines for prophylaxis or treatment of these diseases, and the development and implementation of vaccines against these viruses has proved problematic. Although antiviral molecules with treatment and prophylactic

potential against chikungunya virus have been identified, no successful field trials have been reported. Chemoprophylaxis may be attractive for unvaccinated at-risk populations, but performing a successful chemoprophylaxis trial during a chikungunya outbreak will require a clearly identifiable at-risk population. We propose the application of a household transmission model, as used in testing drugs against respiratory viruses. Current evidence on household clustering of chikungunya and other Aedes mosquito-borne viral infections is supportive. We suggest that this model may improve prophylaxis trial feasibility, as well as focusing research and future treatment on a population likely to benefit.

### Updated spatio-temporal distribution of Aedes (Stegomyia) albopictus in Brazil.

Variza, P., Lorenz, C., de Oliveira, J., Fernansdes, M., Netto, S., Prophiro, J.

11-05-2022

*Acta Trop*

<https://pubmed.ncbi.nlm.nih.gov/35568071>

Aedes albopictus is native to Asia and is ranked among the top 100 invasive species worldwide, with vector competence for dengue, Zika, and chikungunya viruses. Understanding Ae. albopictus dispersal is essential for effective monitoring and vector control strategies. In this study, we analysed and updated the distribution of Ae. albopictus in Brazil using data available from the Ministry of Health through the Rapid Index Survey for Aedes (LIRA) for the years 2015-2020. The results of this research were mapped to visually represent the current distribution of Ae. albopictus in Brazil. In 2015, the presence of the vector was confirmed in 271 of the 1,820 Brazilian municipalities sampled (14.9%), and in 2020 it was detected in 728 of the 2,937 municipalities sampled (24.8%). In 2020, all Brazilian states had recorded the presence of this critical vector with a broader geographic distribution in the Southeast and Midwest regions as compared to the North, Northeast, and South regions. It was possible to note some stabilization of dispersion of this species in the Brazilian territory. The record of Ae. albopictus distribution advanced in Brazilian states and municipalities from 2015 to 2020; it is suggested that surveys of this vector be conducted periodically in all Brazilian municipalities and authorities should develop control strategies for this species together with Ae. aegypti.

### Neglected tropical diseases in Australia: a narrative review.

Revue de littérature

Kurcheid, J., Gordon, C., Clarke, N., Wangdi, K., Kelly, M., Lal, A., Mutombo, P., Wang, D., Mationg, M., Clements, A., Muhi, S., Bradbury, R., Biggs, B., Page, W., Williams, G., McManus, D., Gray, D.

12-05-2022

*Med J Aust*

<https://doi.org/10.5694/mja2.51533>

•Neglected tropical diseases (NTDs) represent a threat to the health, wellbeing and economic prosperity of billions of people worldwide, often causing serious disease or death. •Commonly considered diseases of low and middle-income nations, the presence of NTDs in high income countries such as Australia is often overlooked. •Seven of the 20 recognised NTDs are endemic in Australia: scabies, soil-transmitted helminths and strongyloidiasis, echinococcosis, Buruli ulcer, leprosy, trachoma, and snakebite envenoming. •Dengue, while not currently endemic, poses a risk of establishment in Australia. There are occasional outbreaks of dengue fever, with local transmission, due to introductions in travellers from endemic regions. •Similarly, the risk of introduction of other NTDs from neighbouring countries is a concern. Many NTDs are only seen in Australia in individuals travelling from endemic areas, but they need to be recognised in health settings as the potential consequences of infection can be severe. •In this review, we consider the status of NTDs in Australia, explore the risk of introducing and contracting these infections, and emphasise the negative impact they have on the health of Australians, especially Aboriginal and Torres Strait Islander peoples.

### Clinical significance of differential serum-signatures for early prediction of severe dengue among Eastern Indian patients.

Mukherjee, S., Saha, B., Tripathi, A.

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*Clin Exp Immunol*

<https://doi.org/10.1093/cei/uxac018>

Dengue infection can result in simple dengue fever or life-threatening severe dengue. Early identification of severe patients is needed for proper disease management. Dengue infection was screened among 168 symptomatic patients by qRT-PCR, anti-dengue IgM, and IgG ELISA. Dengue patients were categorized according to WHO classification. Viral load and dengue serotypes were determined by qRT-PCR. Levels of acute-phase-proteins (SAP, SAA2; CRP and ApoA1), endothelial (Ang2, VEGF), coagulation (fibrinogen) markers were determined by sandwich ELISA/immunoturbidimetry/western-blotting. Hepatic (ALT, AST, ALP) and other blood biochemical parameters were studied by autoanalyzer and haematology cell counter. Statistical analysis and protein-protein-interaction network were performed by GraphPad-Prism and STRINGS database, respectively. Among 87 dengue patients, significantly higher levels of Ang2, VEGF, CRP, SAA2, ApoA1, AST, ALT, and AST/ALT ratio and low level of fibrinogen were detected in severe-dengue cases compared to dengue without warning-signs, with seven of them severely altered during febrile-phase. Higher fold-change of Ang2 and VEGF as well as decreased fibrinogen were observed among patients with haemorrhagic-manifestation, clinical-fluid accumulation and thrombocytopenia. Functional network analysis predicted Ang2, VEGF, and CRP to be functionally and physically connected and SAA2 and ApoA1 to be functioning together. Correlation analyses also validated this connectivity by a

strong positive correlation between Ang2, VEGF, and CRP. PCA analysis followed by hierarchical clustering heatmap analysis segregated severe-dengue patients from the rest, with VEGF, Ang2, ApoA1, AST, and ALT clearly distinguishing the severe-dengue group. Thus, serum levels of VEGF, Ang2, ApoA1, AST, and ALT might act as potential biomarkers for predicting dengue severity during the early stage.

### Simple, sensitive, and cost-effective detection of wAlbB Wolbachia in Aedes mosquitoes, using loop mediated isothermal amplification combined with the electrochemical biosensing method.

Thayanukul, P., Lertanantawong, B., Sirawaraporn, W., Charasmongkolcharoen, S., Chaibun, T., Jittungdee, R., Kittayapong, P.

13-05-2022

*PLoS Negl Trop Dis*

<https://doi.org/10.1371/journal.pntd.0009600>

**Background:** Wolbachia is an endosymbiont bacterium generally found in about 40% of insects, including mosquitoes, but it is absent in *Aedes aegypti* which is an important vector of several arboviral diseases dengue, chikungunya, zika, and yellow fever. The evidence that Wolbachia trans-infected *Ae. aegypti* mosquitoes lost their vectorial competence and became less capable of transmitting arboviruses to human hosts highlights the potential of using Wolbachia-based approaches for prevention and control of arboviral diseases. Recently, release of Wolbachia trans-infected *Ae. aegypti* has been deployed widely in many countries for the control of mosquito-borne viral diseases. Field surveillance and monitoring of Wolbachia presence in released mosquitoes is important for the success of these control programs. So far, a number of studies have reported the development of loop mediated isothermal amplification (LAMP) assays to detect Wolbachia in mosquitoes, but the methods still have some specificity and cost issues. **Methodology/Principal findings:** We describe here the development of a LAMP assay combined with the DNA strand displacement-based electrochemical sensor (BIOSENSOR) method to detect wAlbB Wolbachia in trans-infected *Ae. aegypti*. Our developed LAMP primers used a low-cost dye detecting system and 4 oligo nucleotide primers which can reduce the cost of analysis while the specificity is comparable to the previous methods. The detection capacity of our LAMP technique was 1.4 nM and the detection limit reduced to 2.2 fM when combined with the BIOSENSOR. Our study demonstrates that a BIOSENSOR can also be applied as a stand-alone method for detecting Wolbachia; and it showed high sensitivity when used with the crude DNA extracts of macerated mosquito samples without DNA purification. **Conclusions/Significance:** Our results suggest that both LAMP and BIOSENSOR, either used in combination or stand-alone, are robust and sensitive. The methods have good potential for routine detection of Wolbachia in mosquitoes during field surveillance and monitoring of Wolbachia-based release programs, especially in countries with limited resources.

## The Multifaceted Biology of PCSK9.

Revue de littérature

Seidah, N., Prat, A.

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*Endocr Rev*

<https://doi.org/10.1210/endrev/bnab035>

This article reviews the discovery of PCSK9, its structure-function characteristics, and its presently known and proposed novel biological functions. The major critical function of PCSK9 deduced from human and mouse studies, as well as cellular and structural analyses, is its role in increasing the levels of circulating low-density lipoprotein (LDL)-cholesterol (LDLc), via its ability to enhance the sorting and escort of the cell surface LDL receptor (LDLR) to lysosomes. This implicates the binding of the catalytic domain of PCSK9 to the EGF-A domain of the LDLR. This also requires the presence of the C-terminal Cys/His-rich domain, its binding to the secreted cytosolic cyclase associated protein 1, and possibly another membrane-bound "protein X". Curiously, in PCSK9-deficient mice, an alternative to the downregulation of the surface levels of the LDLR by PCSK9 is taking place in the liver of female mice in a 17 $\beta$ -estradiol-dependent manner by still an unknown mechanism. Recent studies have extended our understanding of the biological functions of PCSK9, namely its implication in septic shock, vascular inflammation, viral infections (Dengue; SARS-CoV-2) or immune checkpoint modulation in cancer via the regulation of the cell surface levels of the T-cell receptor and MHC-I, which govern the antitumoral activity of CD8+ T cells. Because PCSK9 inhibition may be advantageous in these processes, the availability of injectable safe PCSK9 inhibitors that reduces by 50% to 60% LDLc above the effect of statins is highly valuable. Indeed, injectable PCSK9 monoclonal antibody or small interfering RNA could be added to current immunotherapies in cancer/metastasis.

## Decision tree based ensemble machine learning model for the prediction of Zika virus T-cell epitopes as potential vaccine candidates.

Bukhari, S., Webber, J., Mehbodniya, A.

12-05-2022

*Sci Rep*

<https://doi.org/10.1038/s41598-022-11731-6>

Zika fever is an infectious disease caused by the Zika virus (ZIKV). The disease is claiming millions of lives worldwide, primarily in developing countries. In addition to vector control strategies, the most effective way to prevent the spread of ZIKV infection is vaccination. There is no clinically approved vaccine to combat ZIKV infection and curb its pandemic. An epitope-based peptide vaccine (EBPV) is seen as a powerful alternative to conventional vaccinations because of its low production cost and short production time. Nonetheless, EBPVs have gotten less attention, despite the fact that they have a significant untapped potential for enhancing vaccine safety, immunogenicity, and cross-reactivity. Such a vaccine technology is based on target pathogen's selected antigenic

peptides called T-cell epitopes (TCE), which are synthesized chemically based on their amino acid sequences. The identification of TCEs using wet-lab experimental approach is challenging, expensive, and time-consuming. Therefore in this study, we present computational model for the prediction of ZIKV TCEs. The model proposed is an ensemble of decision trees that utilizes the physicochemical properties of amino acids. In this way a large amount of time and efforts would be saved for quick vaccine development. The peptide sequences dataset for model training was retrieved from Virus Pathogen Database and Analysis Resource (ViPR) database. The sequences dataset consist of experimentally verified T-cell epitopes (TCEs) and non-TCEs. The model demonstrated promising results when evaluated on test dataset. The evaluation metrics namely, accuracy, AUC, sensitivity, specificity, Gini and Mathew's correlation coefficient (MCC) recorded values of 0.9789, 0.984, 0.981, 0.987, 0.974 and 0.948 respectively. The consistency and reliability of the model was assessed by carrying out the five (05)-fold cross-validation technique, and the mean accuracy of 0.97864 was reported. Finally, model was compared with standard machine learning (ML) algorithms and the proposed model outperformed all of them. The proposed model will aid in predicting novel and immunodominant TCEs of ZIKV. The predicted TCEs may have a high possibility of acting as prospective vaccine targets subjected to in-vivo and in-vitro scientific assessments, thereby saving lives worldwide, preventing future epidemic-scale outbreaks, and lowering the possibility of mutation escape.

## Incidence of chikungunya virus infections among Kenyan children with neurological disease, 2014-2018: A cohort study.

Nyamwaya, D., Otiende, M., Mwango, L., Kariuki, S., Otieno, B., Omuoyo, D., Githinji, G., Kitsao, B., Karanja, H., Gitonga, J., de Laurent, Z., Davies, A., Mwarumba, S., Agoti, C., Thumbi, S., Hamaluba, M., Newton, C., Bejon, P., Warimwe, G.

12-05-2022

*PLoS Med*

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**Background:** Neurological complications due to chikungunya virus (CHIKV) infection have been described in different parts of the world, with children being disproportionately affected. However, the burden of CHIKV-associated neurological disease in Africa is currently unknown and given the lack of diagnostic facilities in routine care it is possible that CHIKV is an unrecognized etiology among children with encephalitis or other neurological illness. **Methods and findings:** We estimated the incidence of CHIKV infection among children hospitalized with neurological disease in Kilifi County, coastal Kenya. We used reverse transcriptase polymerase chain reaction (RT-PCR) to systematically test for CHIKV in cerebrospinal fluid (CSF) samples from children aged <16 years hospitalized with symptoms of neurological disease at Kilifi County Hospital between January 2014 and December 2018. Clinical records were linked to the Kilifi Health and Demographic Surveillance System and population incidence

rates of CHIKV infection estimated. There were 18,341 pediatric admissions for any reason during the 5-year study period, of which 4,332 (24%) had CSF collected. The most common clinical reasons for CSF collection were impaired consciousness, seizures, and coma (47%, 22%, and 21% of all collections, respectively). After acute investigations done for immediate clinical care, CSF samples were available for 3,980 admissions, of which 367 (9.2%) were CHIKV RT-PCR positive. Case fatality among CHIKV-positive children was 1.4% (95% CI 0.4, 3.2). The annual incidence of CHIKV-associated neurological disease varied between 13 to 58 episodes per 100,000 person-years among all children <16 years old. Among children aged <5 years, the incidence of CHIKV-associated neurological disease was 77 per 100,000 person-years, compared with 20 per 100,000 for cerebral malaria and 7 per 100,000 for bacterial meningitis during the study period. Because of incomplete case ascertainment due to children not presenting to hospital, or not having CSF collected, these are likely minimum estimates. Study limitations include reliance on hospital-based surveillance and limited CSF sampling in children in coma or other contraindications to lumbar puncture, both of which lead to under-ascertainment of incidence and of case fatality. **Conclusions:** In this study, we observed that CHIKV infections are relatively more common than cerebral malaria and bacterial meningitis among children hospitalized with neurological disease in coastal Kenya. Given the wide distribution of CHIKV mosquito vectors, studies to determine the geographic extent of CHIKV-associated neurological disease in Africa are essential.

### The knowledge, attitude and practice of community people on dengue fever in Central Nepal: a cross-sectional study.

Phuyal, P., Kramer, I., Kuch, U., Magdeburg, A., Groneberg, D., Lamichhane Dhimal, M., Montag, D., Harapan, H., Wouters, E., Jha, A., Dhimal, M., Müller, R.

12-05-2022

*BMC Infect Dis*

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**Background:** Since 2006, Nepal has experienced frequent Dengue fever (DF) outbreaks. Up to now, there have been no knowledge, attitude and practice (KAP) studies carried out on DF in Nepal that have included qualitative in-depth and quantitative data. Thus, we aimed to explore and compare the KAP of people residing in the lowland (<1500 m) and highland (>1500 m) areas of Nepal. **Methods:** A cross-sectional mixed-method study was conducted in six districts of central Nepal in September-October 2018 including both quantitative (660 household surveys) and qualitative data (12 focus group discussions and 27 in-depth interviews). The KAP assessment was executed using a scoring system and defined as high or low based on 80% cut-off point. Logistic regression was used to investigate the associated factors, in quantitative analysis. The deductive followed by inductive approach was adopted to identify the themes in the qualitative data. **Results:** The study revealed that both the awareness about DF and prevention measures were low. Among the surveyed participants, 40.6%

had previously heard about DF with a significantly higher number in the lowland areas. Similarly, IDI and FGD participants from the lowland areas were aware about DF, and it's associated symptoms, hence they were adopting better preventive practices against DF. The findings of both the qualitative and quantitative data indicate that people residing in the lowland areas had better knowledge on DF compared to people in highland areas. All IDI participants perceived a higher chance of increasing future dengue outbreaks due to increasing temperature and the mobility of infected people from endemic to non-endemic areas. The most quoted sources of information were the television (71.8%) and radio (51.5%). Overall, only 2.3% of the HHS participants obtained high knowledge scores, 74.1% obtained high attitude scores and 21.2% obtained high preventive practice scores on DF. Among the socio-demographic variables, the area of residence, educational level, age, monthly income, SES and occupation were independent predictors of knowledge level, while the education level of the participants was an independent predictor of the attitude level. **Conclusions:** Our study found a very low level of knowledge and insufficient preventive practices. This highlights an urgent need for extensive dengue prevention programs in both highland and lowland communities of Nepal.

### A bacterium-like particle vaccine displaying Zika virus prM-E induces systemic immune responses in mice.

Jin, H., Bai, Y., Wang, J., Jiao, C., Liu, D., Zhang, M., Li, E., Huang, P., Gong, Z., Song, Y., Xu, S., Feng, N., Zhao, Y., Wang, T., Li, N., Gao, Y., Yang, S., Zhang, H., Li, Y., Xia, X., Wang, H.

11-05-2022

*Transbound Emerg Dis*

<https://doi.org/10.1111/tbed.14594>

The emergence of Zika virus (ZIKV) infection, which is unexpectedly associated with congenital defects, has prompted the development of safe and effective vaccines. The gram-positive enhancer matrix-protein anchor (GEM-PA) display system has emerged as a versatile and highly effective platform for delivering target proteins in vaccines. In this study, we developed a bacterium-like particle vaccine, ZI- $\Delta$ PA-GEM, based on the GEM-PA system. The fusion protein ZI- $\Delta$ PA, which contains the prM-E- $\Delta$ TM protein of ZIKV (with a stem-transmembrane region deletion) and the protein anchor PA3, was expressed. The fusion protein was successfully displayed on the GEM surface to form ZI- $\Delta$ PA-GEM. Moreover, the intramuscular immunization of BALB/c mice with ZI- $\Delta$ PA-GEM combined with ISA 201 VG and poly(I:C) adjuvants induced durable ZIKV-specific IgG and protective neutralizing antibody responses. Potent B-cell/DC activation was also stimulated early after immunization. Notable, splenocyte proliferation, the secretion of multiple cytokines, T/B-cell activation and central memory T-cell responses were elicited. These data indicate that ZI- $\Delta$ PA-GEM is a promising bacterium-like particle vaccine candidate for ZIKV. This article is protected by copyright. All rights reserved.

### **Spatial dispersal of *Aedes albopictus* mosquitoes captured by the modified sticky ovitrap in Selangor, Malaysia.**

**Roslan, M., Ngui, R., Marzuki, M., Vythilingam, I., Shafie, A., Musa, S., Wan Sulaiman, W.**

11-05-2022

*Geospat Health*

<https://doi.org/10.4081/gh.2022.1025>

Dengue is a major mosquito-borne disease in many tropical and sub-tropical countries worldwide, with entomological surveillance and control activities as the key management approaches. This study aimed to explore the spatial dispersal of the vector *Aedes albopictus*, captured by the modified sticky ovitrap (MSO) in residential areas with low-rise buildings in Selangor, Malaysia. Distribution maps were created and shown as temporally distinguished classes based on hotspot analysis by Getis-Ord; spatial autocorrelation assessed by semivariograms using the exponential Kernel function; and universal Kriging showing areas with estimated high and low vector densities. Distribution, hotspot and interpolated maps were analysed based on the total number of mosquitoes by month and week. All maps in the present study were generated and visualised in ArcMap. Spatial autocorrelation of *Ae. albopictus* based on the monthly occurrence of *Ae. albopictus* was found in March, April, October, November and December 2018, and when based on the weekly numbers, in weeks 1, 2, 3, 5, 7, 12, 14, 25, 26, 27, 31, 33, 42, 49 and 52. Semivariograms, based on the monthly and weekly numbers of *Ae. albopictus*, indicated spatial autocorrelation of the species extending between 50 and 70 m. The mosquito density maps reported in this study may provide beneficial information to facilitate implementation of more efficient entomological control activities.

### **Dengue: A Growing Problem With New Interventions.**

**Wong, J., Adams, L., Durbin, A., Muñoz-Jordán, J., Poehling, K., Sánchez-González, L., Volkman, H., Paz-Bailey, G.**

11-05-2022

*Pediatrics*

<https://pubmed.ncbi.nlm.nih.gov/35543085>

Dengue is the disease caused by 1 of 3 distinct, but closely related dengue viruses (DENV-1-4) that are transmitted by *Aedes* spp. mosquito vectors. It is the most common arboviral disease worldwide, with the greatest burden in tropical and sub-tropical regions. In the absence of effective prevention and control measures, dengue is projected to increase in both disease burden and geographic range. Given its increasing importance as an etiology of fever in the returning traveler or the possibility of local transmission in regions in the United States with competent vectors, as well as the risk for large outbreaks in endemic US territories and associated states, clinicians should understand its clinical presentation and be familiar with appropriate testing, triage, and management of patients with dengue. Control and prevention efforts reached a milestone in June 2021 when the Advisory Committee on

Immunization Practices (ACIP) recommended Dengvaxia for routine use in children aged 9 to 16 years living in endemic areas with laboratory confirmation of previous dengue virus infection. Dengvaxia is the first vaccine against dengue to be recommended for use in the United States and one of the first to require laboratory testing of potential recipients to be eligible for vaccination. In this review, we outline dengue pathogenesis, epidemiology, and key clinical features for front-line clinicians evaluating patients presenting with dengue. We also provide a summary of Dengvaxia efficacy, safety, and considerations for use as well as an overview of other potential new tools to control and prevent the growing threat of dengue.

### **Arboviral disease record data - Dengue and Chikungunya, Brazil, 2013-2020.**

**da Silva Neto, S., Tabosa de Oliveira, T., Teixeira, I., Medeiros Neto, L., Souza Sampaio, V., Lynn, T., Endo, P.**

10-05-2022

*Sci Data*

<https://doi.org/10.1038/s41597-022-01312-7>

One of the main categories of Neglected Tropical Diseases (NTDs) are arboviruses, of which Dengue and Chikungunya are the most common. Arboviruses mainly affect tropical countries. Brazil has the largest absolute number of cases in Latin America. This work presents a unified data set with clinical, sociodemographic, and laboratorial data on confirmed patients of Dengue and Chikungunya, as well as patients ruled out of infection from these diseases. The data is based on case notification data submitted to the Brazilian Information System for Notifiable Diseases, from Portuguese Sistema de Informação de Agravos de Notificação (SINAN), from 2013 to 2020. The original data set comprised 13,421,230 records and 118 attributes. Following a pre-processing process, a final data set of 7,632,542 records and 56 attributes was generated. The data presented in this work will assist researchers in investigating antecedents of arbovirus emergence and transmission more generally, and Dengue and Chikungunya in particular. Furthermore, it can be used to train and test machine learning models for differential diagnosis and multi-class classification.

### **The distinguishing NS5-M114V mutation in American Zika virus isolates has negligible impacts on virus replication and transmission potential.**

**Peng, N., Amarilla, A., Hugo, L., Modhiran, N., Sng, J., Slonchak, A., Watterson, D., Setoh, Y., Khromykh, A.**

10-05-2022

*PLoS Negl Trop Dis*

<https://doi.org/10.1371/journal.pntd.0010426>

During 2015-2016, outbreaks of Zika virus (ZIKV) occurred in Southeast Asia and the Americas. Most ZIKV infections in humans are asymptomatic, while clinical manifestation is usually a self-limiting febrile disease with maculopapular rash. However, ZIKV is capable of inducing a range of severe

neurological complications collectively described as congenital Zika syndrome (CZS). Notably, the scale and magnitude of outbreaks in Southeast Asia were significantly smaller compared to those in the Americas. Sequence comparison between epidemic-associated ZIKV strains from Southeast Asia with those from the Americas revealed a methionine to valine substitution at residue position 114 of the NS5 protein (NS5-M114V) in all the American isolates. Using an American isolate of ZIKV (Natal), we investigated the impact of NS5-M114V mutation on virus replication in cells, virulence in interferon (IFN)  $\alpha/\beta$  receptor knockout (Ifnar $^{-/-}$ ) mice, as well as replication and transmission potential in *Aedes aegypti* mosquitoes. We demonstrated that NS5-M114V mutation had insignificant effect on ZIKV replication efficiency in cells, its ability to degrade STAT2, and virulence in vivo, albeit viremia was slightly prolonged in mice. Furthermore, NS5-M114V mutation decreased mosquito infection and dissemination rates and had no effect on virus secretion into the saliva. Taken together, our findings support the notion that NS5-M114V mutation is unlikely to be a major determinant for virus replication and transmission potential.

### Seropositivity for *Coxiella burnetii* in suspected patients with dengue in São Paulo state, Brazil.

França, D., Mioni, M., Fornazari, F., de Lima Duré, A., Silva, M., Possebon, F., Richini-Pereira, V., Langoni, H., Megid, J.  
10-05-2022

*PLoS Negl Trop Dis*

<https://doi.org/10.1371/journal.pntd.0010392>

Q fever and brucellosis are zoonoses that cause fever and other systemic clinical signs in humans; their occurrences are neglected and the differential diagnosis for some diseases is disregarded. This study aimed to investigate the seropositivity for *Coxiella burnetii* and *Brucella* spp. antibodies in patients suspected of dengue from 38 municipalities in the state of São Paulo, Brazil. The samples ( $n = 604$ ) were obtained by convenience from the Adolfo Lutz Institute serum bank. Sera were subjected to an indirect immunofluorescence assay (IFA) using in-house and commercial diagnostic protocols to evaluate *C. burnetii* positivity. For *Brucella* spp., sera were subjected to rapid plate serum agglutination with buffered acidified antigen (AAT), slow tube serum agglutination (SAL), and 2-mercaptoethanol (2-ME) techniques. Associations and statistical inferences of the results were performed by logistic regression according to the clinical and demographic variables collected from the patients. Statistical analyses were performed using Statistical Analysis Software (SAS) and associations were considered when  $p$  value was  $<0.05$ . In all, 129 patients showed positive results for Q fever, indicating a seropositivity of 21.4% (95% CI 18.15-24.85). Patients with 14-20 days of symptoms had 2.12 (95% CI 1.34-3.35) times more chances of being seropositive for Q fever than patients with 7-13 days, and patients with 21-27 days of fever had 2.62 (95% CI 1.27-5.41) times more chances of being seropositive for Q fever than patients with 7-13 days. For the other variables analyzed, there were no significant associations between the groups. No positivity for brucellosis was observed. This is the

most comprehensive study of people seropositive for Q fever in São Paulo state and provides additional data for the medical community in Brazil. It is suggested that Q fever may be an important differential diagnosis of febrile illnesses in the region, demanding the government's attention and investment in health.

### Effective interventions to ensure MCH (Maternal and Child Health) services during pandemic related health emergencies (Zika, Ebola, and COVID-19): A systematic review.

Palo, S., Dubey, S., Negi, S., Sahay, M., Patel, K., Swain, S., Mishra, B., Bhuyan, D., Kanungo, S., Som, M., Merta, B., Bhattacharya, D., Kshatri, J., Pati, S.

10-05-2022

*PLoS One*

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**Introduction:** Ensuring accessible and quality health care for women and children is an existing challenge, which is further exacerbated during pandemics. There is a knowledge gap about the effect of pandemics on maternal, newborn, and child well-being. This systematic review was conducted to study maternal and child health (MCH) services utilization during pandemics (Zika, Ebola, and COVID-19) and the effectiveness of various interventions undertaken for ensuring utilization of MCH services. **Methodology:** A systematic and comprehensive search was conducted in MEDLINE/PubMed, Cochrane CENTRAL, Embase, Epistemonikos, ScienceDirect, and Google Scholar. Of 5643 citations, 60 potential studies were finally included for analysis. The included studies were appraised using JBI Critical appraisal tools. Study selection and data extraction were done independently and in duplicate. Findings are presented narratively based on the RMNCHA framework by World Health Organization (WHO). **Results:** Maternal and child health services such as antenatal care (ANC) visits, institutional deliveries, immunization uptake, were greatly affected during a pandemic situation. Innovative approaches in form of health care services through virtual consultation, patient triaging, developing dedicated COVID maternity centers and maternity schools were implemented in different places for ensuring continuity of MCH care during pandemics. None of the studies reported the effectiveness of these interventions during pandemic-related health emergencies. **Conclusion:** The findings suggest that during pandemics, MCH care utilization often gets affected. Many innovative interventions were adopted to ensure MCH services. However, they lack evidence about their effectiveness. It is critically important to implement evidence-based appropriate interventions for better MCH care utilization.

### Intracellular mono-ADP-ribosyltransferases at the host-virus interphase.

Revue de littérature

Lüscher, B., Verheirstraeten, M., Krieg, S., Korn, P.

10-05-2022

Cell Mol Life Sci

<https://doi.org/10.1007/s00018-022-04290-6>

The innate immune system, the primary defense mechanism of higher organisms against pathogens including viruses, senses pathogen-associated molecular patterns (PAMPs). In response to PAMPs, interferons (IFNs) are produced, allowing the host to react swiftly to viral infection. In turn the expression of IFN-stimulated genes (ISGs) is induced. Their products disseminate the antiviral response. Among the ISGs conserved in many species are those encoding mono-ADP-ribosyltransferases (mono-ARTs). This prompts the question whether, and if so how, mono-ADP-ribosylation affects viral propagation. Emerging evidence demonstrates that some mono-ADP-ribosyltransferases function as PAMP receptors and modify both host and viral proteins relevant for viral replication. Support for mono-ADP-ribosylation in virus-host interaction stems from the findings that some viruses encode mono-ADP-ribosylhydrolases, which antagonize cellular mono-ARTs. We summarize and discuss the evidence linking mono-ADP-ribosylation and the enzymes relevant to catalyze this reversible modification with the innate immune response as part of the arms race between host and viruses.

### Detection and typing of dengue virus by one-step RT-PCR-based high-resolution melting assay.

Tian, R., Yan, H., Jiang, Y., Wu, A., Li, L., Yang, Z., Yu, K.

10-05-2022

Virus Genes

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Dengue is a rapidly spreading arboviral disease that can be transmitted through any of the four types of dengue virus (DENV) serotypes. Previous studies have observed that individuals who have a pre-existing secondary infection due to a different dengue serotype, experience severe forms of this disease. During a DENV outbreak, a time-sensitive preliminary diagnosis of the origin of DENV might be useful in controlling the epidemic. Here, we developed a rapid and accurate one-step TB Green RT-PCR-based high-resolution melting (HRM) assay to identify and serotype DENV using serotyping primers based on the alignment with the E gene. This assay had a detection limit of  $7.7 \times 10^2$  (DENV 1),  $3.8 \times 10^2$  (DENV 2),  $6.2 \times 10^2$  (DENV 3), and  $1.2 \times 10^3$  (DENV 4) RNA copies/mL. No cross-reactivity with the Chikungunya, Zika, and Japanese encephalitis viruses was observed. The feasibility of using this assay for clinical diagnosis was evaluated in DENV-positive patient sera. The HRM assay and the RT-qPCR had complete matched results derived from DENV detection, including 51 serum positive and 20 serum negative. Additionally, eight DENV 2 strains in the same serotype were successfully differentiated by an HRM assay. Thus, this assay facilitated accurate detection and serotyping of DENV, along with the time-sensitive identification of the infectious focus of different DENVs.

### Natural Aedes-Borne Virus Infection Detected in Male Adult Aedes aegypti (Diptera: Culicidae) Collected From Urban Settings in Mérida, Yucatán, México.

Kirstein, O., Talavera, G., Wei, Z., Ciau-Carrillo, K., Koyoc-Cardena, E., Puerta-Guardo, H., Rodríguez-Martín, E., Medina-Barreiro, A., Mendoza, A., Piantadosi, A., Manrique-Saide, P., Vazquez-Prokopec, G.

10-05-2022

J Med Entomol

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Aedes-borne viruses (ABVs) such as dengue (DENV), chikungunya (CHIKV), and Zika (ZIKV) contribute significantly to the global burden of infectious diseases, disproportionately affecting disadvantaged populations from tropical and subtropical urban areas. ABVs can be transmitted from female mosquitoes to their progeny by vertical transmission via transovarial and/or trans-egg vertical transmission and contribute to the maintenance of infected-mosquito populations year-round in endemic regions. This study describes the natural infection rate of DENV, CHIKV, and ZIKV in field-caught male Aedes (Sergentomyia) aegypti (Linnaeus) mosquitoes from Mérida, Yucatán, México, as a proxy for the occurrence of vertical virus transmission. We used indoor sequential sampling with Prokopack aspirators to collect all mosquitoes inside houses from ABV hotspots areas. Collections were performed in a DENV and CHIKV post-epidemic phase and during a period of active ZIKV transmission. We individually RT-qPCR tested all indoor collected Ae. aegypti males (1,278) followed by Sanger sequencing analysis for final confirmation. A total of 6.7% male mosquitoes were positive for ABV (CHIKV = 5.7%; DENV = 0.9%; ZIKV = 0.1%) and came from 21.0% (30/143) houses infested with males. Most ABV-positive male mosquitoes were positive for CHIKV (84.8%). The distribution of ABV-positive Ae. aegypti males was aggregated in a few households, with two houses having 11 ABV-positive males each. We found a positive association between ABV-positive males and females per house. These findings suggested the occurrence of vertical arbovirus transmission within the mosquito populations in an ABV-endemic area and, a mechanism contributing to viral maintenance and virus re-emergence among humans in post-epidemic periods.

### Advancement of dengue virus NS1 protein detection by 3D-nanoassembly complex gold nanoparticles utilizing competitive sandwich aptamer on disposable electrode.

Khoris, I., Nasrin, F., Chowdhury, A., Park, E.

09-04-2022

Anal Chim Acta

<https://pubmed.ncbi.nlm.nih.gov/35491045>

Signal amplification have been centralized in developing the highly reliable biosensor for analyte detection with a narrow detection window. We proposed an aptasensor to provide a highly sensitive early-stage diagnostic platform of dengue

virus NS1 protein (DENV-NS1) by dual-approach - colorimetric and electrochemical detection. This work utilized two different aptamers specific to DENV-NS1: One conjugated to gold nanoparticles (AuNPs), forming AuNPs-Apt<sub>1</sub> and its complementary sequence aptamer, forming AuNPs-Apt<sub>2</sub>. The unbound Apt<sub>1</sub> of AuNPs-Apt<sub>1</sub> by DENV-NS1 were to hybridize to AuNPs-Apt<sub>2</sub> and induced a 3D-nanoassembled formation, resulting in DENV-NS1 concentration-dependent plasmonic color change. Occurrence of the hybridization of Apt<sub>1</sub> and Apt<sub>2</sub>, the 3D-assembled hybridized aptamers of AuNPs was incubated with methylene blue (MB) solution, which intercalated a high number of MB molecules within the duplex structure of aptamers, and the complex was captured on the Apt<sub>2</sub>-conjugated disposable gold electrode (DGE). The developed aptamer-based biosensor showed high sensitivity with colorimetric response down to 1.28 pg/mL and electrochemical approach down to 30 fg/mL of DENV-NS1 with good selectivity. This work showcases an advanced utilization of aptamer and its complementary anti-sense aptamer in signal amplification and nanocarrier for biosensing.

### Temporal Correlation Between Urban Microclimate, Vector Mosquito Abundance, and Dengue Cases.

Faridah, L., Fauziah, N., Agustian, D., Mindra Jaya, I., Eka Putra, R., Ekawardhani, S., Hidayath, N., Damar Djati, I., Carvajal, T., Mayasari, W., Ruluwedrata Rinawan, F., Watanabe, K.

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*J Med Entomol*

<https://doi.org/10.1093/jme/tjac005>

Dengue Hemorrhagic Fever (DHF) is a major mosquito-borne viral disease. Studies have reported a strong correlation between weather, the abundance of *Aedes aegypti*, the vector of DHF virus, and dengue incidence. However, this conclusion has been based on the general climate pattern of wide regions. In general, however, the human population, level of infrastructure, and land-use change in rural and urban areas often produce localized climate patterns that may influence the interaction between climate, vector abundance, and dengue incidence. Thoroughly understanding this correlation will allow the development of a customized and precise local early warning system. To achieve this purpose, we conducted a cohort study, during January-December 2017, in 16 districts in Bandung, West Java, Indonesia. In the selected areas, local weather stations and modified light mosquito traps were set up to obtain data regarding daily weather and the abundance of adult female *Ae. aegypti*. A generalized linear model was applied to analyze the effect of local weather and female adult *Ae. aegypti* on the number of dengue cases. The result showed a significant non-linear correlation among mosquito abundance, maximum temperature, and dengue cases. Using our model, the data showed that the addition of a single adult *Ae. aegypti* mosquito increased the risk of dengue infection by 1.8%, while increasing the maximum temperature by one degree decreased the risk by 17%. This finding suggests specific actionable insights needed to supplement existing mosquito eradication programs.

### Global RNAseq of ocular cells reveals gene dysregulation in both asymptomatic and with Congenital Zika Syndrome infants exposed prenatally to Zika virus.

Rosa-Fernandes, L., Bedrat, A., Dos Santos, M., Pinto, A., Lucena, E., Silva, T., Melo, R., Palmisano, G., Cardoso, C., Barbosa, R.

10-03-2022

*Exp Cell Res*

<https://pubmed.ncbi.nlm.nih.gov/35283101>

In 2015, Brazil reported an outbreak identified as Zika virus (ZIKV) infection associated with congenital abnormalities. To date, a total of 86 countries and territories have described evidence of Zika infection and recently the appearance of the African ZIKV lineage in Brazil highlights the risk of a new epidemic. The spectrum of ZIKV infection-induced alterations at both cellular and molecular levels is not completely elucidated. Here, we present for the first time the gene expression responses associated with prenatal ZIKV infection from ocular cells. We applied a recently developed non-invasive method (impression cytology) which use eye cells as a model for ZIKV studies. The ocular profiling revealed significant differences between exposed and control groups, as well as a different pattern in ocular transcripts from Congenital Zika Syndrome (CZS) compared to ZIKV-exposed but asymptomatic infants. Our data showed pathways related to mismatch repair, cancer, and PI3K/AKT/mTOR signaling and genes probably causative or protective in the modulation of ZIKV infection. Ocular cells revealed the effects of ZIKV infection on primordial neuronal cell genes, evidenced by changes in genes associated with embryonic cells. The changes in gene expression support an association with the gestational period of the infection and provide evidence for the resulting clinical and ophthalmological pathologies. Additionally, the findings of cell death- and cancer-associated deregulated genes raise concerns about the early onset of other potential pathologies including the need for tumor surveillance. Our results thus provide direct evidence that infants exposed prenatally to the Zika virus, not only with CZS but also without clinical signs (asymptomatic) express cellular and molecular changes with potential clinical implications.

### miR-383 Regulates Hepatic Lipid Homeostasis and Response to Dengue Virus Infection.

Ahmed, N., Ahmed, N., Pezacki, J.

07-03-2022

*ACS Infect Dis*

<https://doi.org/10.1021/acsinfectdis.1c00470>

Recently, microRNAs (miRNAs), as endogenous noncoding RNAs that inhibit mRNA translation, have been identified to broadly possess functional roles in regulating cellular signaling and metabolic processes due to their chemical and biological properties. In addition, they have emerged to be of critical importance in modulating host-virus interactions, especially for RNA viruses. Herein, we discovered that miR-383-5p targets certain lipid and cholesterol biosynthetic pathways and

restricts Dengue virus (DENV) infection in hepatic cells. Global transcriptomics analysis of Huh7 human hepatoma cells overexpressing miR-383-5p revealed enrichment of lipid and cholesterol metabolic processes. Bioinformatics analysis of genes repressed in miR-383-5p overexpressing cells divulged the repression of a key target PLA2G4A, a pro-viral host factor essential for the production of infectious DENV particles. Our study demonstrated the effectiveness of miRNA mimics as tools to study cellular signaling pathways that contribute to viral pathogenesis. Overall, our study identifies miR-383-5p as an interesting host factor during DENV propagation and highlights a potential therapeutic role in the regulation of hepatic lipid metabolism and an antiviral response to DENV.

### **Mosquito Repellent Potential of *Carpesium abrotanoides* Essential Oil and Its Main Components Against a Dengue Vector, *Aedes aegypti* (Diptera: Culicidae).**

**Haris, A., Azeem, M., Binyameen, M.**

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*J Med Entomol*

<https://doi.org/10.1093/jme/tjac009>

Disease vectoring mosquitoes are a serious threat to humans. However, till today only few mosquito repellents have been identified. The current study was conducted to evaluate the repellent potential of *Carpesium abrotanoides* essential oil against *Aedes aegypti* females by human bait technique. Essential oil was extracted by steam distillation process while the identification of chemical constituents was carried out by gas chromatography-mass spectrometry. Time span repellent bioassays of *C. abrotanoides* essential oil in comparison to DEET were performed at three different doses (33 µg/cm<sup>2</sup>, 165 µg/cm<sup>2</sup>, and 330 µg/cm<sup>2</sup>) under laboratory conditions. Highest repellency periods for essential oil and DEET were observed at the tested dose of 330 µg/cm<sup>2</sup> with 315 min and 720 min, respectively. Lowest repellency period of 45 min for essential oil and 105 min for DEET was recorded at the tested dose of 33 µg/cm<sup>2</sup>. Major constituents caryophyllene (24.3%) and trans-nerolidol (12.0%) of *C. abrotanoides* essential oil were also evaluated as repellents at three different doses (330 µg/cm<sup>2</sup>, 165 µg/cm<sup>2</sup>, and 33 µg/cm<sup>2</sup>) against *Ae. aegypti*. Surprisingly, trans-nerolidol completely inhibited *Ae. aegypti* landings for 45 min when tested at 330 µg/cm<sup>2</sup>. However, caryophyllene did not completely inhibit *Ae. aegypti* landing even after immediate application at the tested dose of 330 µg/cm<sup>2</sup>. At the tested dose of 330 µg/cm<sup>2</sup>, the mixture (trans-nerolidol + caryophyllene) completely inhibited *Ae. aegypti* landing for 60 min indicating the synergistic effect of caryophyllene. Hence, *C. abrotanoides* as well as its major constituent, especially trans-nerolidol, have potential to formulate as mosquito repellent comparable of DEET.

### **The Fauna, Diversity, and Bionomics of Culicinae (Diptera: Culicidae) in Hormozgan Province, Southern Iran.**

**Jaberhashemi, S., Azari-Hamidian, S., Soltani, A., Azizi, K.,**

**Dorzaban, H., Norouzi, M., Daghighi, E.**

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*J Med Entomol*

<https://doi.org/10.1093/jme/tjac003>

Hormozgan Province is one of the important foci of malaria in Iran. In addition to malaria pathogens, mosquitoes also transmit the pathogens that cause dirofilariasis and West Nile fever in the province. Also, the threat of emerging aedine-borne viruses that cause infections, such as Chikungunya, dengue, and Zika, is noticeable. There is little information about the fauna and bionomics of Culicinae in the province. The present investigation aimed to study the fauna, diversity, and bionomics of culicines. The study was conducted from September 2016 to April 2017 in four counties of Bandar Abbas, Bandar Khamir, Bashagard, and Jask. In total, 3,236 larvae and 1,901 adults including 16 culicine species were collected. The larvae of *Culiseta longiareolata* (Macquart) (25.65%), *Culex pipiens* Linnaeus (16.62%), and *Cx. quinquefasciatus* Say (16.16%) were most abundant and *Cx. hortensis* Ficalbi (0.09%) was least abundant. Among adults, *Cx. laticinctus* Edwards (33.19%), *Cx. quinquefasciatus* (31.09%), and *Cx. pipiens* (11.99%) were the most prevalent species and *Cs. longiareolata* (0.47%), *Aedes caballus* (Theobald) (0.90%), and *Cx. bitaeniorhynchus* Giles (0.90%) were the least prevalent species. The pairwise similarities of fauna of the counties and different collecting methods and diversity indices were investigated. More ecological data, especially on host preference, seasonality, and larval habitat characteristics, are needed as a basic knowledge for any intervention measures using integrated vector management.

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## **RAGE**

### **Deactivation of the antiviral state by rabies virus through targeting and accumulation of persistently phosphorylated STAT1.**

**Manokaran, G., Audsley, M., Funakoda, H., David, C., Garnham, K., Rawlinson, S., Deffrasnes, C., Ito, N., Moseley, G.**

16-05-2022

*PLoS Pathog*

<https://doi.org/10.1371/journal.ppat.1010533>

Antagonism of the interferon (IFN)-mediated antiviral state is critical to infection by rabies virus (RABV) and other viruses, and involves interference in the IFN induction and signaling pathways in infected cells, as well as deactivation of the antiviral state in cells previously activated by IFN. The latter is required for viral spread in the host, but the precise mechanisms involved and roles in RABV pathogenesis are poorly defined. Here, we examined the capacity of attenuated and pathogenic strains of RABV that differ only in the IFN-antagonist P protein to overcome an established antiviral state. Importantly, P protein selectively targets IFN-activated phosphorylated STAT1 (pY-STAT1), providing a molecular tool

to elucidate specific roles of pY-STAT1. We find that the extended antiviral state is dependent on a low level of pY-STAT1 that appears to persist at a steady state through ongoing phosphorylation/dephosphorylation cycles, following an initial IFN-induced peak. P protein of pathogenic RABV binds and progressively accumulates pY-STAT1 in inactive cytoplasmic complexes, enabling recovery of efficient viral replication over time. Thus, P protein-pY-STAT1 interaction contributes to 'disarming' of the antiviral state. P protein of the attenuated RABV is defective in this respect, such that replication remains suppressed over extended periods in cells pre-activated by IFN. These data provide new insights into the nature of the antiviral state, indicating key roles for residual pY-STAT1 signaling. They also elucidate mechanisms of viral deactivation of antiviral responses, including specialized functions of P protein in selective targeting and accumulation of pY-STAT1.

### **Analysis of the evolution, infectivity and antigenicity of circulating rabies virus strains.**

**Cai, M., Liu, H., Jiang, F., Sun, Y., Wang, W., An, Y., Zhang, M., Li, X., Di, L., Li, Y., Yu, Y., Huang, W., Wang, Y.**  
16-05-2022

*Emerg Microbes Infect*

<https://doi.org/10.1080/22221751.2022.2078742>

Rabies virus has existed for thousands of years and is circulating in many species. In the present study, a total of 2896 rabies viruses isolated worldwide were phylogenetically classified into ten clusters based on the G gene sequence, and these clusters showed a close relationship with the hosts and regions that they were isolated from. Eighty-three representative G sequences were selected from ten clusters and were used to construct pseudoviruses using the VSV vector. The phylogenetic relationships, infectivity and antigenicity of the representative 83 pseudotyped rabies viruses were comprehensively analyzed. 83 pseudoviruses were divided into four antigenic clusters (GAgV), of which GAgV4 showed poor neutralization to all immunized sera. Further analysis showed that almost all strains in the GAgV4 were isolated from wild animals in the America, especially bats and skunks. No significant relationship in terms of phylogeny, infectivity and antigenicity was proved. Amino acid mutations at residues 231 and 436 can affect the infectivity, while mutations at residues 113, 164 and 254 may affect the sensitivity to immunized animal sera, especially residue 254. We recommend close monitoring of infectivity and antigenicity, which should be more precise than simple genetic analysis.

### **Selective plasticity of callosal neurons in the adult contralesional cortex following murine traumatic brain injury.**

**Empl, L., Chovsepian, A., Chahin, M., Kan, W., Fourneau, J., Van Steenbergen, V., Weidinger, S., Marcantoni, M., Ghanem, A., Bradley, P., Conzelmann, K., Cai, R., Ghasemigharagoz, A., Ertürk, A., Wagner, I., Kreutzfeldt, M., Merkler, D., Liebscher, S.,**

**Bareyre, F.**

12-05-2022

*Nat Commun*

<https://doi.org/10.1038/s41467-022-29992-0>

Traumatic brain injury (TBI) results in deficits that are often followed by recovery. The contralesional cortex can contribute to this process but how distinct contralesional neurons and circuits respond to injury remains to be determined. To unravel adaptations in the contralesional cortex, we used chronic in vivo two-photon imaging. We observed a general decrease in spine density with concomitant changes in spine dynamics over time. With retrograde co-labeling techniques, we showed that callosal neurons are uniquely affected by and responsive to TBI. To elucidate circuit connectivity, we used monosynaptic rabies tracing, clearing techniques and histology. We demonstrate that contralesional callosal neurons adapt their input circuitry by strengthening ipsilateral connections from pre-connected areas. Finally, functional in vivo two-photon imaging demonstrates that the restoration of pre-synaptic circuitry parallels the restoration of callosal activity patterns. Taken together our study thus delineates how callosal neurons structurally and functionally adapt following a contralateral murine TBI.

### **Establishment and clinical validation of an in-cell-ELISA-based assay for the rapid quantification of Rabies virus neutralizing antibodies.**

**Schöler, L., Le-Trilling, V., Dittmer, U., Fiedler, M., Trilling, M.**  
10-05-2022

*PLoS Negl Trop Dis*

<https://doi.org/10.1371/journal.pntd.0010425>

Neutralizing antibodies (nAbs) prevent the entry of viruses into permissive cells. Since nAbs represent correlates of protection against the Rabies lyssavirus, the presence of sufficient nAbs indicates effective vaccination. Accordingly, Rabies lyssavirus-specific nAb titers need to be determined in routine diagnostics to identify individuals being at risk of Rabies lyssavirus infections due to insufficient immunity. The current gold standard for the quantification of Rabies lyssavirus-specific nAbs is the rapid fluorescent focus inhibition test (RFFIT). However, RFFITs are expensive and labor-intensive since multiple microplate wells must be evaluated one-by-one by trained personnel through microscopic inspection, which limits the number of samples that can be processed. To overcome this disadvantage, we established a novel assay for Rabies lyssavirus-specific nAbs relying on an in-cell-ELISA (icELISA)-based neutralization test (icNT). The icNT differs from the RFFIT in the readout phase, and can be automatically quantified in minutes using broadly available microplate readers. During the establishment, icNT parameters such as antibody concentrations, permeabilization procedures, blocking reagents, infectious doses, and the duration of infection were optimized. Afterwards, a dose-dependent detection of Rabies lyssavirus neutralization was demonstrated using the WHO Standard Rabies Immunoglobulin reference. A panel of 200 sera with known

RFFIT titers revealed very good sensitivity and specificity of the icNT. Furthermore, the icNT showed very good intra- and inter-assay precision. By recognizing Rabies lyssavirus-specific antigens, the assay can be applied immediately to automatically quantify the concentration of Rabies lyssavirus nAbs in routine diagnostics or for various basic research questions such as screening for antiviral compounds.

### The effects of geographical distributions of buildings and roads on the spatiotemporal spread of canine rabies: An individual-based modeling study.

Sararat, C., Changruenggam, S., Chumkaeo, A., Wiratsudakul, A., Pan-Ngum, W., Modchang, C.

10-05-2022

*PLoS Negl Trop Dis*

<https://doi.org/10.1371/journal.pntd.0010397>

Rabies is a fatal disease that has been a serious health concern, especially in developing countries. Although rabies is preventable by vaccination, the spread still occurs sporadically in many countries, including Thailand. Geographical structures, habitats, and behaviors of host populations are essential factors that may result in an enormous impact on the mechanism of propagation and persistence of the disease. To investigate the role of geographical structures on the transmission dynamics of canine rabies, we developed a stochastic individual-based model that integrates the exact configuration of buildings and roads. In our model, the spatial distribution of dogs was estimated based on the distribution of buildings, with roads considered to facilitate dog movement. Two contrasting areas with high- and low-risk of rabies transmission in Thailand, namely, Hatyai and Tephra districts, were chosen as study sites. Our modeling results indicated that the distinct geographical structures of buildings and roads in Hatyai and Tephra could contribute to the difference in the rabies transmission dynamics in these two areas. The high density of buildings and roads in Hatyai could facilitate more rabies transmission. We also investigated the impacts of rabies intervention, including reducing the dog population, restricting owned dog movement, and dog vaccination on the spread of canine rabies in these two areas. We found that reducing the dog population alone might not be sufficient for preventing rabies transmission in the high-risk area. Owned dog confinement could reduce more the likelihood of rabies transmission. Finally, a higher vaccination coverage may be required for controlling rabies transmission in the high-risk area compared to the low-risk area.

### Binding induced isothermal amplification reaction to activate CRISPR/Cas12a for amplified electrochemiluminescence detection of rabies viral RNA via DNA nanotweezer structure switching.

Liu, S., Wang, C., Wang, Z., Xiang, K., Zhang, Y., Fan, G., Zhao, L., Han, H., Wang, W.

12-02-2022

*Biosens Bioelectron*

<https://pubmed.ncbi.nlm.nih.gov/35180689>

Rabies is caused by the infection of Rabies virus, it leads to fatal encephalitis, developing a highly sensitive and specific detection method for Rabies virus remains a challenge. Herein, we report an electrochemiluminescence (ECL) biosensor for Rabies viral RNA based on dual-signal amplification and DNA nanotweezers (DTs). Dual-signal amplification process includes target binding induced isothermal amplification and CRISPR-based amplification. In the presence of target RNA, two assisted probes simultaneously hybridized with it to trigger isothermal amplification with the help of polymerase and nicking enzyme. This process generated a large amount of single-stranded DNA (ssDNA) as products. The products hybridized with CRISPR RNA to activate the trans-cleavage activity of Cas12a to indiscriminately cleave predesigned single-stranded trigger (ST) strands. After mixing the cleavage products with DTs and hemin molecules, DTs cannot be closed by cleaved ST strands to capture hemin to the electrode to quench the ECL signal. Therefore, the higher concentration of the target, the stronger intensity of the ECL signal. The detection limit is as low as 2.8 pM and the detection range is from 5 pM to 5 nM with excellent specificity and stability. The proposed method provides a promising strategy for Rabies detection, and can be easily adapted to other analytes via reasonable design as a valuable and versatile tool in bioanalysis.

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## TRACHOME

### Neglected tropical diseases in Australia: a narrative review.

Revue de littérature

Kurcheid, J., Gordon, C., Clarke, N., Wangdi, K., Kelly, M., Lal, A., Mutombo, P., Wang, D., Mationg, M., Clements, A., Muhi, S., Bradbury, R., Biggs, B., Page, W., Williams, G., McManus, D., Gray, D.

12-05-2022

*Med J Aust*

<https://doi.org/10.5694/mja2.51533>

- Neglected tropical diseases (NTDs) represent a threat to the health, wellbeing and economic prosperity of billions of people worldwide, often causing serious disease or death.
- Commonly considered diseases of low and middle-income nations, the presence of NTDs in high income countries such as Australia is often overlooked.
- Seven of the 20 recognised NTDs are endemic in Australia: scabies, soil-transmitted helminths and strongyloidiasis, echinococcosis, Buruli ulcer, leprosy, trachoma, and snakebite envenoming.
- Dengue, while not currently endemic, poses a risk of establishment in Australia. There are occasional outbreaks of dengue fever, with local transmission, due to introductions in travellers from endemic regions.
- Similarly, the risk of introduction of other NTDs from neighbouring countries is a concern. Many NTDs

are only seen in Australia in individuals travelling from endemic areas, but they need to be recognised in health settings as the potential consequences of infection can be severe. •In this review, we consider the status of NTDs in Australia, explore the risk of introducing and contracting these infections, and emphasise the negative impact they have on the health of Australians, especially Aboriginal and Torres Strait Islander peoples.

### Seasonal variation in water use for hygiene in Oromia, Ethiopia, and its implications for trachoma control: An intensive observational study.

Greenland, K., Czerniewska, A., Guye, M., Legesse, D., Ahmed Mume, A., Shafi Abdurahman, O., Abraham Aga, M., Miecha, H., Shumi Bejiga, G., Sarah, V., Burton, M., Last, A.

13-05-2022

*PLoS Negl Trop Dis*

<https://doi.org/10.1371/journal.pntd.0010424>

If facial hygiene practices vary seasonally this could have important implications for the design of interventions for trachoma control. This observational study was conducted to explore seasonal variation in hygiene behaviours in 9 households with at least one child aged 1-9 years-of-age in the West Arsi zone in rural Oromia, Ethiopia. Sixty-one household members were observed intensively over two days in the dry season (January), the rainy season (July) and during the harvest period (October) in 2018. Structured record forms were used to document household water availability and use. Daily water use per capita was very low in all seasons (3.1-4.2 litres). Around one third of water consumed in households in all seasons was associated with body washing. Soap was used during 44 of 677 (6%) of these observed occasions and half of all body washes (n = 340; 50%) included face washing. Overall, 95% of 58 individuals washed their faces at least once between 06:30h and 21:30h in the dry season (21% with soap), compared with 79% in the rainy season (2% with soap) (p = 0.013). Sixty-five percent of householders washed their faces during the harvest observation period (06:30h to 17:30h), none of whom used soap. Twenty-eight percent of 204 children aged 11 and under still had ocular or nasal discharge on their faces after washing. Seventy-three percent of those who washed their faces did so more than once in the dry season, compared with 33% in the rainy season (p<0.001). Face washing occurred throughout the day during the dry season, with a clear peak in the early morning and extra washes in the early evening. Face washing mainly took place in the early morning in the other two seasons. Genuine water scarcity in this area is likely to limit the impact of face washing interventions for trachoma control in the absence of water supply interventions. However, face washing was most common at the time of year when water is the hardest to come by, and seasonal differences in behaviour should be considered in any resulting intervention design.

## ULCERE DE BURULI

### Neglected tropical diseases in Australia: a narrative review.

Revue de littérature

Kurcheid, J., Gordon, C., Clarke, N., Wangdi, K., Kelly, M., Lal, A., Mutombo, P., Wang, D., Mationg, M., Clements, A., Muhi, S., Bradbury, R., Biggs, B., Page, W., Williams, G., McManus, D., Gray, D.

12-05-2022

*Med J Aust*

<https://doi.org/10.5694/mja2.51533>

•Neglected tropical diseases (NTDs) represent a threat to the health, wellbeing and economic prosperity of billions of people worldwide, often causing serious disease or death. •Commonly considered diseases of low and middle-income nations, the presence of NTDs in high income countries such as Australia is often overlooked. •Seven of the 20 recognised NTDs are endemic in Australia: scabies, soil-transmitted helminths and strongyloidiasis, echinococcosis, Buruli ulcer, leprosy, trachoma, and snakebite envenoming. •Dengue, while not currently endemic, poses a risk of establishment in Australia. There are occasional outbreaks of dengue fever, with local transmission, due to introductions in travellers from endemic regions. •Similarly, the risk of introduction of other NTDs from neighbouring countries is a concern. Many NTDs are only seen in Australia in individuals travelling from endemic areas, but they need to be recognised in health settings as the potential consequences of infection can be severe. •In this review, we consider the status of NTDs in Australia, explore the risk of introducing and contracting these infections, and emphasise the negative impact they have on the health of Australians, especially Aboriginal and Torres Strait Islander peoples.

## PIAN

## LEPRE

### Neglected tropical diseases in Australia: a narrative review.

Revue de littérature

Kurcheid, J., Gordon, C., Clarke, N., Wangdi, K., Kelly, M., Lal, A., Mutombo, P., Wang, D., Mationg, M., Clements, A., Muhi, S., Bradbury, R., Biggs, B., Page, W., Williams, G., McManus, D., Gray, D.

12-05-2022

*Med J Aust*

<https://doi.org/10.5694/mja2.51533>

•Neglected tropical diseases (NTDs) represent a threat to the health, wellbeing and economic prosperity of billions of people worldwide, often causing serious disease or death. •Commonly considered diseases of low and middle-income nations, the presence of NTDs in high income countries such as Australia is often overlooked. •Seven of the 20 recognised NTDs are endemic in Australia: scabies, soil-transmitted helminths and strongyloidiasis, echinococcosis, Buruli ulcer, leprosy, trachoma, and snakebite envenoming. •Dengue, while not currently endemic, poses a risk of establishment in Australia. There are occasional outbreaks of dengue fever, with local transmission, due to introductions in travellers from endemic regions. •Similarly, the risk of introduction of other NTDs from neighbouring countries is a concern. Many NTDs are only seen in Australia in individuals travelling from endemic areas, but they need to be recognised in health settings as the potential consequences of infection can be severe. •In this review, we consider the status of NTDs in Australia, explore the risk of introducing and contracting these infections, and emphasise the negative impact they have on the health of Australians, especially Aboriginal and Torres Strait Islander peoples.

### Arginase 1 is a marker of protection against illness in contacts of leprosy patients.

**da Silva Prata, R., Mendes, M., Soares, V., França-Costa, J., Sales, A., Duppré, N., de Matos Borges, V., da Silva, T., Bozza, P., Bozza, M., Sarno, E., Moraes, M., Sperandio da Silva, G., Pinheiro, R.**  
12-05-2022

*Sci Rep*

<https://doi.org/10.1038/s41598-022-11944-9>

Leprosy household contacts are generally more prone to develop the disease compared to the general population. Previous studies have demonstrated that genes related to the alternative activation (M2) profile in macrophages are associated with the increased bacillary load in multibacillary leprosy patients (MB), and that contacts of MB patients have a higher risk of contracting the disease. In addition, positive serological responses to PGL-1 or LID-1 are associated with a higher risk of disease. We performed a 5-year follow-up of contacts of leprosy patients and evaluated the pattern of gene and protein expression in cells from contacts that developed leprosy during this period. Leprosy household contacts had decreased soluble CD163 and heme oxygenase 1 (HO-1) serum levels when compared with healthy donors and leprosy patients. In contrast, arginase 1 activities were higher in contacts when compared with both healthy donors and leprosy patients. Of the contacts, 33 developed leprosy during the follow-up. Gene expression analysis revealed reduced ARG1 expression in these contacts when compared with contacts that did not develop disease. Arginase activity was a good predictive marker of protection in contacts (sensitivity: 90.0%, specificity: 96.77%) and the association with serology for anti-PGL-1 and anti-LID-1 increased the sensitivity to 100%. Altogether, the data presented here demonstrate a positive

role of arginase against leprosy and suggest that the evaluation of arginase activity should be incorporated into leprosy control programs in order to aid in the decision of which contacts should receive chemoprophylaxis.

### Implementation of genetic screening test to reduce the incidence of dapsone hypersensitivity syndrome among patients with leprosy in Papua, Indonesia: a study protocol.

**Krismawati, H., Ferdiana, A., Irwanto, A., Budiawan, T., Imaniar, C., Wahyuni, T., Singh, P., Mieras, L., Pongtiku, A.**

11-05-2022

*BMJ Open*

<https://doi.org/10.1136/bmjopen-2021-057173>

**Introduction:** The mainstay of leprosy treatment is multidrug treatment (MDT), which contains rifampicin, dapsone and clofazimine. The occurrence of dapsone hypersensitivity syndrome (DHS), a sudden, potentially fatal and traumatic adverse reaction due to dapsone, may affect treatment adherence and may result in fatality if untreated. Before MDT administration, screening for *HLA-B\*13:01* in patients with leprosy can potentially reduce DHS risk. The study aims to assess the effectiveness of using a screening test for *HLA-B\*13:01* in reducing the incidence of DHS and to evaluate the feasibility of using the quantitative PCR-based screening tool as DHS predictors before dapsone administration using individual patient testing in a referral centralised-lab model. **Methods and analysis:** A total of 310 newly diagnosed patients with leprosy will be recruited from health centres in two highly endemic districts in Indonesia. Dried blood will be taken on filter paper as the specimen receptacle to collect DNA from the patients and transported at room temperature to the leprosy referral laboratory before MDT administration. Checking for *HLA-B\*13:01* from human DNA is performed using the Nala PGx 1301 V.1 kit. The results will be shared with the leprosy health workers on the site via phone call and courier. Patients with a positive test result will be treated with MDT without dapsone, and patients with a negative result will be treated with complete MDT. Physical examination (weight, height, skin, muscle and nerve function examination), complete blood tests (including renal function test) will be carried out at baseline. Follow-up will be performed at the fourth and eighth weeks to observe any development of adverse drug reactions. **Ethics and dissemination:** The ethical approval for the study was issued by the Ethical Committee of the National Institute of Health Research and Development, Ministry of Health, Indonesia. Written informed consent will be sought from all participants.

## TRYPANOSOMES (TRYPANOSOMIASE ET MALADIE DE CHAGAS)

### Hybrid-Compounds Against Trypanosomiases.

Nunes, J., Ferreira da Silva-Júnior, E.

09-05-2022

*Curr Drug Targets*

<https://doi.org/10.2174/1389450123666220509202352>

Neglected tropical diseases (NTDs) are a global public health problem that is associated with approximately 20 conditions. Among these, Chagas disease (CD), caused by *Trypanosoma cruzi*, and human African trypanosomiasis (HAT), caused by *T. brucei gambiense* or *T. brucei rhodesiense*, which affect mainly the populations of the countries from the American continent and sub-Saharan Africa. Pharmacological therapies used for such illnesses are not yet fully effective. In this context, the search for new therapeutic alternatives against these diseases becomes necessary. A drug design tool, recently recognized for its effectiveness in obtaining ligands capable of modulating multiple targets for complex diseases, concerns molecular hybridization. Therefore, this review aims to demonstrate the importance of applying molecular hybridization in facing the challenges of developing prototypes as candidates for the treatment of parasitic diseases. Therefore, studies involving different chemical classes that investigated and used hybrid compounds in recent years were compiled in this work, such as thiazolidinones, naphthoquinones, quinolines, and others. Finally, this review covers several applications of the exploration of molecular hybridization as a potent strategy in the development of molecules potentially active against trypanosomiases, in order to provide information that can help in designing new drugs with trypanocidal activity.

### Genome Size Variation of Chagas Disease Vectors of the Rhodniini Tribe.

Merle, M., Filée, J., de Oliveira, J., Almeida, C., Mougel, F., Bastide, H., Girondot, M., da Rosa, J., Harry, M.

16-05-2022

*Am J Trop Med Hyg*

<https://doi.org/10.4269/ajtmh.21-0394>

The genome size of five *Rhodnius* species (*R. milesi*, *R. nasutus*, *R. neivai*, *R. prolixus*, and *R. robustus*) and two *Psammolestes* species (*P. coroedes* and *P. tertius*) were estimated using flow cytometry and/or k-mer distributions in genome sequences. Phylogenetic generalized linear mixed models highlighted significant genome size variations among species and between sexes, with *R. prolixus* showing the largest genome. In this study we provide the first data on female genome size in Triatominae. For five species, female genome size did not differ from males, except for *R. robustus*, where females had smaller genomes. Genome size estimations based on the k-mer distribution method were less than those estimated from flow cytometry, but both methods exhibited the same pattern of sexual differences. Further

genomic studies are needed to infer whether genome size variation could be an adaptive trait in *Rhodnius*.

### Use of benznidazole to treat chronic Chagas disease: An updated systematic review with a meta-analysis.

Crespillo-Andújar, C., Comeche, B., Hamer, D., Arevalo-Rodríguez, I., Alvarez-Díaz, N., Zamora, J., Pérez-Molina, J.

16-05-2022

*PLoS Negl Trop Dis*

<https://doi.org/10.1371/journal.pntd.0010386>

**Background:** Approximately 6 million people worldwide are affected by Chagas disease, with many in the chronic phase of the disease (CCD). It is crucial to evaluate the effectiveness of benznidazole for CCD treatment. **Methods/Principal findings:** We updated a meta-analysis published in 2009 up to February 2021, including controlled trials (RCT) and prospective observational studies (OBS) that compared benznidazole vs placebo/no-treatment (P/nT). Main outcomes evaluated were clinical progression (CP) and seroreversion with subgroup analysis performed according to study design and participants' age. Parasitological response and safety were also described. We identified 879 articles and selected nine for inclusion (corresponding to eight studies). After adding the nine articles from the previous meta-analysis, 17 studies were analyzed corresponding to 6640 patients. The odds ratio (OR) for seroreversion in children treated with benznidazole vs P/nT was 38.3 (95%CI: 10.7-137) and 34.9 (95%CI: 1.96-624.09) in RCT and OBS, respectively. In adults the OR for seroreversion in OBS was 17.1 (95%CI: 2.3-129.1). CP was only evaluated in adults, where benznidazole did not demonstrate a beneficial effect: OR 0.93 (95%CI: 0.8-1.1) and OR 0.49 (95%CI: 0.2-1.2) for RCT and OBS, respectively. Most outcomes were deemed to have a low level of certainty, except for the beneficial effect in children and the low efficacy in adults (moderate certainty). **Conclusions:** Benznidazole should be recommended for CCD in children, though this is only based on serological response and a moderate grade of evidence, while in adults benznidazole efficacy remains uncertain. More data on clinical efficacy of benznidazole in CCD is needed in both children and adults.

### Label-free LC-MS/MS proteomics analyses reveal proteomic changes in oxidative stress and the SOD antioxidant strategy in TM cells.

Li, Q., Zhang, L., Xu, Y.

14-05-2022

*Clin Proteomics*

<https://doi.org/10.1186/s12014-022-09350-4>

**Background:** Treatment for glaucoma has traditionally been limited to reducing intraocular pressure (IOP). Inhibiting oxidative stress in the trabecular meshwork (TM) is regarded as a new treatment for glaucoma; however, the effects do not meet expectations. Exploring the mechanism by which oxidative stress and antioxidant stress occur in TM cells will offer clues to aid the development of new treatments. **Methods and results:** In our study, we cultured TM cells and used H<sub>2</sub>O<sub>2</sub> and SOD to induce and inhibit oxidative stress,

respectively. Label-free LC-MS/MS quantitative proteomic analysis was conducted to analyze the differentially expressed proteins and relevant signaling pathways. A total of 24 upregulated proteins and 18 downregulated proteins were identified under oxidative stress. PTGS2, TGF $\beta$ 2 and ICAM-1 are the key proteins. The PTGS2/NF- $\kappa$ B pathway, TGF- $\beta$ /Smad signaling pathway and AGE-RAGE signaling pathway in diabetic complications may be the major signaling pathways under conditions of ROS-induced damage in TM cells. Seventy-eight proteins were upregulated and 73 proteins were downregulated under antioxidant stress in TM cells. The key protein was ICAM-1, which participates in the African trypanosomiasis pathway, one of the most important pathways under antioxidant stress. Combining the results of the Venn diagram with protein-protein interactions (PPIs), ICAM-1 was identified as the major protein. Cell Counting Kit-8 (CCK-8) and western blotting (WB) were used to reveal that suppressing the expression of ICAM-1 would improve the survival of TM cells. **Conclusions:** Key proteins and signaling pathways play important roles in the mechanisms of oxidative stress and antioxidant strategies in TM cells. ICAM-1 knockdown can suppress the apoptosis of TM cells induced by H<sub>2</sub>O<sub>2</sub>, which may reveal new therapeutic targets and biomarkers for glaucoma.

### Unusual neurological presentation of second stage African trypanosomiasis in a young boy: a case report.

Ibrahim, E., Elmahal, M., Ahmed, K., Hasabo, E., Omer, M.  
12-05-2022

*BMC Pediatr*

<https://doi.org/10.1186/s12887-022-03313-2>

**Background:** In South Sudan, sleeping sickness is a frequent condition caused by human African trypanosomiasis. There are two stages that are well-known. When the CNS is affected, especially with *Trypanosoma gambiense* infection, the early hemolymphatic stage and the late encephalitic stage have been observed, including mental, motor, and sensory symptoms. In this case, second-stage African trypanosomiasis manifested itself in an atypical neurological manner. **Case presentation:** A 16-year-old boy from South Sudan referred to Sudan National Centre for Neurological Sciences, Khartoum, Sudan suffering from non-convulsive status epilepticus, mental deterioration and behavioral changes for the last nine months. He was conscious but disorientated. Low hemoglobin concentration, elevated ESR, enlarged spleen and positive card agglutination test for trypanosomiasis was found in this patient. Electro-encephalogram (EEG) found an on-going generalized seizure activity. The patient showed improvement after management with carbamazepine and tonic. **Conclusion:** Our case highlights that late second stage African trypanosomiasis with neurological complications such as non-convulsive status epilepticus should be suspected in any patient who developed progressive cognitive decline and behavioral changes following long standing history of African Trypanosomiasis and routine Electro-encephalogram EEG is the best tool to diagnose non convulsive status epilepticus.

### Monitoring the elimination of gambiense human African trypanosomiasis in the historical focus of Batié, South-West Burkina Faso.

Compaoré, C., Kaboré, J., Ilboudo, H., Thomas, L., Falzon, L., Bamba, M., Sakande, H., Koné, M., Kaba, D., Bougouma, C., Adama, I., Amathe, O., Belem, A., Fèvre, E., Büscher, P., Lejon, V., Jamonneau, V.

11-05-2022

*Parasite*

<https://doi.org/10.1051/parasite/2022024>

The World Health Organisation has targeted the elimination of human African trypanosomiasis (HAT) as zero transmission by 2030. Continued surveillance needs to be in place for early detection of re-emergent cases. In this context, the performance of diagnostic tests and testing algorithms for detection of the re-emergence of *Trypanosoma brucei gambiense* HAT remains to be assessed. We carried out a door-to-door active medical survey for HAT in the historical focus of Batié, South-West Burkina Faso. Screening was done using three rapid diagnostic tests (RDTs). Two laboratory tests (ELISA/T. b. gambiense and immune trypanolysis) and parasitological examination were performed on RDT positives only. In total, 5883 participants were screened, among which 842 (14%) tested positive in at least one RDT. Blood from 519 RDT positives was examined microscopically but no trypanosomes were observed. The HAT Sero-K-Set test showed the lowest specificity of 89%, while the specificities of SD Bioline HAT and rHAT Sero-Strip were 92% and 99%, respectively. The specificity of ELISA/T. b. gambiense and trypanolysis was 99% (98-99%) and 100% (99-100%), respectively. Our results suggest that T. b. gambiense is no longer circulating in the study area and that zero transmission has probably been attained. While a least cost analysis is still required, our study showed that RDT preselection followed by trypanolysis may be a useful strategy for post-elimination surveillance in Burkina Faso.

### Novel trypanocidal thiophen-chalcone cruzain inhibitors: structure- and ligand-based studies.

de Oliveira, A., Valli, M., Ferreira, L., Souza, J., Krogh, R., Meier, L., Abreu, H., Voltolini, B., Llanes, L., Nunes, R., Braga, A., Andricopulo, A.

11-05-2022

*Future Med Chem*

<https://doi.org/10.4155/fmc-2022-0013>

**Background:** Chagas disease is a neglected tropical disease that affects millions of people worldwide and for which no effective treatment is available. **Materials & methods:** 17 chalcones were synthesized, for which the inhibition of cruzain and trypanocidal activity were investigated. **Results:** Chalcone **C8** showed the highest cruzain inhibitory (IC<sub>50</sub> = 0.536  $\mu$ m) and trypanocidal activity (IC<sub>50</sub> = 0.990  $\mu$ m). Molecular docking studies showed interactions involving Asp161 and the thiophen group interacting with the S2 subsite. Furthermore, quantitative structure-activity relationship ( $q^2 = 0.786$ ;  $r^2 = 0.953$ ) and density functional

theory studies were carried out, and a correlation between the lowest unoccupied molecular orbital surface and trypanocidal activity was observed. **Conclusion:** These results demonstrate that these chalcones are worthwhile hits to be further optimized in Chagas disease drug discovery programs.

### Presence of Anti-*T. cruzi* Antibodies in Inhabitants and Dogs of Two Rural Settlements in the Sierra de Los Tuxtlas, Veracruz, Mexico.

Benítez-Villa, G., López-Monteon, A., Waleckx, E., Dumonteil, E., Márquez-Fernández, A., Roviroso-Hernández, M., Orduña-García, F., Guzmán-Gómez, D., Ramos-Ligonio, A.

10-05-2022

*Acta Parasitol*

<https://doi.org/10.1007/s11686-022-00557-x>

**Purpose:** The aim of this study was to identify the risk factors associated with house infestation by *Triatoma dimidiata* as well as with *Trypanosoma cruzi* infection in humans and owned dogs in two rural communities from the municipality of Catemaco, Veracruz, Mexico. **Methods:** One hundred and 16 human blood samples and 34 dog blood samples were collected. The presence of anti-*T. cruzi* antibodies was determined using four different ELISA assays. Moreover, reactive ELISA sera from humans and dogs were processed by indirect immunofluorescence (IFI) to confirm the presence of anti-*T. cruzi* antibodies. **Results:** Serologic tests for *T. cruzi* infection showed a prevalence of 5.1% (6/116) in humans and of 50% (17/34) in owned dogs. **Conclusion:** The presence of animals (dogs, chickens and wild animals), as well as some characteristics of house construction were identified as risk factors for infestation and infection. Complementary studies must be carried out to allow a better understanding of the transmission dynamics in the state of Veracruz, Mexico, and the implementation of adequate control programs.

### Microevolution of *Trypanosoma cruzi* reveals hybridization and clonal mechanisms driving rapid genome diversification.

Matos, G., Lewis, M., Talavera-López, C., Yeo, M., Grisard, E., Messenger, L., Miles, M., Andersson, B.

10-05-2022

*Elife*

<https://doi.org/10.7554/eLife.75237>

Protozoa and fungi are known to have extraordinarily diverse mechanisms of genetic exchange. However, the presence and epidemiological relevance of genetic exchange in *Trypanosoma cruzi*, the agent of Chagas disease, has been controversial and debated for many years. Field studies have identified both predominantly clonal and sexually recombining natural populations. Two of six natural *T. cruzi* lineages (TcV and TcVI) show hybrid mosaicism, using analysis of single-gene locus markers. The formation of hybrid strains in vitro has been achieved and this provides a framework to study the mechanisms and adaptive significance of genetic exchange. Using whole genome sequencing of a set of experimental

hybrids strains, we have confirmed that hybrid formation initially results in tetraploid parasites. The hybrid progeny showed novel mutations that were not attributable to either (diploid) parent showing an increase in amino acid changes. In long-term culture, up to 800 generations, there was a variable but gradual erosion of progeny genomes towards triploidy, yet retention of elevated copy number was observed at several core housekeeping loci. Our findings indicate hybrid formation by fusion of diploid *T. cruzi*, followed by sporadic genome erosion, but with substantial potential for adaptive evolution, as has been described as a genetic feature of other organisms, such as some fungi.

## LEISHMANIOSE

### Role of Chemokines in the Pathogenesis of Visceral Leishmaniasis.

Kumar, R., Bhatia, M., Pai, K.

09-05-2022

*Curr Med Chem*

<https://doi.org/10.2174/0929867329666220509171244>

Visceral leishmaniasis (VL; also known as kala-azar), caused by the protozoan parasite *Leishmania donovani* is characterized by the inability of the host to generate an effective immune response. The manifestations of the disease depends on involvement of various immune components such as activation of macrophages, cell mediated immunity, secretion of cytokines and chemokines, etc. Macrophages are the final host cells for *Leishmania* parasites to multiply, and they are the key to a controlled or aggravated response that leads to clinical symptoms. The two most common macrophage phenotypes are M1 and M2. The pro-inflammatory microenvironment (mainly by IL-1 $\beta$ , IL-6, IL-12, IL-23, and TNF- $\alpha$  cytokines) and tissue injury driven by classically activated macrophages (M1-like) and wound healing driven by alternatively activated macrophages (M2-like) in an anti-inflammatory environment (mainly by IL-10, TGF- $\beta$ , chemokine ligand (CCL)1, CCL2, CCL17, CCL18, and CCL22). Moreover, on polarized Th cells, chemokine receptors are expressed differently. Typically, CXCR3 and CCR5 are preferentially expressed on polarized Th1 cells, whereas CCR3, CCR4 and CCR8 have been associated with the Th2 phenotype. Further, the ability of the host to produce a cell-mediated immune response capable of regulating and/or eliminating the parasite is critical in the fight against the disease. Here, we review the interactions between parasites and chemokines and chemokines receptors in the pathogenesis of VL.

### Forging Ahead the Repositioning of Multitargeted Drug Ivermectin.

Atmakuri, S., Nene, S., Khatri, D., Singh, S., Sinha, V., Srivastava, S.

16-05-2022

*Curr Drug Deliv*
<https://doi.org/10.2174/1567201819666220516163242>

With the advent of ivermectin, tremendous improvement in public health has been observed, especially in the treatment of onchocerciasis and lymphatic filariasis that created chaos mostly in rural, sub-Saharan Africa and Latin American countries. The discovery of ivermectin became a boon to millions of people that had suffered in the pandemic and still hold its pharmacological potential against these. Ivermectin continued to surprise scientists because of its notable role in the treatment of various other tropical diseases (Chagas, leishmaniasis, worm infections, etc.) and is viewed as the safest drug with the least toxic effects. The current review highlights its role in unexplored avenues towards forging ahead of the repositioning of this multitargeted drug in cancer, viral (the evaluation of the efficacy of ivermectin against SARS-Cov-2 is under investigation) and bacterial infection and malaria. This article also provides a glimpse of regulatory considerations of drug repurposing and current formulation strategies. Due to its broad-spectrum activity, multitargeted nature and promising efforts are put towards the repurposing of this drug throughout the field of medicine. This single drug originated from a microbe, changed the face of global health by proving its unmatched success and progressive efforts continue in maintaining its bequest in the management of global health by decreasing the burden of various diseases worldwide.

### Understanding the risk perception of visceral leishmaniasis exposure and the acceptability of sandfly protection measures among migrant workers in the lowlands of Northwest Ethiopia: a health belief model perspective.

Berhe, R., Spigt, M., Schneider, F., Paintain, L., Adera, C., Nigusie, A., Gizaw, Z., Tesfaye, Y., Elnaiem, D., Alemayehu, M.  
16-05-2022

*BMC Public Health*
<https://doi.org/10.1186/s12889-022-13406-3>

**Background:** Visceral leishmaniasis (VL) is the leading cause of health concerns among Ethiopian migrant workers. Understanding risk perception and health-protective behavior are significant challenges in the prevention and eradication of the disease. As a result, studies are required to assess these important epidemiological factors, which will provide guidance on how to assist migrant workers in taking preventive measures against VL. **Method:** We conducted qualitative research among migrant workers on seasonal agricultural farms in Northwest Ethiopia between June and November 2019 to assess their perception of the risk of contracting VL and their willingness to use protective measures against the disease. Seventeen focus group discussions and 16 key informant interviews were conducted to study migrant workers' risk perception in relation to sandfly bite exposure and use of sandfly control measures. For analysis, all interviews were recorded, transcribed, and

translated. ATLAS.ti was used to perform qualitative content analysis on the data. **Result:** Migrant workers are fearful of VL because of previous exposure and the disease's prevalence in the area. They believe, however, that VL is a minor illness that is easily treated. While Insecticide Treated Nets (ITNs) are widely accepted as a protective measure, there are still reservations about using them due to the seasonality of the transmission, difficulties in hanging them on farm areas, and a preference for alternative traditional practices. Regardless of perceived self-efficacy, the central cues were the message delivered by the health workers and an increase in sandfly bite irritation. Based on the findings, three levels of intervention modalities are suggested: 1) increasing pre-arrival awareness through outdoor media (posters, stickers, billboards), 2) encouraging proper use of protective measures upon arrival at farm camps, and 3) informing departing workers on disease recognition and best practices for health-seeking continuous use of protective measures at home. **Conclusion:** This finding suggests that VL prevention interventions should focus on individuals' perceptions in order to promote consistent use of protective measures. The findings are highly useful in planning effective interventions against VL.

### False-positive rapid diagnostic test for malaria in new world cutaneous leishmaniasis: a tale of two travelers.

Unterborn, R., Henao-Cordero, J., Kousari, A., Ramanan, P., Franco-Paredes, C., Madinger, N.  
09-05-2022

*Ther Adv Infect Dis*
<https://doi.org/10.1177/20499361221097791>

We report two immigrants from Cuba seen in a US travel clinic with a confirmed diagnosis of cutaneous leishmaniasis in whom we also suspected malaria co-infection. Both individuals likely acquired leishmaniasis in the Darien Gap region of Panama during their migratory path to the United States. As part of their clinical workup to rule out malaria, a rapid malaria antigen testing for *P. falciparum* was obtained and reported positive in both patients. However, both a qualitative reverse transcription-polymerase chain reaction (RT-PCR) for *Plasmodium falciparum* in blood and repeated thick-and-thin smear direct microscopy were negative in both, deeming the rapid malaria test as a false-positive. Thus, confirmation of malaria in travelers requires thick-and-thin film microscopy. Clinicians should be aware of the growing recognition of the possibility of false-positive malaria rapid diagnostic tests in those with some forms of leishmaniasis.

### Splenic nodules as guiding signs in pediatric population with visceral leishmaniasis.

Casero-González, M., Izquierdo-Palomares, L., Cañuelo-Ruiz, O., Montero-Yéboles, R., de la Torre-Aguilar, M., Ruiz-Sáez, B.  
12-05-2022

*An Pediatr (Engl Ed)*
<https://pubmed.ncbi.nlm.nih.gov/35570190>

### Visceral leishmaniasis versus treated multiple myeloma relapse: Spleen as the main clue.

Boulevard-Chollet, X., Cañete-Sánchez, F., Hernández-Pérez, P., Romero-Robles, L., Garrastachu-Zumarán, P.

12-05-2022

*Rev Esp Med Nucl Imagen Mol (Engl Ed)*

<https://pubmed.ncbi.nlm.nih.gov/35570142>

### Burden and risk factors of cutaneous leishmaniasis in Ethiopia: a systematic review and meta-analysis.

Revue de littérature

Shita, E., Nibret, E., Munshea, A., Gashaw, B.

15-05-2022

*Int J Dermatol*

<https://doi.org/10.1111/ijd.16265>

**Introduction:** Cutaneous leishmaniasis (CL) is a major public health problem in Ethiopia. About 30 million people are at risk, and there are 20,000 to 50,000 new cases annually. It is maintained by rock hyraxes and Phlebotomus sand flies. Different studies showed the presence and risk factors of CL. However, there is no study on the pooled prevalence and risk factors. This study aimed to determine the pooled prevalence and risk factors of CL in Ethiopia. **Method:** We retrieved published articles from different databases. The review was conducted based on PRISMA guidelines. The meta-analysis was done with Stata software version 14. The forest plot with random-effect model and inverse variance index was used to estimate the pooled prevalence with 95% confidence interval and heterogeneity of articles, respectively. **Results:** A total of 99,226 people from 19 studies were screened. The overall pooled prevalence of CL was 20.4% with 95% CI (15.67-25.13%). The pooled prevalence is a weighted average of results of the included 19 studies. Highest pooled prevalence, 65.39% (95% CI: 61.14-69.47%), was in Southern Nations, Nationalities and Peoples' Region (SNNPR), and the lowest was 1.53% (95% CI: 1.43-1.63%) in Amhara Region. Children were the most affected age group. Living in a home close to farmlands, outdoor sleeping behavior, the presence of gorge, hyrax, cracked walls, animal dung, and other cases in the neighborhood were identified as risk factors for CL.

**Conclusion:** There is high burden of CL in Ethiopia. Larger surveys are required. Health education on the prevention and control strategies shall be implemented.

### Tissue tropism: Is it an intrinsic characteristic of Leishmania species?

Revue de littérature

Maatallah, I., Akarid, K., Lemrani, M.

11-05-2022

*Acta Trop*

<https://pubmed.ncbi.nlm.nih.gov/35568069>

The genus *Leishmania* comprises a wide range of species, some of which are pathogenic to humans and each of which has a different tissue preference, resulting in one of the three clinical forms of human leishmaniasis: visceral, cutaneous, or

mucocutaneous. Although, all pathogenic species are deposited intradermally in the mammalian host upon an infectious sand fly bite, only the viscerotropic strains can leave the skin and reach the internal organs. We assume that *Leishmania* tissue tropism is not only the result of *Leishmania* genetic determinism but is also governed by the interaction of the parasite with different vectorial and human host elements. To shed light on these elements and key steps determining the course of the infection, we describe throughout this review the disease's progression from the early stages of infection taking place in the skin to the late stages succeeding in the parasite's visceral dissemination. Hence, we address the question of *Leishmania* tropism, through providing relevant hypotheses and answers gathered from the literature.

### Translationally Controlled Tumor Protein-Mediated Stabilization of Host Antiapoptotic Protein MCL-1 Is Critical for Establishment of Infection by Intramacrophage Parasite *Leishmania donovani*.

Giri, J., Basu, M., Roy, S., Mishra, T., Jana, K., Chande, A., Ukil, A.

13-05-2022

*J Immunol*

<https://pubmed.ncbi.nlm.nih.gov/35562118>

In the early phase of infection, the intramacrophage pathogen *Leishmania donovani* protects its niche with the help of the antiapoptotic protein myeloid cell leukemia-1 (MCL-1). Whether *Leishmania* could exploit MCL-1, an extremely labile protein, at the late phase is still unclear. A steady translational level of MCL-1 observed up to 48 h postinfection and increased caspase-3 activity in MCL-1-silenced infected macrophages documented its importance in the late hours of infection. The transcript level of MCL-1 showed a sharp decline at 6 h postinfection, and persistent MCL-1 expression in cyclohexamide-treated cells negates the possibility of de novo protein synthesis, thereby suggesting infection-induced stability. Increased ubiquitination, a prerequisite for proteasomal degradation of MCL-1, was also found to be absent in the late hours of infection. Lack of interaction with its specific E3 ubiquitin ligase MULE (MCL-1 ubiquitin ligase E3) and specific deubiquitinase USP9X prompted us to search for blockade of the ubiquitin-binding site in MCL-1. To this end, TCTP (translationally controlled tumor protein), a well-known binding partner of MCL-1 and antiapoptotic regulator, was found to be strongly associated with MCL-1 during infection. Phosphorylation of TCTP, a requirement for MCL-1 binding, was also increased in infected macrophages. Knockdown of TCTP decreased MCL-1 expression and short hairpin RNA-mediated silencing of TCTP in an infected mouse model of visceral leishmaniasis showed decreased parasite burden and induction of liver cell apoptosis. Collectively, our investigation revealed a key mechanism of how *L. donovani* exploits TCTP to establish infection within the host.

### **Pintomyia evansi (Diptera: Psychodidae) larvae susceptibility to hydrated lime under laboratory conditions.**

Ortega, E., Estrada, L., Bejarano, E., Cadena, H.  
10-05-2022

*Acta Trop*

<https://pubmed.ncbi.nlm.nih.gov/35562088>

This study evaluated the effect of Calcium hydroxide (Ca(OH)<sub>2</sub> Mg(OH)<sub>2</sub>) on third stages *P. evansi* larvae mortality under experimental laboratory conditions. Three treatments containing a mixture of phlebotomine natural breeding soil (substrate) and Calcium hydroxide at different concentrations were used: Treatment 1 (T1), 1 kg of substrate mixed with 56.2 g of lime; Treatment 2 (T2), 1 kg of substrate mixed with 62.5 g of lime; and Treatment 3 (T3), 1 kg of substrate mixed with 70 g of lime. In addition, a sample of substrate without lime was used as a control for each treatment. The mortality in T1 was 1% at 24 h and 12% at 48 h, reaching a maximum of 56% at 72 h of exposure. For T2, mortality was progressive, starting with 12% at 12 h, 36% at 24 h, 52% at 48 h, and 100% at 72 h; while T3 showed mortality percentages of 94% and 100% between 12 h and 24 h of exposure. Therefore, T3 was the most effective according to the Kaplan-Meier survival analysis. This study showed that treatments over 62 g of Calcium hydroxide per 1 kg of substrate offer a starting point for immature stage control under laboratory conditions. With these results, we propose to evaluate the cost-effectiveness and feasibility of the application, of the latter concentration, under field conditions in urban environments for its application in vector control programs.

### **Dermoscopy findings of various cutaneous morphologies of post-kala-azar dermal leishmaniasis.**

Swarnkar, B., Sathyan, A., Gupta, S., Arava, S.  
12-05-2022

*Int J Dermatol*

<https://doi.org/10.1111/ijd.16257>

### **Can floral nectars reduce transmission of Leishmania?**

Palmer-Young, E., Schwarz, R., Chen, Y., Evans, J.  
12-05-2022

*PLoS Negl Trop Dis*

<https://doi.org/10.1371/journal.pntd.0010373>

**Background:** Insect-vector-borne *Leishmania* are responsible for loss of more disability-adjusted life years than any parasite besides malaria. Elucidation of the environmental factors that affect parasite transmission by vectors is essential to develop sustainable methods of parasite control that do not have off-target effects on beneficial insects or environmental health. Many phytochemicals that inhibit growth of sand fly-vector-borne *Leishmania* which have been exhaustively studied in the search for phytochemical-based drugs are abundant in nectars, which provide sugar-based meals to infected sand

flies. **Principle findings:** In a quantitative meta-analysis, we compare inhibitory phytochemical concentrations for *Leishmania* to concentrations present in floral nectar and pollen. We show that nectar concentrations of several flowering plant species exceed those that inhibit growth of *Leishmania* cell cultures, suggesting an unexplored, landscape ecology-based approach to reduce *Leishmania* transmission.

**Significance:** If nectar compounds are as effective against parasites in the sand fly gut as predicted from experiments in vitro, strategic planting of antiparasitic phytochemical-rich floral resources or phytochemically enriched baits could reduce *Leishmania* loads in vectors. Such interventions could provide an environmentally friendly complement to existing means of disease control.

### **Discriminator for Cutaneous Leishmaniasis Using MALDI-MSI in a Murine Model.**

Barajas-Solano, C., Muñoz, B., Chicano-Gálvez, E., Escobar, P., Mejía-Ospino, E.  
12-05-2022

*J Am Soc Mass Spectrom*

<https://doi.org/10.1021/jasms.2c00015>

Cutaneous leishmaniasis is a skin disease caused by flagellate protozoa of the genus *Leishmania* and transmitted by sandflies of the genus *Lutzomyia*. Around 1 million new cases occur in the world annually, with a total of 12 million people affected, mainly in rural areas with low access to health services and adequate treatments. In the area of the Americas, Colombia has one of the highest infection rates after Brazil. Topical treatments with pentamidine isethionate (PMD) present an attractive alternative due to their ease of application and low costs. However, cutaneous leishmaniasis lesions present nodules with seropurulent exudate that, when drying, form hyperkeratotic lesions, hindering the effective penetration of drugs for their treatment. The use of molecular histology techniques, such as MALDI-MSI, allow in situ evaluation of the penetration of the treatment to the sections of the dermis where the disease-causing parasite resides. However, the large volume of information generated makes it impossible to process it manually. Machine learning techniques allow the unsupervised processing of large amounts of information, generating prediction models for the classification of new information. This work proposes a low-cost method to generate cutaneous leishmaniasis detection and classification models using MALDI-MSI images taken from murine models. The proposed models allow a 95% efficiency when separating healthy samples from infected samples and an effectiveness of 67% when separating effectively treated samples from unsuccessfully treated samples.

### **Exogenous IL-13 exacerbates Leishmania major infection and abrogates acquired immunity to re-infection.**

Zaatar, M., Simaan, Y., Karam, M.  
10-05-2022

*Parasitol Res*

<https://doi.org/10.1007/s00436-022-07539-y>

Cutaneous leishmaniasis is a major global health issue, affecting more than 88 countries with 0.7-1.2 million new cases per year. T helper polarization plays a significant role in disease outcome, with Th1 responses being associated with resistance and Th2 responses being associated with susceptibility. IL-13 is an important Th2 cytokine with structural and functional similarities to IL-4. In this study, we demonstrate that administering exogenous IL-13 to Leishmania major-infected BALB/c mice increases parasite load in the infected paw and decreases tissue levels of the key Th1/Th2 cytokines IFN- $\gamma$  and IL-4, respectively. Infecting BALB/c mice with a low dose of L. major has previously been shown to confer resistance to re-infection with a higher dose. In this study, we demonstrate that administration of exogenous IL-13 early in the course of the initial low-dose infection abrogates acquired resistance to high-dose re-infection, as measured by infected paw thickness.

### **In silico screening, molecular dynamic simulations, and in vitro activity of selected natural compounds as an inhibitor of Leishmania donovani 3-mercaptopyruvate sulfurtransferase.**

**Kant, V., Kumar, P., Ranjan, R., Kumar, P., Mandal, D., Vijayakumar, S.**  
10-05-2022

*Parasitol Res*

<https://doi.org/10.1007/s00436-022-07532-5>

In Leishmania sp., the enzymes of de novo cysteine biosynthesis pathway require sulfide. Other organisms utilize sulfide through the sulfide reduction pathway, but Leishmania lacks the gene that encodes these enzymes. Hence, the major source of sulfide for Leishmania is believed to be from the action of 3-mercaptopyruvate sulfurtransferase (3MST) on 3-mercapto-pyruvate (3MP). There has been no effort reported in the past to screen inhibitors against L. donovani 3MST (Ld3MST). As a result, this study examines natural compounds that are potent against Ld3MST and validates it by in vitro activity and cytotoxicity tests. Initially, a library of ~5000 natural compounds was subjected to molecular docking approach for screening, and the best hit was validated using a long-term molecular dynamic simulation (MD). Among the docking results, quercetine-3-rutinoside (Rutin) was deemed the best hit. The results of the MD indicated that Rutin was highly capable of interacting with the varied active site segments, possibly blocking substrate access. Additionally, promastigotes and amastigotes were tested for Rutin activity and the IC<sub>50</sub> was found to be 40.95 and 90.09  $\mu$ M, respectively. Similarly, the cytotoxicity assay revealed that Rutin was not toxic even at a concentration of 819.00  $\mu$ M to THP-1 cell lines. Additionally, the Ld3MST was cloned, purified, and evaluated for enzyme activity in the presence of Rutin. Reduction in the enzyme activity (~85%) was observed in the presence of ~40  $\mu$ M Rutin. Thus, this study suggests that Rutin may act as a potent inhibitor of Ld3MST. With further in vivo investigations, Rutin could be a small molecule of choice for combating leishmaniasis.

### **Quantitative monitoring of experimental and human Leishmaniasis employing amastigote specific genes.**

**Roy, M., Sarkar, D., Chatterjee, M.**

10-05-2022

*Parasitology*

<https://doi.org/10.1017/S0031182022000610>

### **Leishmania tropica and Leishmania infantum infection in dogs and cats in central Israel.**

**Baneth, G., Nachum-Biala, Y., Adamsky, O., Gunther, I.**

10-05-2022

*Parasit Vectors*

<https://doi.org/10.1186/s13071-022-05272-0>

**Background:** Three species of Leishmania cause disease in humans in Israel and are endemic in the Middle East: Leishmania infantum, Leishmania tropica and Leishmania major. These species infect dogs and cats, but little is known about their prevalence in pet populations and their clinical manifestations. A study on dog and cat Leishmania infection was conducted in a focus of human L. tropica infection in central Israel with the aim of getting insight on leishmaniasis in pets in an area where human infection is highly prevalent. **Methods:** Blood, demographic and clinical data were collected from dogs and cats brought for veterinary care in a focus of human L. tropica infection during 2018-2020. kDNA PCR and internal transcribed spacer1 high-resolution melt analysis PCR (ITS1 HRM PCR) with DNA sequencing were performed for the detection of Leishmania and species determination. **Results:** Forty-three of 189 dogs (22.8%) and 44 of 152 cats (28.9%) were positive for Leishmania spp. infection by kDNA PCR. The ITS1 HRM PCR detected six dogs (3.3%) infected with L. infantum and one (0.5%) with L. tropica, whereas six cats (3.9%) were found infected by L. infantum and five (3.3%) by L. tropica. Four of the five L. tropica-positive cats suffered from weight loss, four had azotemia, two with mild and two with severe azotemia and progressive renal disease. Three cats had gingivostomatitis; three had skin lesions with abscess and ulcers in two and scales and hair loss in another cat, which was also FIV+. This is the first report of feline L. tropica infection in Israel. Clinical information on cats with this infection from previous studies elsewhere is scarce. **Conclusions:** A high rate of Leishmania spp. infection, mostly estimated as sub-clinical, was found in dogs and cats admitted for veterinary care in an L. tropica focus. Among the animals in which infection could be characterized to the species level, more dogs were infected with L. infantum than with L. tropica while 5 of 11 cats were infected with L. tropica and had signs of systemic and skin disease not described before in feline L. tropica infection.

### **Association between feline immunodeficiency virus and Leishmania infantum infections in cats: a retrospective matched case-control study.**

**Priolo, V., Masucci, M., Donato, G., Solano-Gallego, L.,**

**Martínez-Orellana, P., Persichetti, M., Raya-Bermúdez, A., Vitale, F., Pennisi, M.**

10-05-2022

*Parasit Vectors*

<https://doi.org/10.1186/s13071-022-05230-w>

**Background:** Feline leishmaniosis caused by *Leishmania infantum* is often associated with feline immunodeficiency virus (FIV) infection; however, the role and clinical significance of this coinfection remain unknown. This study aimed to assess whether FIV is associated with *L. infantum* infection in cats from canine leishmaniosis endemic areas and to report the clinical signs and hematological alterations associated with coinfection. **Methods:** A retrospective matched case-control study (ratio 1:2) was conducted. Data of clinical examination and complete blood count (CBC) were selected from a cohort of 705 cats examined for epidemiological studies on feline leishmaniosis conducted between 2012 and 2019. Ninety-one FIV seropositive cases and 182 FIV seronegative control cats were selected. Matching was done according to age, sex, lifestyle and geographic provenience of case cats. Rapid ELISA devices were mainly used to detect anti-FIV antibodies. Anti-*Leishmania* IgG antibodies were detected by indirect-immunofluorescence test (IFAT). *Leishmania* DNA was searched in blood, oral and conjunctival swabs by quantitative real-time PCR. **Results:** Feline immunodeficiency virus seropositive cats had no hematological abnormalities suggestive of an advanced stage of FIV infection and were statistically more frequently IFAT positive, and their risk of being *L. infantum* antibody positive was 2.8 greater than in the FIV seronegatives. The association of FIV seropositivity with *L. infantum* antibody positivity was confirmed in the univariable model of logistic regression. A multivariate model found FIV infection and *L. infantum* PCR positivity as predictors of a positive *L. infantum* IFAT result. Male outdoor cats from rural or suburban areas were at risk for FIV and *L. infantum* antibody positivity. Clinical signs more frequently associated with the coinfection were oral lesions, pale mucous membranes and low body condition score (BCS). **Conclusions:** This study documents that FIV seropositive cats with no hematological abnormalities suggestive of an advanced stage of FIV infection are more prone to be *L. infantum* seroreactive by IFAT in endemic areas. Therefore, FIV seropositive cats should be tested for *L. infantum* antibodies and treated for preventing sand fly bites. Pale mucous membranes, low BCS and oral lesions but no CBC abnormalities were significantly associated with the coinfection.

### Detection of specific antibodies against *Leishmania infantum* in canine serum and oral transudate using an in-house ELISA.

**Baxarias, M., Viñals, J., Álvarez-Fernández, A., Alcover, M., Solano-Gallego, L.**

10-05-2022

*Parasit Vectors*

<https://doi.org/10.1186/s13071-022-05246-2>

**Background:** Canine leishmaniosis caused by the protozoan

*Leishmania infantum* is a complex infection due to its variable clinical signs and laboratory findings. Therefore, a broad range of techniques is available for diagnosis. Testing for specific antibodies in serum is the most commonly used technique, although the testing of other body fluids, such as oral transudate (OT), can be an alternative as its collection is non-invasive and testing can be performed by untrained personnel. The aim of this study was to assess and compare the detection of *L. infantum*-specific antibodies in paired samples of serum and OT collected from apparently healthy dogs and dogs with clinical leishmaniosis using an in-house enzyme-linked immunosorbent assay (ELISA). **Methods:** Serum and OT were collected from 407 dogs, which varied in breed, sex, age, lifestyle and clinical status, by many practicing veterinarians in Spain. The main geographical areas of sampling included Barcelona (n=110), Mallorca (n=94), Cadiz (n=54) and Asturias (n=47). The majority of infected dogs were apparently healthy (89.9%) while 41 presented clinical signs and/or clinicopathological abnormalities compatible with *L. infantum* infection and subsequently diagnosed with leishmaniosis (10.1%). An in-house ELISA was performed to quantify the anti-*Leishmania* antibodies in serum and OT. **Results:** The *L. infantum* infection rate determined by the in-house ELISA was 37.1% in serum samples and 32.7% in OT samples. Serum and OT ELISA results showed a positive correlation (Spearman's correlation coefficient  $r_s=0.6687$ ,  $P<0.0001$ ). The percent agreement between the serum and OT ELISA results was 84%, while agreement according to Cohen's kappa statistic ( $\kappa$ ) was substantial (0.66) when all samples were analyzed. The highest percent agreement (92.1%) between both tests was found in dogs from low endemicity regions and from sick dogs, with both groups presenting almost perfect agreement according to Cohen's  $\kappa$  agreement test (0.84). Few seronegative dogs (n=23) tested positive by the OT ELISA. The agreement between serum and OT went from almost perfect to moderate when the geographical distribution and clinical status were analyzed. **Conclusions:** The results of this study demonstrated an almost perfect to moderate agreement between OT and serum samples tested using the in-house ELISA. These results are particularly promising in sick dogs with high antibody levels while the results seem less optimal in apparently healthy dogs with low antibody levels.

### Detection of vector-borne pathogens in owned dogs with cranial cruciate ligament rupture living in the Mediterranean area.

**Tabar, M., Tabar, J., Naranjo, C., Altet, L., Roura, X.**

10-05-2022

*Parasit Vectors*

<https://doi.org/10.1186/s13071-022-05205-x>

**Background:** Cranial cruciate ligament rupture (CCLR) results from a multifactorial degenerative process that leads to rupture of the ligament. Vector-borne pathogens (VBP) in dogs can induce joint disease but their role in CCLR has not been previously investigated. The aim of the present work is to evaluate the prevalence of VBP in dogs with CCLR.

**Methods:** This was a prospective study that included 46 dogs presented for CCLR surgical treatment and 16 control dogs euthanized for diseases unrelated to the joints. Specimens collected included blood, synovial fluid, and synovial membrane biopsy. Pathogen testing consisted of serology for *Leishmania infantum* (quantitative ELISA), *Ehrlichia canis/ewingii*, *Borrelia burgdorferi*, *Anaplasma phagocytophilum/platys*, and *Dirofilaria immitis* (4DX IDEXX test), and PCR for *L. infantum*, *Ehrlichia/Anaplasma* spp., *Bartonella* spp., piroplasms (*Babesia* spp. and *Theileria* spp.), and filariae (*D. immitis*, *Dirofilaria repens*, *Acanthocheilonema dracunculoides*, *Acanthocheilonema reconditum*, and *Cercopithifilaria* spp.) on both EDTA-whole blood (EB) and synovial fluid (SF) samples. SF cytology and histopathological evaluation of synovial membrane were also performed.

**Results:** The prevalence of VBP was 19.6% in the CCLR group and 18.8% in the control group, with no statistical difference among them. The presence of synovitis was not more frequent in CCLR dogs (45.6%) than in control dogs (43.7%). Lymphoplasmacytic infiltration was the most common inflammatory pattern detected in the joints of both groups of dogs. **Conclusions:** This study failed to demonstrate a role of canine VBP in CCLR or the presence or different pattern of joint inflammation in pathogen-positive dogs.

### Use of preventive measures and serological screening tools for *Leishmania infantum* infection in dogs from Europe.

**Baxarias, M., Homedes, J., Mateu, C., Attipa, C., Solano-Gallego, L.**

10-05-2022

*Parasit Vectors*

<https://doi.org/10.1186/s13071-022-05251-5>

**Background:** There are several screening tools for detecting *Leishmania infantum* infection in dogs and various preventive measures to protect against it. Some studies have investigated them, but not many have described their current use. The aim of this study was to investigate which preventive measures and serological screening tools for *L. infantum* infection were employed from 2012 to 2018 in dogs from different endemic European countries. **Methods:** A set of electronic datasheets was completed for each dog from several veterinary centres. Classification of preventive measures included: (1) repellents, (2) vaccines and (3) immunomodulators. Classification of serological tests included the: (1) direct agglutination test (DAT), (2) enzyme-linked immunosorbent assay (ELISA), (3) indirect immunofluorescence (IFI), (4) rapid tests and (5) other assays. Dogs were also classified depending on their risk of exposure and living area. **Results:** Information from 3762 dogs was gathered. Preventive measures were applied in 91.5% of dogs and the most frequently used were repellents (86.2%) followed by vaccines (39.8%) and Leisguard® (15.3%). The different types of repellents (collar and spot-on) were used similarly. A combination of a vaccine and repellents was preferred in the high-risk group while the low-risk preferred a combination of Leisguard® and a repellent (Chi-square test:  $\chi^2=88.41$ ,  $df=10$ ,  $P<0.001$ ). Furthermore, all preventive

measures were similarly used through the years except for repellents, which were predicted to have a small increase of use each year. Regarding serological screening tools, the most used were rapid and ELISA tests. Rapid tests, ELISA tests and DAT were used similarly through the years, but a significant change was found in the use of IFI and other assays whose use decreased a little each year. **Conclusions:** Repellents were the preferred measure, while vaccines and Leisguard® were second-line options. Some dogs were not treated by any measures, which highlights the need for dog owner education. Moreover, there seems to be a preference for rapid tests in the clinical setting to detect specific *L. infantum* antibodies while ELISA or IFI are less often employed. This underlines an increasing problem, as qualitative rapid tests have a variable diagnostic performance limiting the adequate diagnosis of seropositive dogs in endemic areas.

### Intracellular localization of MyosinXXI discriminates *Leishmania* spp and *Leptomonas seymouri*.

**Kajuluri, L., Gargvanshi, S., Sahasrabudhe, A.**

04-03-2022

*Biochem Biophys Res Commun*

<https://pubmed.ncbi.nlm.nih.gov/35299073>

The patients with the most dreaded *Leishmania donovani* infections are now regularly been detected with co-infecting monoxenous trypanosomatid, *Leptomonas seymouri*, of which pathological consequence is obscure. Due to high degree of morphological similarity, its presence remains unmarked in the culture which leads to anomalous research outcomes. The available methods to detect *Leptomonas* in cultures are cumbersome and are not quantitative. We report here that MyosinXXI serves as a distinguishing biomarker that can be used to mark the presence of *L. seymouri* in *Leishmania* cultures. The method uses *Leishmania* MyosinXXI antibodies employed in immunofluorescence microscopy that shows a specialized localization pattern in *Leishmania* but not in *Leptomonas* (Patent application No. IN201711014439). This method is not only qualitative, but can also quantify the *L. seymouri* load in the cultured field isolates and serves as a remarkable tool to ascertain laboratory strains of *Leishmania*.

### Phlebotomine Sandfly (Diptera: Psychodidae) Fauna and The Association Between Climatic Variables and The Abundance of *Lutzomyia longipalpis* sensu lato in an Intense Transmission Area for Visceral Leishmaniasis in Central Western Brazil.

**de Souza Fernandes, W., de Oliveira Moura Infran, J., Falcão de Oliveira, E., Etelvina Casaril, A., Petilim Gomes Barrios, S., Lopes de Oliveira, S., Gutierrez de Oliveira, A.**

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*J Med Entomol*

<https://doi.org/10.1093/jme/tjac006>

The presence, abundance, and distribution of sandflies are

strongly influenced by climate and environmental changes. This study aimed to describe the sandfly fauna in an intense transmission area for visceral leishmaniasis and to evaluate the association between the abundance of *Lutzomyia longipalpis* sensu lato (Lutz & Neiva 1912) (Diptera: Psychodidae) and climatic variables. Captures were carried out 2 yr (July 2017 to June 2019) with automatic light traps in 16 sites of the urban area of Campo Grande, Mato Grosso do Sul state. The temperature (°C), relative humidity (%), precipitation (mm3), and wind speed (km/h) were obtained by a public domain database. The Wilcoxon test compared the absolute frequencies of the species by sex. The association between climatic variables and the absolute frequency of *Lu. longipalpis* s.l. was assessed using the Spearman's correlation coefficient. A total of 1,572 sandflies into four species were captured. *Lutzomyia longipalpis* s.l. was the most abundant species and presented a significant correlation with the average temperature, humidity, and wind speed in different periods. *Lutzomyia longipalpis* s.l. was captured in all months, showing its plasticity in diverse weather conditions. We emphasize the importance of regular monitoring of vectors and human and canine cases, providing data for surveillance and control actions to continue to be carried out in the municipality.

### Treating leishmaniasis in Amazonia, part 2: Multi-target evaluation of widely used plants to understand medicinal practices.

Houël, E., Ginouves, M., Azas, N., Bourreau, E., Eparvier, V., Hutter, S., Knittel-Obrecht, A., Jahn-Oyac, A., Prévot, G., Villa, P., Vonthron-Sénécheau, C., Odonne, G.

05-02-2022

*J Ethnopharmacol*

<https://pubmed.ncbi.nlm.nih.gov/35131338>

**Ethnopharmacological relevance:** Leishmaniasis are widely distributed among tropical and subtropical countries, and remains a crucial health issue in Amazonia. Indigenous groups across Amazonia have developed abundant knowledge about medicinal plants related to this pathology. **Aim of the study:** We intend to explore the weight of different pharmacological activities driving taxa selection for medicinal use in Amazonian communities. Our hypothesis is that specific activity against *Leishmania* parasites is only one factor along other (anti-inflammatory, wound healing, immunomodulating, antimicrobial) activities. **Materials and methods:** The twelve most widespread plant species used against leishmaniasis in Amazonia, according to their cultural and biogeographical importance determined through a wide bibliographical survey (475 use reports), were selected for this study. Plant extracts were prepared to mimic their traditional preparations. Antiparasitic activity was evaluated against promastigotes of reference and clinical New-World strains of *Leishmania* (*L. guyanensis*, *L. braziliensis* and *L. amazonensis*) and *L. amazonensis* intracellular amastigotes. We concurrently assessed the extracts immunomodulatory properties on PHA-stimulated human PBMCs and RAW264.7 cells, and on *L. guyanensis* antigens-stimulated PBMCs obtained from

*Leishmania*-infected patients, as well as antifungal activity and wound healing properties (human keratinocyte migration assay) of the selected extracts. The cytotoxicity of the extracts against various cell lines (HFF1, THP-1, HepG2, PBMCs, RAW264.7 and HaCaT cells) was also considered. The biological activity pattern of the extracts was represented through PCA analysis, and a correlation matrix was calculated.

**Results:** *Spondias mombin* L. bark and *Anacardium occidentale* L. stem and leaves extracts displayed high anti-promastigotes activity, with  $IC_{50} \leq 32 \mu\text{g/mL}$  against *L. guyanensis* promastigotes for *S. mombin* and  $IC_{50}$  of 67 and 47  $\mu\text{g/mL}$  against *L. braziliensis* and *L. guyanensis* promastigotes, respectively, for *A. occidentale*. In addition to the antiparasitic effect, antifungal activity measured against *C. albicans* and *T. rubrum* (MIC in the 16-64  $\mu\text{g/mL}$  range) was observed. However, in the case of *Leishmania* amastigotes, the most active species were *Bixa orellana* L. (seeds), *Chelonantus alatus* (Aubl.) Pulle (leaves), *Jacaranda copaia* (Aubl.) D. Don. (leaves) and *Plantago major* L. (leaves) with  $IC_{50} < 20 \mu\text{g/mL}$  and infection rates of 14-25% compared to the control. Concerning immunomodulatory activity, *P. major* and *B. orellana* were highlighted as the most potent species for the wider range of cytokines in all tested conditions despite overall contrasting results depending on the model. Most of the species led to moderate to low cytotoxic extracts except for *C. alatus*, which exhibited strong cytotoxic activity in almost all models. None of the tested extracts displayed wound healing properties. **Conclusions:** We highlighted pharmacologically active extracts either on the parasite or on associated pathophysiological aspects, thus supporting the hypothesis that antiparasitic activities are not the only biological factor useful for antileishmanial evaluation. This result should however be supplemented by in vivo studies, and attracts once again the attention on the importance of the choice of biological models for an ethnopharmacologically consistent study. Moreover, plant cultural importance, ecological status and availability were discussed in relation with biological results, thus contributing to link ethnobotany, medical anthropology and biology.

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## CYSTICERCOSE

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## DRACUNCULOSE

## ECHINOCOCCOSIS

### Bio-Membrane SELEX as a new approach for selecting ss-DNA aptamers that bind to the hydatid cyst laminated layer.

Dehkordi, A., Khanahmad, H., Azizi, Y., Mirian, M., Pestehchian, N., Darani, H.

16-05-2022

*Curr Mol Med*

<https://doi.org/10.2174/1566524022666220516140451>

**Background:** Hydatid cyst (HC) is the larval stage of the canine intestinal tapeworm (cestode), *Echinococcus granulosus*. In addition to the high global economic cost to livestock farming, the infection can lead to dangerous problems for human health. Therefore, research into new diagnosis and treatment approaches is valuable. This study is set out to explore aptamers that bind to HC antigens. **Methods:** The similarity between HC genotype in sheep and humans, sheep HCs were collected and were used as a biological membrane for aptamer selection. Four Bio-Membrane SELEX rounds were conducted and ssDNA aptamers were selected. Selected aptamers' affinity and specificity to the laminated layer antigens were evaluated using membrane staining by fluorescein primer as a probe. Biotinylated primer was used as a probe for aptahistochemistry and dot blot techniques. Subsequently, cloning and plasmid extraction was conducted. The affinity and specificity of sequenced aptamers were examined with the dot blot method. **Results:** Selected aptamers reacted with HC wall in aptahistochemistry, aptahistofluorescent, and dot blot experiments. Following cloning and sequencing, 20 sequences were achieved. A strong reaction between HC total antigens and sequenced aptamers has emerged in the dot blot method. **Conclusion:** In this investigation, we propose a novel method to determine specific aptamers. Bio-Membrane SELEX, could be assumed as a practical and sensitive method for aptamer selection. Selected aptamers in this study possibly may be used for specific HC antigens detection.

### Epidemiological study of gastrointestinal helminths among dogs from Northeastern Nigeria: a potential public health concern.

Jajere, S., Lawal, J., Shittu, A., Waziri, I., Goni, D., Fasina, F.

11-05-2022

*Parasitol Res*

<https://doi.org/10.1007/s00436-022-07538-z>

Understanding the epidemiology of canine parasitic infections, gastrointestinal helminthic infections in particular, is crucial for designing an efficient control programs targeted at minimizing the risks of zoonotic transmission. A total of 470 dogs attending veterinary clinics in Northeastern Nigeria were screened for gastrointestinal helminths using standard parasitological techniques. Epidemiological risk factors associated with the canine parasitic infections were assessed using multivariable logistic regression analysis. In total, 77.9%

(366/470) of dogs had harboured one or more species of the gastrointestinal helminths: *Ancylostoma caninum* (40.2%), *Toxocara canis* (35.1%) *Trichuris vulpis* (26.6%), *Spirocerca lupi* (5.7%), *Taenia/Echinococcus* (12.3%), *Dipylidium caninum* (10.9%) and *Diphyllobothriid ova* (2.8%). Female dogs (OR=2.1;  $p=0.02$ ), local breeds (OR=2.3;  $p<0.01$ ), younger dogs (OR=3.2;  $p<0.001$ ), dogs adopted as security guards (OR=1.8;  $p<0.01$ ) and poor body condition score (OR=3.1;  $p<0.001$ ) were strongly associated with *A. caninum* infection. For *T. canis* and *T. vulpis*, younger dogs (OR=2.5;  $p=0.02$  and OR=2.3;  $p<0.01$ ) and poor body condition score (OR=4.2;  $p<0.001$  and OR=2.2;  $p<0.01$ ) were the strong predictors for infection, whereas female dogs (OR=2.8;  $p=0.02$ ), younger dogs (OR=4.1;  $p<0.001$ ) and poor body condition score (OR=4.0;  $p<0.001$ ) were strongly associated with *D. caninum* infection in dogs. The results revealed high prevalence of gastrointestinal helminths-some of which have zoonotic potential-among dogs underlying huge public health risk.

### First Report of Alveolar Hydatid Disease (*Echinococcus multilocularis*) in a Golden Jackal (*Canis aureus*).

Marinković, D., Gavrilović, P., Vidanović, D., Čirović, D., Kuručki, M., Vasković, N., Aničić, M.

10-05-2022

*Acta Parasitol*

<https://doi.org/10.1007/s11686-022-00556-y>

**Background:** Alveolar hydatid disease caused by the tapeworm *Echinococcus multilocularis* is a parasitic disease present in the northern hemisphere. *Echinococcus multilocularis* is a parasite of canid and felid carnivores as definitive hosts, and small mammals, particularly rodents as intermediate hosts. Other animal species and humans can be aberrant intermediate hosts for this parasite. It is known that besides acting as definitive hosts, domestic dogs can rarely become infected with the larval form of *E. multilocularis* and develop alveolar echinococcosis; however, a role of wild canids as aberrant intermediate hosts has not been documented until now. To the best of our knowledge the present paper provides the first description of alveolar hydatid disease in a golden jackal (*Canis aureus*). **Case Presentation:** Necropsy of the yearling female animal found a large, round, tumor-like mass, 20 cm in diameter, with a rough, multilobulated surface in the abdominal cavity, connected to the liver and omentum. On the cut surface this tumor-like lesion was multicystic, with a number of locular cavities filled with a clear yellowish to orange watery fluid and a large area of necrosis in the central part of the mass. Histopathology revealed multiple cystic spaces separated by fibrous sheaths and inflammatory cells-lymphocytes, plasma cells, neutrophil and eosinophil granulocytes. The cysts contained either pale, hyaline, eosinophilic laminar and occasionally amorphous, acellular, PAS-positive structures, or metacystodes with invaginated protoscolices. In several cysts round calcified bodies (calcareous corpuscles) were noted. Microscopic examination showed everted and inverted protoscolices which were attached to fragments of the brood capsule or free in hydatid

fluid. By comparing consensus nucleotide sequence of 457 bp obtained by PCR reaction with sequences deposited in NCBI GenBank it is determined that it was 100% identical with *E. multilocularis* sequences under accession numbers MH259778.1, MH259776.1, AB668376.1, EU704124.1 and AB018440.2. **Conclusion:** The present paper provides a proof that the golden jackal, besides being a definitive host, can also serve as the aberrant intermediate host for *E. multilocularis*.

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## TREMATODOSES D'ORIGINE ALIMENTAIRE (CLONORCHIOSE, OPISTHORCHIOSE, FASCIOLASE ET PARAGONIMOSE)

### Exploration of animal models to study the life cycle of *Fasciola hepatica*.

Fang, W., Yang, J., Wang, H., Chen, S., Li, K., Liu, Y., Duan, Y., Li, T.

16-05-2022

*Parasitology*

<https://doi.org/10.1017/S0031182022000609>

### Efficacy of flukicides on *Fasciola gigantica*, a food borne zoonotic helminth affecting livestock in Bangladesh.

Hasan, M., Roy, B., Biswas, H., Rahman, M., Anisuzzaman, A., Alam, M., Talukder, M.

10-05-2022

*Parasitology*

<https://doi.org/10.1017/S0031182022000580>

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## FILARIOSE LYMPHATIQUE

### Forging Ahead the Repositioning of Multitargeted Drug Ivermectin.

Atmakuri, S., Nene, S., Khatri, D., Singh, S., Sinha, V., Srivastava, S.

16-05-2022

*Curr Drug Deliv*

<https://doi.org/10.2174/1567201819666220516163242>

With the advent of ivermectin, tremendous improvement in public health has been observed, especially in the treatment of onchocerciasis and lymphatic filariasis that created chaos mostly in rural, sub-Saharan Africa and Latin American countries. The discovery of ivermectin became a boon to millions of people that had suffered in the pandemic and still

hold its pharmacological potential against these. Ivermectin continued to surprise scientists because of its notable role in the treatment of various other tropical diseases (Chagas, leishmaniasis, worm infections, etc.) and is viewed as the safest drug with the least toxic effects. The current review highlights its role in unexplored avenues towards forging ahead of the repositioning of this multitargeted drug in cancer, viral (the evaluation of the efficacy of ivermectin against SARS-Cov-2 is under investigation) and bacterial infection and malaria. This article also provides a glimpse of regulatory considerations of drug repurposing and current formulation strategies. Due to its broad-spectrum activity, multitargeted nature and promising efforts are put towards the repurposing of this drug throughout the field of medicine. This single drug originated from a microbe, changed the face of global health by proving its unmatched success and progressive efforts continue in maintaining its bequest in the management of global health by decreasing the burden of various diseases worldwide.

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## MYCETOME

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## ONCHOCERCOSE

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## SCHISTOSOMIASIS

### Impact of Three to Five Rounds of Mass Drug Administration on Schistosomiasis and Soil-Transmitted Helminths in School-Aged Children in North-Central Nigeria.

Griswold, E., Eigege, A., Adelamo, S., Mancha, B., Kenrick, N., Sambo, Y., Ajiji, J., Zam, G., Solomon, J., Urude, R., Kadimbo, J., Danboyi, J., Miri, E., Nute, A., Rakers, L., Nebe, O., Anyaike, C., Weiss, P., Noland, G., Richards, F.

16-05-2022

*Am J Trop Med Hyg*

<https://doi.org/10.4269/ajtmh.21-1207>

Nasarawa and Plateau states of north-central Nigeria have implemented programs to control schistosomiasis (SCH) and soil-transmitted helminths (STH) in children since the 1990s. Statewide mapping surveys were conducted in 2013, when 11,332 school-aged children were sampled from 226 schools. The local government areas (LGAs) then received varying combinations of mass drug administration (MDA) for the next 5 years. We revisited 196 (87%) schools in 2018 plus an additional six (202 schools in total), sampling 9,660 children. We calculated overall prevalence and intensity of infection

and evaluated associations with gender; age; behaviors; water, sanitation, and hygiene (WASH); and treatment regimen. Urine heme detection dipsticks were used for *Schistosoma haematobium* in both surveys, with egg counts added in 2018. Stool samples were examined by Kato-Katz for *Ascaris lumbricoides*, *Trichuris trichiura*, *Schistosoma mansoni*, and hookworm. Schistosomiasis prevalence among sampled students dropped from 12.9% (95% confidence interval [CI]: 11.1-14.9%) to 9.0% (95% CI: 7.5-10.9%), a statistically significant change ( $P < 0.05$ ). In 2018, eight LGAs still had  $> 1\%$  of children with heavy-intensity schistosome infections. Prevalence of STH infection did not significantly change, with 10.8% (95% CI: 9.36-12.5%) of children positive in 2013 and 9.4% (95% CI: 8.0-10.9%) in 2018 ( $P = 0.182$ ). Heavy-intensity STH infections were found in  $< 1\%$  of children with hookworm, and none in children with *A. lumbricoides* or *T. trichiura* in either study. The WASH data were collected in 2018, indicating 43.6% of schools had a latrine and 14.4% had handwashing facilities. Although progress is evident, SCH remains a public health problem in Nasarawa and Plateau states.

### Expression of microRNA-223 and microRNA-146b in serum and liver tissue of mice infected with *Schistosoma mansoni*.

El-Taweel, H., Issa, Y., Mady, R., Shehata, G., Youssef, E., Tolba, M.

16-05-2022

*Parasitol Res*

<https://doi.org/10.1007/s00436-022-07542-3>

MicroRNAs (miRNAs) play regulatory roles in several diseases. In schistosomiasis, the main pathological changes are caused by the granulomatous reaction induced by egg deposition. We aimed to study the changes in host miRNA-223 and miRNA-146b expression in relation to egg deposition and development of hepatic pathology in murine schistosomiasis *mansoni*. Blood and liver tissue samples were collected from non-infected mice (group I), *S. mansoni*-infected mice at the 4th, 8th, and 12th weeks post-infection (p.i.) (groups II-IV), and 4 weeks after praziquantel treatment (group V). The collected samples were processed for RNA extraction, reverse transcription, and real-time PCR analysis of miRNA-223 and miRNA-146b. miRNAs' relative expression was estimated by the  $\Delta\Delta C_t$  method. Liver tissue samples were examined for egg count estimation and histopathological evaluation. Results revealed that miRNA-223 was significantly downregulated in liver tissues 8 and 12 weeks p.i., whereas miRNA-146b expression increased gradually with the progression of infection with a significantly higher level at week 12 p.i. compared to week 4 p.i. Serum expression levels nearly followed the same pattern as the tissue levels. The dysregulated expression of miRNAs correlated with liver egg counts and was more obvious with the demonstration of chronic granulomas, fibrous transformation, and distorted hepatic architecture 12 weeks p.i. Restoration of normal expression levels was observed 4 weeks after treatment. Collectively, these findings provide new insights for in-depth

understanding of host-parasite interaction in schistosomiasis and pave a new way for monitoring the progress of hepatic pathology before and after treatment.

### *Schistosoma mansoni* miracidia: revisiting motility and survival parameters for improved computational modelling.

de Souza, R., Pascoal, V., Vilches, T., Bittencourt, H., Utz, L., Teixeira, C.

16-05-2022

*Parasitology*

<https://doi.org/10.1017/S0031182022000579>

### Potential risk of colonization of *Bulinus globosus* in the mainland of China under climate change.

Wang, X., Juma, S., Li, W., Suleman, M., Muhsin, M., He, J., He, M., Xu, D., Zhang, J., Bergquist, R., Yang, K.

13-05-2022

*Infect Dis Poverty*

<https://doi.org/10.1186/s40249-022-00980-2>

**Background:** *Bulinus globosus*, the main intermediate snail host of *Schistosoma haematobium*. The increased contacts between Africa and China could even lead to large-scale dissemination of *B. globosus* in China. Temperature is the key factor affecting fresh-water snail transmission. This study predicted potential risk of colonization of *B. globosus* in the mainland of China under climate change. **Methods:** We investigated minimum and maximum temperatures for *B. globosus* eggs, juveniles and adult snails kept under laboratory conditions to find the most suitable range by pinpointing the median effective temperatures (ET50). We also assessed the influence of temperature on spawning and estimated the accumulated temperature (AT). The average air temperatures between 1955 and 2019 in January and July, the coldest and hottest months in China, respectively, were collected from national meteorological monitoring stations and investigated in a geographic information system (GIS) using empirical Bayesian Kriging to evaluate the theoretical possibility for distribution of *B. globosus* in southern China based on temperature. **Results:** The effective minimum temperature (ET50<sub>min</sub>) for eggs, juveniles, adult snails and spawning were 8.5, 7.0, 7.0, 14.9 °C, respectively, with the corresponding maximum values (ET50<sub>max</sub>) of 36.6, 40.5, 40.2 and 38.1 °C. The AT was calculated at 712.1±64.9 °C-d. In 1955, the potential *B. globosus* distribution would have had a northern boundary stretching from the coastal areas of Guangdong Province and Guangxi Autonomous Region to southern Yunnan Province. Since then, this line has gradually moved northward. **Conclusions:** Annual regeneration of *B. globosus* can be supported by the current climate conditions in the mainland of China, and a gradual expansion trend from south to north is shown in the study from 2015 to 2019. Thus, there is a potential risk of colonization of *B. globosus* in the mainland of China under climate change.

**The Novodiag® Stool parasites assay, an innovative high-plex technique for fast detection of protozoa, helminths and microsporidia in stool samples: a retrospective and prospective study.**

Hartuis, S., Lavergne, R., Nourrisson, C., Verweij, J., Desoubeaux, G., Lussac-Sorton, F., Lemoine, J., Cateau, E., Jeddi, F., Poirier, P., Le Pape, P., Morio, F.

13-05-2022

Parasite

<https://doi.org/10.1051/parasite/2022026>

**Objectives:** We provide the first evaluation of the CE-IVD marked Novodiag® stool parasites assay (NVD), allowing rapid and high-plex detection of 26 distinct targets, encompassing protozoans, helminths and microsporidia in stool samples.

**Methods:** A total of 254 samples (n = 205 patients) were prospectively processed by the NVD and our routine procedure (RP). Performances of the NVD were compared with RP. Samples only positive by the NVD assay were investigated by external PCR assays. Sensitivity and specificity (Se/Sp) and time from sample receipt to results were determined for each method. The NVD was also evaluated against 77 additional samples positive for a wide range of parasites. **Results:** Overall positivity rate was 16.9% for RP compared with 34% using the NVD assay, and 164 samples (66%) were negative by both methods. Only 30 positive samples (12%) showed full concordance between RP and NVD. Fifty-three discordant samples were sent for external investigations. Except for *Giardia intestinalis* and *Trichuris* spp., higher Se was observed for the NVD assay for *Blastocystis* spp. (100% vs. 63%), *Dientamoeba fragilis* (100% vs. 0%), *Schistosoma* spp. (100% vs. 17%), and *Enterobius vermicularis* (100% vs. 67%) but roughly similar to RP for the remaining parasites tested. False-positive results were identified for *Blastocystis* spp., *G. intestinalis*, and *Trichuris* spp. using the NVD assay. The NVD mostly provides a diagnosis on the day of sample receipt compared with a mean of three days with RP. **Conclusions:** Besides some limitations, the NVD is a new diagnostic strategy allowing rapid and high-plex detection of gastrointestinal parasites from unpreserved stools.

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## HELMINTHIASES TRANSMISES PAR LE SOL (ASCARIDIOSE, TRICHURIASE, ANKYLOSTOMIASE)

**Impact of Three to Five Rounds of Mass Drug Administration on Schistosomiasis and Soil-Transmitted Helminths in School-Aged Children in North-Central Nigeria.**

Griswold, E., Eigege, A., Adelamo, S., Mancha, B., Kenrick, N., Sambo, Y., Ajiji, J., Zam, G., Solomon, J., Urude, R., Kadimbo, J., Danboyi, J., Miri, E., Nute, A., Rakers, L., Nebe, O., Anyaïke, C.,

Weiss, P., Noland, G., Richards, F.

16-05-2022

*Am J Trop Med Hyg*

<https://doi.org/10.4269/ajtmh.21-1207>

Nasarawa and Plateau states of north-central Nigeria have implemented programs to control schistosomiasis (SCH) and soil-transmitted helminths (STH) in children since the 1990s. Statewide mapping surveys were conducted in 2013, when 11,332 school-aged children were sampled from 226 schools. The local government areas (LGAs) then received varying combinations of mass drug administration (MDA) for the next 5 years. We revisited 196 (87%) schools in 2018 plus an additional six (202 schools in total), sampling 9,660 children. We calculated overall prevalence and intensity of infection and evaluated associations with gender; age; behaviors; water, sanitation, and hygiene (WASH); and treatment regimen. Urine heme detection dipsticks were used for *Schistosoma hematobium* in both surveys, with egg counts added in 2018. Stool samples were examined by Kato-Katz for *Ascaris lumbricoides*, *Trichuris trichiura*, *Schistosoma mansoni*, and hookworm. Schistosomiasis prevalence among sampled students dropped from 12.9% (95% confidence interval [CI]: 11.1-14.9%) to 9.0% (95% CI: 7.5-10.9%), a statistically significant change ( $P < 0.05$ ). In 2018, eight LGAs still had > 1% of children with heavy-intensity schistosome infections. Prevalence of STH infection did not significantly change, with 10.8% (95% CI: 9.36-12.5%) of children positive in 2013 and 9.4% (95% CI: 8.0-10.9%) in 2018 ( $P = 0.182$ ). Heavy-intensity STH infections were found in < 1% of children with hookworm, and none in children with *A. lumbricoides* or *T. trichiura* in either study. The WASH data were collected in 2018, indicating 43.6% of schools had a latrine and 14.4% had handwashing facilities. Although progress is evident, SCH remains a public health problem in Nasarawa and Plateau states.

**Epidemiology of Soil-Transmitted Helminth Infections among Primary School Children in the States of Chhattisgarh, Telangana, and Tripura, India, 2015-2016.**

Ganguly, S., Barkataki, S., Sanga, P., Boopathi, K., Kanagasabai, K., Devika, S., Karmakar, S., Chowdhury, P., Sarkar, R., Raj, D., James, L., Dutta, S., Campbell, S., Murhekar, M.

16-05-2022

*Am J Trop Med Hyg*

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Soil-transmitted helminth (STH) infections are highly prevalent in many developing countries, affecting the poorest and most deprived communities. We conducted school-based surveys among children studying in first to fifth standard in government schools in the Indian States of Chhattisgarh, Telangana, and Tripura to estimate the prevalence and intensity of STH infections during November 2015 and January 2016. We adopted a two-stage cluster sampling design, with a random selection of districts within each agro-climatic zone in the first stage. In the second stage, government primary

schools were selected by probability proportional to size method from the selected districts. We collected information about demographic details, water, sanitation, and hygiene (WASH) characteristics and stool samples from the school children. Stool samples were tested using Kato-Katz method. Stool samples from 3,313 school children (Chhattisgarh: 1,442, Telangana: 1,443, and Tripura: 428) were examined. The overall prevalence of any STH infection was 80.2% (95% confidence interval [CI]: 73.3-85.7) in Chhattisgarh, 60.7% (95% CI: 53.8-67.2) in Telangana, and 59.8% (95% CI: 49.0-69.7) in Tripura. *Ascaris lumbricoides* was the most prevalent STH infection in all three states. Most of the STH infections were of light intensity. Our study findings indicate that STH infections were highly prevalent among the school children in Chhattisgarh, Telangana, and Tripura, indicating the need for strengthening STH control program in these states. The prevalence estimates from the survey would serve as a baseline for documenting the impact of the National Deworming Day programs in these states.

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## GALE

### Crusted Scabies in a Patient With Intellectual Disability.

Cho, M., Kim, H.

16-05-2022

*J Korean Med Sci*

<https://doi.org/10.3346/jkms.2022.37.e151>

### Neglected tropical diseases in Australia: a narrative review.

Revue de littérature

Kurcheid, J., Gordon, C., Clarke, N., Wangdi, K., Kelly, M., Lal, A., Mutombo, P., Wang, D., Mationg, M., Clements, A., Muhi, S., Bradbury, R., Biggs, B., Page, W., Williams, G., McManus, D., Gray, D.

12-05-2022

*Med J Aust*

<https://doi.org/10.5694/mja2.51533>

•Neglected tropical diseases (NTDs) represent a threat to the health, wellbeing and economic prosperity of billions of people worldwide, often causing serious disease or death. •Commonly considered diseases of low and middle-income nations, the presence of NTDs in high income countries such as Australia is often overlooked. •Seven of the 20 recognised NTDs are endemic in Australia: scabies, soil-transmitted helminths and strongyloidiasis, echinococcosis, Buruli ulcer, leprosy, trachoma, and snakebite envenoming. •Dengue, while not currently endemic, poses a risk of establishment in Australia. There are occasional outbreaks of dengue fever, with local transmission, due to introductions in travellers from endemic regions. •Similarly, the risk of introduction of other

NTDs from neighbouring countries is a concern. Many NTDs are only seen in Australia in individuals travelling from endemic areas, but they need to be recognised in health settings as the potential consequences of infection can be severe. •In this review, we consider the status of NTDs in Australia, explore the risk of introducing and contracting these infections, and emphasise the negative impact they have on the health of Australians, especially Aboriginal and Torres Strait Islander peoples.

### First Report of 'Candidatus Phytoplasma asteris' (16SrI group) Associated with *Murraya exotica* Witches'-Broom Disease in Taiwan.

Tseng, Y., Chang, H., Chang, C., Jan, F.

12-05-2022

*Plant Dis*

<https://doi.org/10.1094/PDIS-02-22-0312-PDN>

*Murraya exotica* L., commonly known as orange jasmine, is an evergreen shrub belonging to the Rutaceae family. It has long been used as traditional Chinese medicine for treating abdominal pain, toothache, scabies, and other disorders (Liu et al. 2018). *M. exotica* is widely grown as a garden bush in Taiwan. A prokaryotic pathogen, 'Candidatus Liberibacter asiaticus' (Damsteegt et al. 2010), reportedly could infect *M. exotica*, but there is no reported phytoplasma disease in *M. exotica*. In June 2020, *M. exotica* plants exhibiting witches'-broom (WB), leaf yellowing, and small leaves (Fig. s1) were observed in a horticultural landscaping field in Taichung City, Taiwan. It was estimated that more than 70% of *M. exotica* plants within a single area were affected. DNA was extracted separately from petioles of five symptomatic and one asymptomatic plants using a modified CTAB method (Echevarría-Machado et al. 2005) and used for nested PCR with two universal primers, P1 (Deng and Hiruki 1991)/P7 (Schneider et al. 1995) followed by R16F2n/R16R2 (Gundersen and Lee 1996) to amplify a 1.2-kb 16S rRNA fragment. PCR was also conducted by primers, rp(I)F1A/rp(I)R1A to amplify a partial ribosomal protein S3 and L22 (rpLV-rpsC) fragment (Lee et al. 2004). Expected 1.2-kb bands were amplified from DNA extracted from all symptomatic plants, whereas no bands were amplified from that of the asymptomatic plant. The amplicons were cloned, sequenced with an ABI 3730 automatic sequencer (Applied Biosystems, Hammon, NJ, USA) in Biotechnology Centre DNA-sequencing facility at National Chung Hsing University (NCHU) and deposited in GenBank. BLAST analysis revealed that 16S rDNA sequences (MZ373297 and MZ373298) shared 100% identity to each other and both shared 99.4% identity with those of several phytoplasma strains, e.g., rapeseed phyllody phytoplasma (CP055264), Brassica sp. phyllody phytoplasma (MN877914), *Plumbago auriculata* leaf yellowing phytoplasma (MN239504), and aster yellows phytoplasma (MK992774), which all belonging to the 16SrI group, by using the CLUSTAL W Methods of MegAlign program (DNASTAR, Inc., Madison, WI, USA). Further analysis using iPhyClassifier tool (<https://plantpathology.ba.ars.usda.gov>) indicated that the virtual restriction fragment length polymorphism (RFLP)

patterns derived from the 16S rDNA F2nR2 fragment of the *M. exotica* WB phytoplasma was most similar to the reference pattern of the 16SrI-B subgroup, with a pattern similarity coefficient of 0.97 and shared 99.3% sequence identity to 'Candidatus Phytoplasma asteris' (M30790). The partial rplV-rpsC gene sequence (OM275408) showed 99.7% of sequence identities to those of rapeseed phyllody phytoplasma (CP055264), plum witches'-broom phytoplasma (MH061366) and oilseed rape phytoplasma (KX551965), by using the CLUSTAL W Methods of MegAlign program. Taken together, we concluded that the phytoplasma strain associated with *M. exotica* WB disease was a strain belonging to a 16SrI. To the best of our knowledge, this is the first report of *M. exotica* being infected by a phytoplasma in the aster yellows group, and *M. exotica* may also serve as an intermediate reservoir host to other plants, e.g., wax apple, periwinkle and roselle, of 16SrI phytoplasma.

### Prevalence and burden of skin diseases among the elderly in Singapore: A 15-year clinical cohort study.

Yew, Y., Kuan, A., George, P., Zhao, X., Tan, S.  
10-05-2022

*J Eur Acad Dermatol Venereol*

<https://doi.org/10.1111/jdv.18205>

**Background:** Populations around the world are rapidly ageing. The profile of skin diseases in the elderly is likely to present unique demands on the healthcare system. **Objectives:** To provide current data on the burden of skin diseases in Singaporean patients and identify differences in the pattern of skin diseases between elderly patients and the rest of the population. **Methods:** This was a retrospective cohort study of 858,117 patients who attended the National Skin Centre between 2004 to 2018. Prevalence was calculated by grouping International Classification of Diseases codes into different categories of skin conditions based on Global Burden of Disease and American Academy of Dermatology classifications. Years lost to disability (YLD) and disability-adjusted life years (DALY) were calculated to report the morbidity and mortality of skin diseases. Differences of each skin condition between age groups were compared. **Results:** The three most prevalent dermatoses across all age groups were dermatitis (33.3%), acne vulgaris (8.3%) and viral skin diseases (7.5%). The top three most common skin conditions among the elderly were dermatitis (37.7%), viral skin diseases (6.2%), and fungal skin diseases (4.3%). Decubitus ulcers, keratinocyte carcinomas and scabies represented a significant proportion of YLD per 100,000 in the elderly ( $p < 0.001$ ). Malignant melanomas, keratinocyte carcinomas, cellulitis, pyoderma, and decubitus ulcers contributed to high DALY in patients aged 70 - 80 years old. Aligning health systems with specific healthcare needs will reduce the disproportionately high burden of skin disease observed in the elderly.

## MORSURES DE SERPENT

### Phytochemical analysis and preclinical toxicological, antioxidant, and anti-inflammatory evaluation of hydroethanol extract from the roots of *Harpalyce brasiliana* Benth (Leguminosae).

Torres-Rêgo, M., Silva de Aquino-Vital, A., Cavalcanti, F., Azevedo Rocha, E., Daniele-Silva, A., Furtado, A., Pontes da Silva, D., Galvão Ururahy, M., Silveira, E., de Freitas Fernandes-Pedrosa, M., Araújo, R.

09-05-2022

*J Ethnopharmacol*

<https://pubmed.ncbi.nlm.nih.gov/35551979>

**Ethnopharmacological relevance:** *Harpalyce brasiliana* Benth (Leguminosae) is a shrub endemic to Brazil, popularly known as "snake's root." This species is used in folk medicine for the treatment of inflammation and snakebites. However, up to now there is no scientific research to justify its popular use.

**Aim of the study:** The study aimed to characterize the phytochemical profile of the hydroethanol extract from the roots of *H. brasiliana* (Hb), to evaluate its antioxidant and anti-inflammatory potential, as well as to investigate its cytotoxicity and acute toxicity. **Materials and methods:** The extract was obtained by maceration method using a solution of ethanol:water (70: 30, v/v). The phytochemical profile was obtained by liquid chromatography coupled to mass spectrometry. The cytotoxicity of extract (31-2000 µg/mL) was evaluated in vitro, by the 3-methyl-[4-5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide (MTT) method using murine macrophage and fibroblast cell lines (RAW 247.6 and 3T3, respectively) and by the hemolytic assay. For the in vivo acute toxicity, the extract (2000 mg/kg) was administered and after 14 days the weight (body and organs) and hematological and biochemical parameters were analyzed. Chemical free radical scavenging effect of the extract (125-2000 µg/mL) was investigated through diphenylpicryl hydrazine reduction, total antioxidant capacity, reducing power, hydroxyl radical scavenging, and iron and copper chelating assays. In vitro anti-inflammatory effect of the extract (125, 500, and 2000 µg/mL) was demonstrated through of nitric oxide (NO) analyzed in lipopolysaccharides stimulated RAW 264.7 cells. In vivo anti-inflammatory activities were evaluated in carrageenan-induced paw edema and zymosan-air-pouch models, with gavage administration (post-treatment) of extract at 100, 200, and 400 mg/kg. For the first animal model, the anti-edematogenic activity and myeloperoxidase (MPO) levels were investigated, while in the zymosan-air-pouch model the leukocyte number, MPO, total protein and pro-inflammatory cytokine (IL-1 $\beta$ , IL-6, and TNF- $\alpha$ ) levels were quantified. In addition, the oxidative parameters such as malondialdehyde (MDA) and reduced glutathione (GSH) were determined.

**Results:** The phytochemical profile revealed the presence of 20 compounds, mainly prenylated and geranylated pterocarpanes. The extract demonstrated no cytotoxicity in erythrocytes, macrophages and fibroblasts cells at the tested concentrations, as well as no sign of toxicity and mortality or significant alterations on the hematological and biochemical

parameters in the acute toxicity model. The extract was also able to neutralize chemical free radicals, with copper and iron chelating effect. For the NO dosage, the extract evidenced the reduction of expression of NO after the administration of the extract (500 and 2000 µg/mL). The edematogenic model revealed a decrease in paw edema and MPO level, while the zymosan-air-pouch model evidenced a reduction of leukocyte number (especially of polymorphonuclears), MPO production, and total protein and cytokine levels, and demonstrated the antioxidant effect through a decrease in MDA and increase in GSH parameters. **Conclusion:** This approach demonstrates for the first time that Hb is not cytotoxic, has low acute toxicity, and possesses antioxidant and anti-inflammatory properties in preclinical analyses, corroborating its popular use.

**A mechanistic model of snakebite as a zoonosis: Envenoming incidence is driven by snake ecology, socioeconomics and its impacts on snakes.**

**Martín, G., Erinjery, J., Ediriweera, D., de Silva, H., Lalloo, D., Iwamura, T., Murray, K.**

12-05-2022

*PLoS Negl Trop Dis*

<https://doi.org/10.1371/journal.pntd.0009867>

Snakebite is the only WHO-listed, not infectious neglected tropical disease (NTD), although its eco-epidemiology is similar to that of zoonotic infections: envenoming occurs after a vertebrate host contacts a human. Accordingly, snakebite risk represents the interaction between snake and human factors, but their quantification has been limited by data availability. Models of infectious disease transmission are instrumental for the mitigation of NTDs and zoonoses. Here, we represented snake-human interactions with disease transmission models to approximate geospatial estimates of snakebite incidence in Sri Lanka, a global hotspot. Snakebites and envenomings are described by the product of snake and human abundance, mirroring directly transmitted zoonoses. We found that human-snake contact rates vary according to land cover (surrogate of occupation and socioeconomic status), the impacts of humans and climate on snake abundance, and by snake species. Our findings show that modelling snakebite as zoonosis provides a mechanistic eco-epidemiological basis to understand snakebites, and the possible implications of global environmental and demographic change for the burden of snakebite.