



Veille scientifique

Maladies tropicales négligées

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06 au 12 mars 2023

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Dengue, chikungunya et maladie à virus Zika

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

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

07-03-2023

Vaccine.

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

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

Behrouz S, Kühl N, Klein CD.

01-03-2023

Eur J Med Chem.

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

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

Self-assembly of dengue virus empty capsid-like particles in solution.

Neves-Martins TC, Mebus-Antunes NC, Neto CHG, Barbosa GM, Almeida FCL, Caruso IP, Da Poian AT.

14-02-2023

iScience.

<https://pubmed.ncbi.nlm.nih.gov/36890794/>

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

Hussain M, Etebari K, Asgari S.

03-03-2023

Virology.

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

Impact of regional climate change on the mosquito vector *Aedes albopictus* in a tropical island environment: La Réunion.

Lamy K, Tran A, Portafaix T, Leroux MD, Baldet T.

Mar-2023

Sci Total Environ.

<https://pubmed.ncbi.nlm.nih.gov/36889019/>

The recent expansion of *Aedes albopictus* across continents in both tropical and temperate regions and the exponential growth of dengue cases over the past 50 years represent a significant risk to human health. Although climate change is not the only factor responsible for the increase and spread of dengue cases worldwide, it might increase the risk of disease transmission at global and regional scale. Here we show that regional and local variations in climate can induce differential impacts on the abundance of *Ae. albopictus*. We use the instructive example of Réunion Island with its varied climatic and environmental conditions and benefiting from the availability of meteorological, climatic, entomological and epidemiological data. Temperature and precipitation data based on regional climate model simulations (3 km × 3 km) are used as inputs to a mosquito population model for three different climate emission scenarios. Our objective is to study the impact of climate change on the life cycle dynamics of *Ae. albopictus* in the 2070-2100 time horizon. Our results show the joint influence of temperature and precipitation on *Ae. albopictus* abundance as a function of elevation and geographical subregion. At low-elevations areas, decreasing precipitation is expected to have a negative impact on environmental carrying capacity and, consequently, on *Ae. albopictus* abundance. At mid- and high-elevations, decreasing precipitation is expected to be counterbalanced by a significant warming, leading to faster development rates at all life stages, and consequently increasing the abundance of this important dengue vector in 2070-2100.

Diagnostic performance of the rapid test for the detection of NS1 antigen and IgM and IgG anti-antibodies against dengue virus.

Valdivia-Conroy B, Vasquez-Calderón JM, Silva-Caso W, Martins-Luna J, Aguilar-Luis MA, Del Valle-Mendoza J, Puyén ZM.

Oct-Dec2022

Rev Peru Med Exp Salud Publica.

<https://pubmed.ncbi.nlm.nih.gov/36888805/>

Study of karyotype and constitutive heterochromatin of *Mansonia* spp. (Diptera: Culicidae) in the area surrounding the Jirau Hydroelectric Dam, Rondônia, Brazil.

Rafael MS, Meireles SDF, Ferreira VDC, Tadei WP, Roque RA.

06-03-2023

Rev Soc Bras Med Trop.

<https://pubmed.ncbi.nlm.nih.gov/36888782/>

Immunogenicity and safety of concomitant and sequential administration of yellow fever YF-17D vaccine and tetravalent dengue vaccine

candidate TAK-003: A phase 3 randomized, controlled study.

Tricou V, Essink B, Ervin JE, Turner M, Escudero I, Rauscher M, Brose M, Lefevre I, Borkowski A, Wallace D. 08-03-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/36888687/>

Background: Yellow fever (YF) vaccination is often mandatory for travelers to YF-endemic areas. The areas with risk of YF partially overlap with those of dengue, for which there is currently no recommended vaccine available for dengue-naïve individuals. This phase 3 study assessed the immunogenicity and safety of concomitant and sequential administration of YF (YF-17D) and tetravalent dengue (TAK-003) vaccines in healthy adults aged 18-60 years living in areas of the US non-endemic for either virus. **Methods:** Participants were randomized 1:1:1 to receive the following vaccinations at Months 0, 3, and 6, respectively: YF-17D+placebo, TAK-003, and TAK-003 (Group 1); TAK-003+placebo, TAK-003, and YF-17D (Group 2); or YF-17D+TAK-003, TAK-003, and placebo (Group 3). The primary objective was to demonstrate non-inferiority (upper bound of 95% confidence interval [UB95%CI] of difference <5%) of YF seroprotection rate one month following concomitant administration of YF-17D and TAK-003 (Group 3) compared with YF-17D plus placebo (Group 1). The secondary objectives included demonstration of non-inferiority of YF and dengue geometric mean titers (GMTs) (UB95%CI for GMT ratio <2.0), and safety. **Results:** 900 adults were randomized. YF seroprotection rates one month post-YF-17D (Month 1) were 99.5% and 99.1% in Group 1 and 3, respectively, and non-inferiority was demonstrated (UB95%CI = 2.69% i.e. <5%). Non-inferiority was also demonstrated for GMTs against YF one month post-YF-17D, and against DENV-2, -3, and -4 (UB95%CI <2), but not DENV-1 (UB95%CI: 2.22), one month post-second TAK-003 vaccination. Adverse event rates following TAK-003 were consistent with previous results, and no important safety risks were identified. **Conclusions:** In this study, YF-17D vaccine and TAK-003 were immunogenic and well tolerated when sequentially or concomitantly administered. The non-inferiority of immune responses to YF-17D and TAK-003 was demonstrated for concomitant administration of the 2 vaccines compared to separate vaccination, except against DENV-1 but with GMTs similar to those observed in other TAK-003 trials.

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

Abbo SR, Nguyen W, Abma-Henkens MHC, van de Kamer D, Savelkoul NHA, Geertsema C, Le TTT, Tang B, Yan K, Dumenil T, van Oers MM, Suhrbier A, Pijlman GP. 08-03-2023

J Virol.

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

Mayaro virus (MAYV) is a mosquito-transmitted alphavirus that causes often debilitating rheumatic disease in tropical Central and South America. There are currently no licensed vaccines or antiviral drugs available for MAYV disease. Here, we generated Mayaro virus-like particles

(VLPs) using the scalable baculovirus-insect cell expression system. High-level secretion of MAYV VLPs in the culture fluid of Sf9 insect cells was achieved, and particles with a diameter of 64 to 70 nm were obtained after purification. We characterize a C57BL/6J adult wild-type mouse model of MAYV infection and disease and used this model to compare the immunogenicity of VLPs from insect cells with that of VLPs produced in mammalian cells. Mice received two intramuscular immunizations with 1 µg of nonadjuvanted MAYV VLPs. Potent neutralizing antibody responses were generated against the vaccine strain, BeH407, with comparable activity seen against a contemporary 2018 isolate from Brazil (BR-18), whereas neutralizing activity against chikungunya virus was marginal. Sequencing of BR-18 illustrated that this virus segregates with genotype D isolates, whereas MAYV BeH407 belongs to genotype L. The mammalian cell-derived VLPs induced higher mean neutralizing antibody titers than those produced in insect cells. Both VLP vaccines completely protected adult wild-type mice against viremia, myositis, tendonitis, and joint inflammation after MAYV challenge. **IMPORTANCE** Mayaro virus (MAYV) is associated with acute rheumatic disease that can be debilitating and can evolve into months of chronic arthralgia. MAYV is believed to have the potential to emerge as a tropical public health threat, especially if it develops the ability to be efficiently transmitted by urban mosquito vectors, such as *Aedes aegypti* and/or *Aedes albopictus*. Here, we describe a scalable virus-like particle vaccine against MAYV that induced neutralizing antibodies against a historical and a contemporary isolate of MAYV and protected mice against infection and disease, providing a potential new intervention for MAYV epidemic preparedness.

Correction for Li et al., "Different Degrees of 5'-to-3' DAR Interactions Modulate Zika Virus Genome Cyclization and Host-Specific Replication".

Li XD, Deng CL, Yuan ZM, Ye HQ, Zhang B.

08-03-2023

J Virol.

<https://pubmed.ncbi.nlm.nih.gov/36883811/>

The stability analysis of a co-circulation model for COVID-19, dengue, and zika with nonlinear incidence rates and vaccination strategies.

Omame A, Abbas M.

Nov-2023

Healthc Anal (N Y).

<https://pubmed.ncbi.nlm.nih.gov/36883137/>

This paper aims to study the impacts of COVID-19 and dengue vaccinations on the dynamics of zika transmission by developing a vaccination model with the incorporation of saturated incidence rates. Analyses are performed to assess the qualitative behavior of the model. Carrying out bifurcation analysis of the model, it was concluded that co-infection, super-infection and also re-infection with same or different disease could trigger backward bifurcation. Employing well-formulated Lyapunov functions, the

model's equilibria are shown to be globally stable for a certain scenario. Moreover, global sensitivity analyses are performed out to assess the impact of dominant parameters that drive each disease's dynamics and its co-infection. Model fitting is performed on the actual data for the state of Amazonas in Brazil. The fittings reveal that our model behaves very well with the data. The significance of saturated incidence rates on the dynamics of three diseases is also highlighted. Based on the numerical investigation of the model, it was observed that increased vaccination efforts against COVID-19 and dengue could positively impact zika dynamics and the co-spread of triple infections.

Metabolic reprogramming and lipid droplets are involved in Zika virus replication in neural cells.

Dias SSG, Cunha-Fernandes T, Souza-Moreira L, Soares VC, Lima GB, Azevedo-Quintanilha IG, Santos J, Pereira-Dutra F, Freitas C, Reis PA, Rehen SK, Bozza FA, Souza TML, de Almeida CJG, Bozza PT.

08-03-2023

J Neuroinflammation.

<https://pubmed.ncbi.nlm.nih.gov/36882750/>

International Travel Vaccine Recommendations for Children.

Machicao MF, Yashar-Gershman S, Romero JR, Bernstein HH.

Mar-2023

Pediatr Ann.

<https://pubmed.ncbi.nlm.nih.gov/36881794/>

Re-examination of the risk of autoimmune diseases after dengue virus infection: A population-based cohort study.

Shih HI, Chi CY, Tsai PF, Wang YP, Chien YW.

07-03-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/36881559/>

Previous studies suggested that dengue was associated with an increased risk of several autoimmune diseases. However, this association still needs to be explored due to the limitations of these studies. A population-based cohort study was conducted using national health databases in Taiwan and included 63,814 newly diagnosed, laboratory-confirmed dengue patients between 2002 and 2015 and 1:4 controls (n = 255,256) matched by age, sex, area of residence and symptom onset time. Multivariate Cox proportional hazard regression models were used to investigate the risk of autoimmune diseases after dengue infection. Dengue patients had a slightly higher risk of overall autoimmune diseases than non-dengue controls (aHR 1.16; P = 0.0002). Stratified analyses by specific autoimmune diseases showed that only autoimmune encephalomyelitis remained statistically significant after Bonferroni correction for multiple testing (aHR 2.72; P < 0.0001). Sixteen (0.025%) dengue patients and no (0%) controls developed autoimmune encephalomyelitis in the first month of follow-up (HR >9999, P < 0.0001), but the

risk between groups was not significantly different thereafter. Contrary to previous studies, our findings showed that dengue was associated with an increased short-term risk of a rare complication, autoimmune encephalomyelitis, but not associated with other autoimmune diseases.

Association between rapid renal function deterioration and cancer mortality in the elderly: A retrospective cohort study.

Kuo IC, Chu YC, Chen YH, Chan TC.

07-03-2032

Cancer Med.

<https://pubmed.ncbi.nlm.nih.gov/36880220/>

Interaction of the Zika virus with the cytoplasmic dynein-1.

Zavala-Vargas DI, Visoso-Carbajal G, Cedillo-Barrón L, Filisola-Villaseñor JG, Rosales-Ramirez R, Ludert JE, Morales-Ríos E.

06-03-2023

Virology.

<https://pubmed.ncbi.nlm.nih.gov/36879270/>

Zika virus (ZIKV) infection is a major public health threat, making the study of its biology a matter of great importance. By analyzing the viral-host protein interactions, new drug targets may be proposed. In this work, we showed that human cytoplasmic dynein-1 (Dyn) interacts with the envelope protein (E) of ZIKV. Biochemical evidence indicates that the E protein and the dimerization domain of the heavy chain of Dyn binds directly without dynactin or any cargo adaptor. Analysis of this interactions in infected Vero cells by proximity ligation assay suggest that the E-Dyn interaction is dynamic and finely tuned along the replication cycle. Altogether, our results suggest new steps in the replication cycle of the ZIKV for virion transport and indicate a suitable molecular target to modulate infection by ZIKV.

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

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

06-03-2023

Am J Trop Med Hyg.

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

Efficient generation and characterization of chimeric dengue viral-like particles.

Veena Rani N, Kapoor N, Krishnan A.

26-02-2023

Biochem Biophys Res Commun.

<https://pubmed.ncbi.nlm.nih.gov/36878035/>

Viral-like particles (VLPs) because of their non-infectious and high immunogenic properties have important applications in diagnostics, drug delivery, and vaccine

production. They also serve as an attractive model system to study virus assembly and fusion processes. Unlike other flaviviruses, Dengue virus (DENV) is not very efficient in the production of VLPs on the expression of DENV structural proteins. On the other hand, the stem region and transmembrane region (TM) of G protein of Vesicular Stomatitis virus (VSV) alone are sufficient for budding. Here we generated chimeric VLPs replacing regions of stem and transmembrane domain (STEM) or only transmembrane domain (TM) of E protein of DENV-2 with corresponding regions of VSV G protein. Both chimeric proteins secreted VLPs at higher levels than the wild type (2-4 folds) without any significant change in the expression in the cell. Chimeric VLPs could be recognized by a conformational monoclonal antibody, 4G2. They were also found to interact with dengue-infected patient sera effectively thus implying that their antigenic determinants are preserved. In addition, they were able to bind to its putative receptor, heparin with similar affinity as the parent counterpart thus retaining its functional property. However, cell-cell fusion revealed that there is no significant increase in the fusion ability of chimeras as compared to the parent clone, whereas VSV G protein displayed high cell-cell fusion activity. Overall, this study suggests that chimeric dengue VLPs can be taken forward for their likely potential as vaccine production and serodiagnosis.

Current evidences of the efficacy of mosquito mass-trapping interventions to reduce *Aedes aegypti* and *Aedes albopictus* populations and *Aedes*-borne transmission.

Jaffal A, Fite J, Baldet T, Delaunay P, Jourdain F, Mora-Castillo R, Olive MM, Roiz D.

06-03-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/36877728/>

Background: Over the past decades, several viral diseases transmitted by *Aedes* mosquitoes-dengue, chikungunya, Zika-have spread outside of tropical areas. To limit the transmission of these viruses and preserve human health, the use of mosquito traps has been developed as a complement or alternative to other vector control techniques. The objective of this work was to perform a systematic review of the existing scientific literature to assess the efficacy of interventions based on adult mosquito trap to control *Aedes* population densities and the diseases they transmit worldwide. **Methods and findings:** Following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, a systematic review was conducted using the PubMed and Scopus databases. Among the 19 selected papers, lethal ovitraps were used in 16 studies, host-seeking female traps in 3 studies. Furthermore, 16 studies focused on the control of *Ae. aegypti*. Our review showed great heterogeneity in the indicators used to assess trap efficacy: e.g., the number of host-seeking females, the number of gravid females, the proportion of positive containers, the viral infection rate in female mosquitoes or serological studies in residents. Regardless of the type of studied traps, the results of various studies support the

efficacy of mass trapping in combination with classical integrated vector control in reducing *Aedes* density. More studies with standardized methodology, and indicators are urgently needed to provide more accurate estimates of their efficacy. **Conclusions:** This review highlights gaps in the demonstration of the efficacy of mass trapping of mosquitoes in reducing viral transmission and disease. Thus, further large-scale cluster randomized controlled trials conducted in endemic areas and including epidemiological outcomes are needed to establish scientific evidence for the reduction of viral transmission risk by mass trapping targeting gravid and/or host-seeking female mosquitoes.

Complex network analysis of arboviruses in the same geographic domain: Differences and similarities.

Santos ES, Miranda JGV, Saba H, Skalinski LM, Araújo MLV, Veiga RV, Costa MDCN, Cardim LL, Paixão ES, Teixeira MG, Andrade RFS, Barreto ML.

Mar-2023

Chaos Solitons Fractals.

<https://pubmed.ncbi.nlm.nih.gov/36876054/>

Virulence network of interacting domains of influenza A and mouse proteins.

Ng TA, Rashid S, Kwok CK.

17-02-2023

Front Bioinform.

<https://pubmed.ncbi.nlm.nih.gov/36875146/>

S-Adenosyl-L-Homocysteine Exhibits Potential Antiviral Activity Against Dengue Virus Serotype-3 (DENV-3) in Bangladesh: A Viroinformatics-Based Approach.

Shill DK, Jahan S, Alam MM, Limon MBH, Alam M, Rahman MZ, Rahman M.

27-02-2023

Bioinform Biol Insights.

<https://pubmed.ncbi.nlm.nih.gov/36873305/>

Dengue outbreak is one of the concerning issues in Bangladesh due to the annual outbreak with the alarming number of death and infection. However, there is no effective antiviral drug available to treat dengue-infected patients. This study evaluated and screened antiviral drug candidates against dengue virus serotype 3 (DENV-3) through viroinformatics-based analyses. Since 2017, DENV-3 has been the predominant serotype in Bangladesh. We selected 3 non-structural proteins of DENV-3, named NS3, NS4A, and NS5, as antiviral targets. Protein modeling and validation were performed with VERIFY-3D, Ramachandran plotting, MolProbity, and PROCHECK. We found 4 drug-like compounds from DRUGBANK that can interact with these non-structural proteins of DENV-3. Then, the ADMET profile of these compounds was determined by admetSAR2, and molecular docking was performed with AutoDock, SWISSDOCK, PatchDock, and FireDock. Furthermore, they were subjected to molecular dynamics (MD) simulation

study using the DESMOND module of MAESTRO academic version 2021-4 (force field OPLS_2005) to determine their solution's stability in a predefined body environment. Two drug-like compounds named Guanosine-5'-Triphosphate (DB04137) and S-adenosyl-L-homocysteine (DB01752) were found to have an effective binding with these 3 proteins (binding energy > 33.47 KJ/mole). We found NS5 protein was stable and equilibrated in a 100 ns simulation run along with a negligible (<3Å) root-mean-square fluctuation value. The root-mean-square deviation value of the S-adenosyl-L-homocysteine-NS5 complex was less than 3Å, indicating stable binding between them. The global binding energy of S-adenosyl-L-homocysteine with NS5 was -40.52 KJ/mole as ΔG . Moreover, these 2 compounds mentioned above are non-carcinogenic according to their ADMET (chemical absorption, distribution, metabolism, excretion, and toxicity) profile (in silico). These outcomes suggest the suitability of S-adenosyl-L-homocysteine as a potential drug candidate for dengue drug discovery research.

Association of Hematological and Biochemical Parameters with Serological Markers of Acute Dengue Infection during the 2022 Dengue Outbreak in Nepal.

Bhattarai BR, Mishra A, Aryal S, Chhusyabaga M, Bhujel R.

23-02-2023

J Trop Med.

<https://pubmed.ncbi.nlm.nih.gov/36873099/>

Background: Nepal faced a major dengue outbreak in 2022. The majority of hospitals and laboratories had limited resources for dengue confirmation and had to rely on rapid dengue diagnostic tests. The purpose of the study is to find the predictive hematological and biochemical parameters in each serological phase of dengue infection (NS1 and IgM) that may assist in dengue diagnosis, severity assessment, and patient management via the use of rapid serological tests. **Method:** A laboratory-based cross-sectional study was conducted among dengue patients. Rapid antigen (NS1) and serological test (IgM/IgG) was performed to diagnose positive dengue cases. Furthermore, hematological and biochemical investigations were carried out and compared between NS1 and/or IgM-positive participants. A logistic regression analysis was used to identify the validity of the hematological and biochemical characteristics for dengue diagnosis as well as patient management. Receiver-operating characteristic (ROC) curve analysis was used to define the best cut-off, sensitivity, and specificity. **Result:** Multiple logistic regression showed thrombocytopenia ($OR_A = 1.000$; $p = 0.006$), leukopenia ($OR_A = 0.999$; $p < 0.001$), glucose level ($OR_A = 1.028$; $p = 0.029$), aspartate aminotransferase ($OR_A = 1.131$; $p = 0.001$), and monocytosis ($OR_A = 2.332$; $p = 0.020$) as significant parameters in the NS1-only positive group. Similarly, thrombocytopenia ($OR_A = 1.000$; $p = 0.001$), glucose level ($OR_A = 1.037$; $p = 0.004$), and aspartate aminotransferase ($OR_A = 1.141$; $p < 0.001$) were significant in IgM-only positive patients. Moreover, thrombocytopenia ($OR_A = 1.000$; $p < 0.001$), leukopenia ($OR_A = 0.999$; $p < 0.001$),

glucose ($OR_A = 1.031$; $p = 0.017$), aspartate aminotransferase ($OR_A = 1.136$; $p < 0.001$), and lymphopenia ($OR_A = 0.520$; $p = 0.067$) were independent predictors in both NS1 + IgM positive groups. Platelets consistently demonstrated a higher area under the curve with increased sensitivity and specificity throughout all models, while aspartate aminotransferase (AUC = 0.811) and glucose (AUC = 0.712) demonstrated better results when single IgM positivity was observed. The total leukocyte count performed better when both NS1 + IgM were positive (AUC = 0.814). **Conclusion:** Hence, thrombocytopenia, elevated AST, high glucose level, leukopenia with monocytosis, and leukopenia with lymphopenia may predict dengue diagnosis and its severity during an active infection. Therefore, these laboratory parameters can be used to complement less sensitive rapid tests, improve dengue diagnosis, and help with proper patient management.

The resurgence of dengue epidemic and climate change in India.

Mondal N.

04-03-2023

Lancet.

<https://pubmed.ncbi.nlm.nih.gov/36870720/>

Identification of an effective fraction from *Ampelopsis radix* with anti-dengue virus activities in vitro and in vivo.

Tian C, Huang H, Zheng Y, He X, Yan L, Shi L, Yang T, Chen X, Yang J, Lu Z, Cao H, Zhao W, Qin Z, Yu J, Tang Q, Tong X, Liu J, Yu L.

02-03-2023

J Ethnopharmacol.

<https://pubmed.ncbi.nlm.nih.gov/36870463/>

Flavivirus nonstructural proteins and replication complexes as antiviral drug targets.

van den Elsen K, Chew BLA, Ho JS, Luo D.

02-03-2023

Curr Opin Virol.

<https://pubmed.ncbi.nlm.nih.gov/36870091/>

Many flaviviruses are well-known pathogens, such as dengue, Zika, Japanese encephalitis, and yellow fever viruses. Among them, dengue viruses cause global epidemics and threaten billions of people. Effective vaccines and antivirals are in desperate need. In this review, we focus on the recent advances in understanding viral nonstructural (NS) proteins as antiviral drug targets. We briefly summarize the experimental structures and predicted models of flaviviral NS proteins and their functions. We highlight a few well-characterized inhibitors targeting these NS proteins and provide an update about the latest development. NS4B emerges as one of the most promising drug targets as novel inhibitors targeting NS4B and its interaction network are entering clinical studies. Studies aiming to elucidate the architecture and molecular basis of viral replication will offer new opportunities for novel antiviral discovery. Direct-acting agents against

dengue and other pathogenic flaviviruses may be available very soon.

[Kawasaki disease cytokine release syndrome and Kawasaki disease shock syndrome: A case report].

Montero-Vázquez RA.

01-02-2023

Rev Alerg Mex.

<https://pubmed.ncbi.nlm.nih.gov/36869015/>

Background: Kawasaki disease is a vasculitis of small and medium vessels, with a high prevalence throughout the world. In addition to coronary aneurysms, this vasculitis can lead to a number of systemic complications, including Kawasaki disease shock syndrome and Kawasaki disease cytokine storm syndrome. **Case report:** : Case report: A 12-year-old male patient, who began his condition with heartburn, sudden fever of 40 °C and jaundice, for which he was prescribed treatment with antipyretics and bismuth subsalicylate, without satisfactory reaction. Gastrointestinal content was added three times, and centripetal maculopapular dermatosis. After 12 hospital stays, he was evaluated by personnel from the Pediatric Immunology service, who reported data on hemodynamic instability due to persistent tachycardia for hours, immediate capillary refill, intense pulse, oliguria of 0.3 mL/kg/h of partial urinary output with condensed urine; the systolic blood pressure figures were below the 50% percentile, and there was polypnea and limit saturation in 93%. In the paraclinical studies, the rapid decrease in platelet count (from 297,000 to 59,000 in 24 hours), as well as a neutrophil-lymphocyte index of 12, drew attention. The concentrations of NS1 size, IgM and IgG for dengue and PCR for SARS virus were determined. -CoV-2, which were negative. The definitive diagnosis of Kawasaki disease was established with Kawasaki disease shock syndrome. The evolution of the patient was satisfactory, with a decrease in fever after the administration of gamma globulin on the tenth day of hospitalization, and a new protocol with prednisone (50 mg/day) was started, when the cytokine storm syndrome due to illness was integrated. Kawasaki syndrome simultaneous with pre-existing disorders, that is, Kawasaki disease and Kawasaki disease shock syndrome due to thrombocytopenia, hepatosplenomegaly, fever, lymphadenopathy; in addition, ferritin of 605 mg/dL and transaminasemia. The control echocardiogram did not show coronary abnormalities and hospital discharge was granted 48 hours after starting treatment with the corticosteroid, with a 14-day follow-up plan. **Conclusions:** Kawasaki disease is an autoimmune vasculitis that can worsen with simultaneous syndromes associated with high mortality. It is important to know this type of alterations and their differences to properly discern and implement effective and timely treatment.

Prevalence and Epidemiological Aspects of Chikungunya Fever in States of the Northeast Region of Brazil: a systematic review.

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

28-02--2023

Acta Trop.

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

Pandemic city: Village-in-a-dish unlocks dynamic genetic effects in the brain.

Seah C, Brennand KJ.

02-03-2023

Cell Stem Cell.

<https://pubmed.ncbi.nlm.nih.gov/36868190/>

In this issue, Wells et al. combine genetic multiplexing ("village-in-a-dish") and Stem-cell-derived NGN2-accelerated Progenitors (SNaPs) to evaluate genotype-phenotype relationships across 100 donors in the context of Zika virus infection in the developing brain. This resource will be broadly applicable in uncovering how genetic variation underlies risk for neurodevelopmental disorders.

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

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

03-02-2023

Public Health.

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

Objectives: There are concerns about the potential effect of social distancing used to control COVID-19 on the incidence of cardiovascular diseases (CVD). **Study design:** Retrospective cohort study. **Methods:** We examined the association between lockdown and CVD incidence in a Zero-COVID country, New Caledonia. Inclusion criteria were defined by a positive troponin sample during hospitalization. The study period lasted for 2 months, starting March 20, 2020 (strict lockdown: first month; loose lockdown: second month) compared with the same period of the three previous years to calculate incidence ratio (IR). Demographic characteristics and main CVD diagnoses were collected. The primary endpoint was the change in incidence of hospital admission with CVD during lockdown compared with the historical counterpart. The secondary endpoint included influence of strict lockdown, change in incidence of the primary endpoint by disease, and outcome incidences (intubation or death) analyzed with inverse probability weighting method. **Results:** A total of 1215 patients were included: 264 in 2020 vs 317 (average of the historical period). CVD hospitalizations were reduced during strict lockdown (IR 0.71 [0.58-0.88]), but not during loose lockdown (IR 0.94 [0.78-1.12]). The incidence of acute coronary syndromes was similar in both periods. The incidence of acute decompensated heart failure was reduced during strict lockdown (IR 0.42 [0.24-0.73]), followed by a rebound (IR 1.42 [1-1.98]). There was no association between lockdown and short-term outcomes. **Conclusions:** Our study showed that lockdown was associated with a striking reduction in CVD hospitalizations, independently from viral spread, and a

rebound of acute decompensated heart failure hospitalizations during looser lockdown.

A systematic review of published literature on mosquito control action thresholds across the world.

Aryaprema VS, Steck MR, Peper ST, Xue RD, Qualls WA.

03-03-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/36867651/>

Congenital Zika syndrome.

Crisanto-López IE, Jesús PL, López-Quecho J, Flores-Alonso JC.

2023

Bol Med Hosp Infant Mex.

<https://pubmed.ncbi.nlm.nih.gov/36867568/>

In February 2016, the World Health Organization declared Zika virus (ZIKV) infection a public health emergency of international concern because it caused congenital Zika syndrome (CZS). The CZS is considered a specific pattern of birth defects caused by ZIKV infection, which is transmitted by the bite of the *Aedes aegypti* mosquito. The CZS clinical manifestations are broad and nonspecific, including microcephaly, subcortical calcifications, ocular alterations, congenital contractures, early hypertonia, and pyramidal as well as extrapyramidal symptoms. The ZIKV has gained great importance because it has affected a large percentage of the population worldwide during the last few years, despite the measures implemented by international organizations. The pathophysiology and non-vectorial transmission routes of the virus are still under study. The diagnosis is made upon suspicion of ZIKV infection, the patient's clinical manifestations, and it is confirmed by molecular laboratory tests demonstrating the presence of viral particles. Unfortunately, there is no specific treatment or vaccine for this condition; however, patients receive multidisciplinary care and constant monitoring. Therefore, the strategies that have been implemented are directed toward preventive measures and vector control.

The role of glial cells in Zika virus-induced neurodegeneration.

Quincozes-Santos A, Bobermin LD, Costa NLF, Thomaz NK, Almeida RRS, Beys-da-Silva WO, Santi L, Rosa RL, Capra D, Coelho-Aguiar JM, DosSantos MF, Heringer M, Cirne-Lima EO, Guimarães JA, Schuler-Faccini L, Gonçalves CA, Moura-Neto V, Souza DO.

03-03-2023

Glia.

<https://pubmed.ncbi.nlm.nih.gov/36866453/>

Concurrent Dengue-Malaria Infection: The Importance of Acute Febrile Illness in Endemic Zones.

González-Macea O, Martínez-Ávila MC, Pérez M, Tibocho Gordon I, Arroyo Salgado B.

27-02-2023

Clin Med Insights Case Rep.

<https://pubmed.ncbi.nlm.nih.gov/36865392/>

Context: Acute febrile disease (AFI) in endemic tropical areas is a frequent reason for consulting the emergency services. Infection by 2 or more etiological agents may modify clinical and laboratory parameters, making diagnosis and treatment a challenge. **Case report:** We report the case of a patient who came from Africa and consults in Colombia, with AFI with thrombocytopenia that was eventually diagnosed to have concurrent infection with *Plasmodium falciparum* malaria and dengue. **Conclusions:** Dengue-malaria coinfection infection reports are scarce; it should be suspected in patients living or returning from areas where both diseases are endemic or during dengue outbreaks. This case serves as a reminder of this important condition that causes high morbidity and mortality if it is not early diagnosed and treated.

The La Crosse virus class II fusion glycoprotein ij loop contributes to infectivity and cholesterol-dependent entry.

Thannickal SA, Spector SN, Stapleford KA.

23-02-2023

bioRxiv.

<https://pubmed.ncbi.nlm.nih.gov/36865275/>

Arthropod-borne viruses (arboviruses) are an emerging and evolving global public health threat with little to no antiviral treatments. La Crosse virus (LACV) from the *Bunyavirales* order is responsible for pediatric encephalitis cases in the United States, yet little is known about the infectivity of LACV. Given the structural similarities between class II fusion glycoproteins of LACV and chikungunya virus (CHIKV), an alphavirus from the *Togaviridae* family, we hypothesized that LACV would share similar entry mechanisms to CHIKV. To test this hypothesis, we performed cholesterol-depletion and repletion assays and used cholesterol modulating compounds to study LACV entry and replication. We found that LACV entry was cholesterol-dependent while replication was less affected by cholesterol manipulation. In addition, we generated single point mutants in the LACV *ij* loop that corresponded to known CHIKV residues important for virus entry. We found that a conserved histidine and alanine residue in the Gc *ij* loop impaired virus infectivity and attenuate LACV *in vitro* and *in vivo*. Finally, we took an evolution-based approach to explore how the LACV glycoprotein evolution in mosquitoes and mice. We found multiple variants that cluster in the Gc glycoprotein head domain, supporting the Gc glycoprotein as a target for LACV adaptation. Together, these results begin to characterize the mechanisms of LACV infectivity and how the LACV glycoprotein contributes to infectivity and pathogenesis. **Importance:** Vector-borne arboviruses are significant health threats leading to devastating disease worldwide. This emergence and the fact that there are little to no vaccines or antivirals targeting these viruses highlights the need to study how arboviruses replicate at the molecular level. One potential antiviral target is the class II fusion glycoprotein. Alphaviruses, flaviviruses, and bunyaviruses encode a class II fusion glycoprotein that contain strong structural similarities in the tip of domain II. Here we show that the bunyavirus La Crosse virus uses

similar mechanisms to entry as the alphavirus chikungunya virus and residues in the *ij* loop are important for virus infectivity. These studies show that genetically diverse viruses use similar mechanisms through conserved structure domains, suggesting these may be a target for broad-spectrum antivirals to multiple arbovirus families.

Assessing the potential of NS2B/NS3 protease inhibitors biomarker in curbing dengue virus infections: In silico vs. In vitro approach.

Norshidah H, Leow CH, Ezleen KE, Wahab HA, Vignesh R, Rasul A, Lai NS.

14-02-2023

Front Cell Infect Microbiol.

<https://pubmed.ncbi.nlm.nih.gov/36864886/>

Prevalence, clinical, and demographic characteristics of concomitant dengue fever and leptospirosis among acute dengue fever patients in The Western Province of Sri Lanka.

Samarakoon PSMJU, Karunanayake L, Muthugala R, Karunanayake P.

Jul-Dec 2022

WHO South East Asia J Public Health.

<https://pubmed.ncbi.nlm.nih.gov/36861631/>

Model-based risk assessment of dengue fever transmission in Xiamen City, China.

Guo Z, Liu W, Liu X, Abudunaibi B, Luo L, Wu S, Deng B, Yang T, Huang J, Wu S, Lei L, Zhao Z, Li Z, Li P, Liu C, Zhan M, Chen T.

13-02-2023

Front Public Health.

<https://pubmed.ncbi.nlm.nih.gov/36860401/>

Background: Quantitative assessment of the risk of local transmission from imported dengue cases makes a great challenge to the development of public health in China. The purpose of this study is to observe the risk of mosquito-borne transmission in Xiamen City through ecological and insecticide resistance monitoring. Quantitative evaluation of mosquito insecticide resistance, community population and the number of imported cases affecting the transmission of dengue fever (DF) in Xiamen was carried out based on transmission dynamics model, so as to reveal the correlation between key risk factors and DF transmission. **Methods:** Based on the dynamics model and combined with the epidemiological characteristics of DF in Xiamen City, a transmission dynamics model was built to simulate the secondary cases caused by imported cases to evaluate the transmission risk of DF, and to explore the influence of mosquito insecticide resistance, community population and imported cases on the epidemic situation of DF in Xiamen City. **Results:** For the transmission model of DF, when the community population is between 10,000 and 25,000, changing the number of imported DF cases and the mortality rate of mosquitoes will have an impact on the spread of indigenous DF cases, however, changing the

birth rate of mosquitoes did not gain more effect on the spread of local DF transmission. **Conclusions:** Through the quantitative evaluation of the model, this study determined that the mosquito resistance index has an important influence on the local transmission of dengue fever caused by imported cases in Xiamen, and the Brayton index can also affect the local transmission of the disease.

Association between genetic variants in TREM1, CXCL10, IL4, CXCL8 and TLR7 genes with the occurrence of congenital Zika syndrome and severe microcephaly.

Santos CNO, Magalhães LS, Fonseca ABL, Bispo AJB, Porto RLS, Alves JC, Dos Santos CA, de Carvalho JV, da Silva AM, Teixeira MM, de Almeida RP, Dos Santos PL, de Jesus AR.

01-03-2023

Sci Rep.

<https://pubmed.ncbi.nlm.nih.gov/36859461/>

Congenital Zika syndrome (CZS) is a cluster of malformations induced by Zika virus (ZIKV) infection and the underlying mechanisms involved in its occurrence are yet not fully understood. Along with epidemiological and environmental factors, the genetic host factors are suggested as important to the CZS occurrence and development, however, few studies have evaluated this. This study enrolled a total of 245 individuals in a case-control association study composed a cohort of high specific interest constituted by 75 mothers who had delivered CZS infants, their 76 infants, and 47 mothers that had delivered healthy infants, and their 47 infants. Sixteen single-nucleotide polymorphisms on TREM1, CXCL10, IL4, CXCL8, TLR3, TLR7, IFNR1, CXCR1, IL10, CCR2 and CCR5 genes were genotyped to investigate their association as risk factors to CZS. The results show an association between C allele at TREM1 rs2234246 and C allele at IL4 rs224325 in mothers infected with ZIKV during pregnancy, with the increased susceptibility to CZS occurrence in their infants and the SNP CXCL8 rs4073 and the G allele at CXCL10 rs4508917 with presence of CZS microcephaly in the infants. Furthermore, the T allele at CXCL8 rs4073 and TLR7 rs179008 SNPs were associated with the severity of microcephaly in children with CZS. These results suggest that these polymorphisms in genes of innate immune responses addressed here are associated to increased risk of occurrence and severity of CZS in pregnant mothers infected with ZIKV and their CZS infants.

The pipeline for drugs for control and elimination of neglected tropical diseases: 1. Anti-infective drugs for regulatory registration.

Pfarr KM, Krome AK, Al-Obaidi I, Batchelor H, Vaillant M, Hoerauf A, Opoku NO, Kuesel AC.

01-03-2023

Parasit Vectors.

<https://pubmed.ncbi.nlm.nih.gov/36859332/>

Challenges on the development of a dengue vaccine: a comprehensive review of the state of the art.

Pintado Silva J, Fernandez-Sesma A.

Mar-2023

J Gen Virol.

<https://pubmed.ncbi.nlm.nih.gov/36857199/>

Dengue virus (DENV) is the mosquito-borne virus of greatest human health concern. There are four serotypes of DENV (1-4) that co-circulate in endemic areas. Each serotype of DENV is individually capable of causing the full spectrum of disease, ranging from self-resolving dengue fever to the more severe dengue haemorrhagic fever (DHF) or dengue shock syndrome (DSS). Based on data published by the CDC, one in four people who become infected with dengue will become ill. Of those that do develop symptomatology, the symptoms can range from mild to severe. Symptoms can vary from rash, ocular aches and pains to more intense symptoms in the manifestation of severe dengue. Roughly, 1 in 20 people who become ill will develop severe dengue, which can result in shock, internal bleeding and death. There is currently no specific treatment for dengue and only one licensed vaccine (Dengvaxia) for children 9 through 16 years of age in just a few countries. Despite its licensure for clinical use, Dengvaxia has performed with low efficacy in children and dengue naïve individuals and critically has resulted in increased risk of developing severe dengue in young, vaccinated recipients. Currently, there are various novel strategies for the development of a dengue vaccine. In this review we have conducted a detailed overview of the DENV vaccine landscape, focusing on nine vaccines in the pipeline to provide a comprehensive overview of the most state-of-the-art developments in strategies for vaccines against DENV.

Some features on methodology of dengue modelling linked to data: Comment on "Mathematical modelling for dengue fever epidemiology: a 10-year systematic review" by M. Aguiar et al.

Pinho STR.

Mar-2023

Phys Life Rev.

<https://pubmed.ncbi.nlm.nih.gov/36821892/>

Natural variation in gene expression and viral susceptibility revealed by neural progenitor cell villages.

Wells MF, Nemesh J, Ghosh S, Mitchell JM, Salick MR, Mello CJ, Meyer D, Pietilainen O, Piccioni F, Guss EJ, Raghunathan K, Tegtmeyer M, Hawes D, Neumann A, Worringer KA, Ho D, Kommineni S, Chan K, Peterson BK, Raymond JJ, Gold JT, Siekmann MT, Zuccaro E, Nehme R, Kaykas A, Eggan K, McCarroll SA.

02-03-2023

Cell Stem Cell.

<https://pubmed.ncbi.nlm.nih.gov/36796362/>

Bioinformatics Analysis of Mutations Sheds Light on the Evolution of Dengue

NS1 Protein With Implications in the Identification of Potential Functional and Druggable Sites.

Sharma A, Krishna S, Sowdhamini R.

04-03-2023

Mol Biol Evol.

<https://pubmed.ncbi.nlm.nih.gov/36795614/>

Non-structural protein (NS1) is a 350 amino acid long conserved protein in the dengue virus. Conservation of NS1 is expected due to its importance in dengue pathogenesis. The protein is known to exist in dimeric and hexameric states. The dimeric state is involved in its interaction with host proteins and viral replication, and the hexameric state is involved in viral invasion. In this work, we performed extensive structure and sequence analysis of NS1 protein, and uncovered the role of NS1 quaternary states in its evolution. A three-dimensional modeling of unresolved loop regions in NS1 structure is performed. "Conserved" and "Variable" regions within NS1 protein were identified from sequences obtained from patient samples and the role of compensatory mutations in selecting destabilizing mutations were identified. Molecular dynamics (MD) simulations were performed to extensively study the effect of a few mutations on NS1 structure stability and compensatory mutations. Virtual saturation mutagenesis, predicting the effect of every individual amino acid substitution on NS1 stability sequentially, revealed virtual-conserved and variable sites. The increase in number of observed and virtual-conserved regions across NS1 quaternary states suggest the role of higher order structure formation in its evolutionary conservation. Our sequence and structure analysis could enable in identifying possible protein-protein interfaces and druggable sites. Virtual screening of nearly 10,000 small molecules, including FDA-approved drugs, permitted us to recognize six drug-like molecules targeting the dimeric sites. These molecules could be promising due to their stable interactions with NS1 throughout the simulation.

Data-rich modeling helps answer increasingly complex questions on variant and disease interactions: Comment on "Mathematical models for dengue fever epidemiology: A 10-year systematic review" by Aguiar et al.

Roster KO.

Mar-2023

Phys Life Rev.

<https://pubmed.ncbi.nlm.nih.gov/36773393/>

Genome sequencing of dengue virus serotype 4 in a bat brain sample (*Platyrrhinus helleri*) from the Brazilian Amazon.

Franco Filho LC, Barata RR, Coelho MS, Cardoso JF, Lemos PDS, Dos Reis HS, Favacho JDFR, Faria NR, Nunes MRT.

Apr-2023

Infect Genet Evol.

<https://pubmed.ncbi.nlm.nih.gov/36764633/>

The existence of sylvatic transmission of dengue virus in communities of neotropical bats remains uncertain. In this work we present a near-complete genome of dengue virus serotype 4 obtained from the brain sample of a bat from *Platyrrhinus helleri* specie collected in the Brazilian Amazon region. The presence of the virus in the brain sample may indicate a possible tropism for the central nervous system in bats, which may justify negative results in previous studies that focused on analysis of other tissues, such as liver and spleen. Besides the duration of dengue virus circulation in the Americas (circa 40 years) may be too short for an implementation of a sylvatic dengue virus cycle. Our findings suggest that continued monitoring is needed to confirm with the neotropical bats could potentially act as a natural reservoir of dengue in the region.

Neem-based products as potential eco-friendly mosquito control agents over conventional eco-toxic chemical pesticides-A review.

Chatterjee S, Bag S, Biswal D, Sarkar Paria D, Bandyopadhyay R, Sarkar B, Mandal A, Dangar TK.
Apr-2023
Acta Trop.
<https://pubmed.ncbi.nlm.nih.gov/36750152/>

Mosquitoes cause serious health hazards for millions of people across the globe by acting as vectors of deadly communicable diseases like malaria, filariasis, dengue and yellow fever. Use of conventional chemical insecticides to control mosquito vectors has led to the development of biological resistance in them along with adverse environmental consequences. In this light, the recent years have witnessed enormous efforts of researchers to develop eco-friendly and cost-effective alternatives with special emphasis on plant-derived mosquitocidal compounds. Neem oil, derived from neem seeds (*Azadirachta indica* A. Juss, Meliaceae), has been proved to be an excellent candidate against a wide range of vectors of medical and veterinary importance including mosquitoes. It is environment-friendly, and target-specific at the same time. The active ingredients of neem oil include limonoids like azadirachtin A, nimbin, salannin and numerous other substances that are still waiting to be discovered. Of these, azadirachtin has been shown to be very effective and is mainly responsible for its toxic effects. The quality of the neem oil depends on its azadirachtin content which, in turn, depends on its manufacturing process. Neem oil can be used directly or as nanoemulsions or nanoparticles or even in the form of effervescent tablets. When added to natural breeding habitat waters they exert their mosquitocidal effects by acting as ovicides, larvicides, pupicides and/or oviposition repellents. The effects are generated by impairing the physiological pathways of the immature stages of mosquitoes or directly by causing physical deformities that impede their development. Neem oil when used directly has certain disadvantages mainly related to its disintegration under atmospheric conditions rendering it ineffective. However, many of its formulations have been reported to remain stable under environmental conditions retaining its efficiency for a long time. Similarly, neem seed

cake has also been found to be effective against the mosquito vectors. The greatest advantage is that the target species do not develop resistance against neem-based products mainly because of the innumerable number of chemicals present in neem and their combinations. This makes neem-based products highly potential yet unexplored candidates of mosquito control agents. The current review helps to elucidate the roles of neem oil and its various derivatives on mosquito vectors of public health concern.

Development of novel antiviral peptides against dengue serotypes 1-4.

Lee MF, Anasir MI, Poh CL.
Mar-2023
Virology.
<https://pubmed.ncbi.nlm.nih.gov/36739680/>

Pupal productivity of larval habitats of *Aedes aegypti* in Msambweni, Kwale County, Kenya.

Mwakutwaa AS, Ngugi HN, Ndenga BA, Krystosik A, Ngari M, Abubakar LU, Yonge S, Kitron U, LaBeaud AD, Mutuku FM.
Mar-2023
Parasitol Res.
<https://pubmed.ncbi.nlm.nih.gov/36683088/>

Aedes aegypti is an important vector of several arboviruses including dengue and chikungunya viruses. Accurate identification of larval habitats of *Ae. aegypti* is considered an essential step in targeted control. This study determined *Ae. aegypti* productivity in selected larval habitats in Msambweni, Kwale County, Kenya. Three sequential larval habitat surveys were conducted. The first survey was habitat census (baseline) through which 83 representative larval habitats were identified and selected. The second and third surveys involved estimating daily productivity of the 83 selected larval habitats for 30 consecutive days during a wet and a dry season, respectively. Of 664 larval habitats examined at baseline, 144 larval habitats (21.7%) were found to be infested with *Ae. aegypti* larvae. At baseline, majority (71%) of the pupae were collected from two (2/6) larval habitat types, tires and pots. Multivariate analysis identified habitat type and the habitat being movable as the predictors for pupal abundance. During the 30-day daily pupal production surveys, only a few of the habitats harbored pupae persistently. Pupae were found in 28% and 12% of the larval habitats during the wet and dry seasons, respectively. In the wet season, drums, tires, and pots were identified as the key habitat types accounting for 85% of all pupae sampled. Three habitats (all drums) accounted for 80% of all the pupae collected in the dry season. Predictors for pupal productivity in the wet season were habitat type, place (whether the habitat is located at the back or front of the house), habitat purpose (use of the water in the habitat), and source of water. Although the multivariate model for habitat type did not converge, habitat type and habitat size were the only significant predictors during the dry season. Drums, pots, and tires were sources of more than 85% of *Ae. aegypti* pupae,

reinforcing the "key container concept." Targeting these three types of habitats makes epidemiological sense, especially during the dry season.

Field Evaluation of In2Care Mosquito Traps to Control *Aedes aegypti* and *Aedes albopictus* (Diptera: Culicidae) in Hawai'i Island.

Brisco KK, Jacobsen CM, Seok S, Wang X, Lee Y, Akbari OS, Cornel AJ.

06-03-2023

J Med Entomol.

<https://pubmed.ncbi.nlm.nih.gov/36656078/>

2021 U.S. Virgin Islands Zika health brigade: Providing recommended pediatric health screenings for children born to mothers with laboratory evidence of possible Zika virus infection during pregnancy.

de Wilde LH, Harrison CJ, Ceesay BE, Mayers CS, Ferrol-Hawley J, Canton J, Godfred-Cato S, Reynolds MR, Brown-Shuler L, Randhawa S, Schoelles D, Hillman B, Carlos MP, Ambrose T, Bitner D, Holgado S, Jones C, Lattin DJ, Mulkey SB, Nguyen A, Payne M, Prkalapakorn SG, Shue A, Ellis EM.

15-03-2023

Birth Defects Res.

<https://pubmed.ncbi.nlm.nih.gov/36574736/>

Background: The United States Virgin Islands (USVI) Department of Health (DOH) conducted a second Zika health brigade (ZHB) in 2021 to provide recommended Zika-related pediatric health screenings, including vision, hearing, neurologic, and developmental screenings, for children in the USVI. This was replicated after the success of the first ZHB in 2018, which provided recommended Zika-related pediatric health screenings to 88 infants and children exposed to Zika virus (ZIKV) during pregnancy.

Methods: Ten specialty pediatric care providers were recruited and traveled to the USVI to conduct the screenings. USVI DOH scheduled appointments for children included in CDC's U.S. Zika Pregnancy and Infant Registry (USZPIR). During the ZHB, participants were examined by pediatric ophthalmologists, pediatric audiologists, and pediatric neurologists. We report the percentage of participants who were referred for additional follow-up care or given follow-up recommendations in the 2021 ZHB and compare these referrals and recommendations to those given in the 2018 ZHB. **Results:** Thirty-three children born to mothers with laboratory evidence of ZIKV infection during pregnancy completed screenings at the 2021 ZHB, of which 15 (45%) children were referred for additional follow-up care. Ophthalmological screenings resulted in the highest number of new referrals for a specialty provider among ZHB participants, with 6 (18%) children receiving referrals for that specialty. Speech therapy was the most common therapy referral, with 10 (30%) children referred, of which 9 (90%) were among those who attended the 2018 ZHB.

Conclusions: Thirty-three children in a jurisdiction with reduced access to healthcare specialists received

recommended Zika-related pediatric health screenings at the ZHB. New and continuing medical and developmental concerns were identified and appropriate referrals for follow-up care and services were provided. The ZHB model was successful in creating connections to health services not previously received by the participants.

Astrocytes in the pathophysiology of neuroinfection.

Zorec R, Verkhatsky A.

03-03-2032

Essays Biochem.

<https://pubmed.ncbi.nlm.nih.gov/36562155/>

Optimizing the Application Timing and Dosage of *Metarhizium brunneum* (Hypocreales: Clavicipitaceae) as a Biological Control Agent of *Aedes aegypti* (Diptera: Culicidae) Larvae.

Alkhaibari AM, Wood MJ, Yavasoglu SI, Bull JC, Butt TM.

06-03-2023

J Med Entomol.

<https://pubmed.ncbi.nlm.nih.gov/36539333/>

Thresholds, bifurcation and chaos in biological phenomena: Comment on "Mathematical models for Dengue fever epidemiology: A 10-year systematic review" by M. Aguiar et al.

Yang HM.

Mar-2023

Phys Life Rev.

<https://pubmed.ncbi.nlm.nih.gov/36455475/>

GCaMP Imaging in Mosquitoes: Central Nervous System.

Zhao Z, Weiss L, McBride CS.

01-03-2023

Cold Spring Harb Protoc.

<https://pubmed.ncbi.nlm.nih.gov/36446531/>

Mosquitoes spread dengue, Zika, malaria, and other pathogens to hundreds of millions of people every year. A better understanding of mosquito behavior and its underlying neural mechanisms may lead to new control strategies, but such an understanding requires the development of tools and approaches for exploring the nervous system of key vector species. For example, we can now image neural activity in mosquito brains using genetically encoded calcium sensors like GCaMP. Compared with other types of neural recording, GCaMP imaging has the advantage of allowing one to record from many neurons simultaneously and/or to record from specific neuronal types. Successful implementation requires careful consideration of many factors, including the choice of microscope and how to make the brains of experimental animals visible and stable while minimizing damage. Here, we elaborate on these points and provide a concise introduction to GCaMP imaging in the mosquito central nervous system.

Comprehensive analysis of multivariable models for predicting severe dengue prognosis: systematic review and meta-analysis.

Lee H, Hyun S, Park S.

01-03-2023

Trans R Soc Trop Med Hyg.

<https://pubmed.ncbi.nlm.nih.gov/36445309/>

Region-specific improvisation on WHO case definition and environmental risk factors associated with dengue: a case-control analysis from Kerala, India.

Anish TS, Valamparampil MJ, Rahul A, Saini P, Prajitha KC, Suresh MM, Reghukumar A, Kumar NP.

01-03-2023

Trans R Soc Trop Med Hyg.

<https://pubmed.ncbi.nlm.nih.gov/36326789/>

Background: Region-specific variations may occur in symptomatic manifestations that need to be addressed by dynamic case definitions. Environmental risk factors for dengue also vary widely across geographic settings. Our aim was to study the test positivity rate of the World Health Organization (WHO) 2009 probable dengue case definition and to suggest region-specific improvisations to it. The study also analyses the sociodemographic and environmental risk factors of dengue fever in South Kerala, India. **Methods:** A case-control study was conducted in South Kerala from 2017 to 2019. Dengue reverse transcription polymerase chain reaction (RT-PCR)-positive and RT-PCR-negative 'probable dengue' patients were compared to identify significant symptoms for a modified definition of dengue. A group of afebrile community controls was compared with RT-PCR-positive dengue cases to study the environmental and behavioural risk factors. **Results:** Arthralgia, palmar erythema and rashes have high discriminatory power (odds ratio [OR] >3) for identifying dengue. Redness of eyes, altered consciousness, abdominal distension and chills were found to moderately discriminate (OR 2-3) dengue. The adjusted analysis showed the presence of mosquito breeding sites (indoor $p=0.02$, outdoor $p=0.03$), solid waste dumping ($p<0.001$) and open water drainage in the compound ($p=0.007$) as significant predictors. **Conclusions:** Regional modifications should be considered when using the WHO definition in endemic settings. Control of mosquito breeding at the household level is the key towards dengue prevention.

Identifying hidden Zika hotspots in Pernambuco, Brazil: a spatial analysis.

Freitas LP, Lowe R, Koepp AE, Alves SV, Dondero M, Marteleto LJ.

01-03-2023

Trans R Soc Trop Med Hyg.

<https://pubmed.ncbi.nlm.nih.gov/36326785/>

Surveillance for Zika, Chikungunya, and Dengue Virus Incidence and RNAemia in Blood Donors at 4 Brazilian Blood Centers During 2016-2019.

Custer B, Grebe E, Buccheri R, Bakkour S, Stone M, Capuani L, Alencar C, Amorim L, Loureiro P, Carneiro-Proietti AB, Mendrone-Junior A, Gonzalez T, Gao K, Livezey KW, Linnen JM, Brambilla D, McClure C, Busch MP, Sabino EC; Recipient Epidemiology and Donor Evaluation Study (REDS-III) International Component Brazil.

01-03-2023

J Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/35687888/>

Background: Except for public health case reports, the incidence of Zika virus (ZIKV), chikungunya virus (CHIKV), and dengue virus (DENV) infection are not available to assess the potential blood transfusion safety threat in Brazil.

Methods: Pools of 6 donation samples (MP6) left over from human immunodeficiency virus, hepatitis B virus, and hepatitis C virus nucleic acid testing were combined to create MP18 pools (3 MP6 pools). Samples were tested using the Grifols triplex ZIKV, CHIKV, and DENV real-time transcription mediated amplification assay to estimate prevalence of RNAemia and incidence, and to compare these results to case reports in São Paulo, Belo Horizonte, Recife, and Rio de Janeiro, from April 2016 through June 2019.

Results: ZIKV, CHIKV, and DENV RNAemia were found from donors who donated without overt symptoms of infection that would have led to deferral. The highest RNAemic donation prevalence was 1.2% (95% CI, .8%-1.9%) for DENV in Belo Horizonte in May 2019. Arbovirus infections varied by location and time of year, and were not always aligned with annual arbovirus outbreak seasons in different regions of the country.

Conclusions: Testing donations for arboviruses in Brazil can contribute to public health. Transfusion recipients were likely exposed to ZIKV, CHIKV, and DENV viremic blood components during the study period.

A systematic review to describe patterns of animal and human viral research in Rwanda.

Dutuze MF, Byukusenge M, Shyaka A, Christofferson RC.

01-03-2023

Int Health.

<https://pubmed.ncbi.nlm.nih.gov/35650601/>

Rage

Analysis of available animal testing data to propose peer-derived quantitative thresholds for determining adequate surveillance capacity for rabies.

Minhaj FS, Bonaparte SC, Boutelle C, Wallace RM.

09-03-2023

Sci Rep.

<https://pubmed.ncbi.nlm.nih.gov/36894610/>

Historical targets for country-level animal rabies testing volumes were abandoned due to ethical and welfare concerns, and interpretation challenges of testing healthy

animals. To-date, no quantitative threshold has been established for evaluating adequate surveillance capacity specific to suspected rabid animals. The purpose here is to establish quantitative testing thresholds for rabies suspected animals to assess a country's rabies surveillance capacity. Animal rabies testing data was obtained from official and unofficial rabies surveillance platforms from 2010 to 2019 and supplemented with official country reports and published literature. Testing rates were determined for all-animal and domestic animals, and standardized per 100,000 estimated human population; the domestic animal rate was also standardized per 100,000 estimated dog population. There were 113 countries that reported surveillance data eligible for analysis. Countries reporting the most data were under WHO categories as having endemic human rabies or no dog rabies. The annual median all-animal testing rate for all countries was 1.53 animals/100,000 human population (IQR 0.27-8.78). Three proposed testing rate thresholds are an all-animal rate of 1.9 animals/100,000 humans, a domestic animal per human rate of 0.8 animals/100,000 humans, and a domestic animal per dog rate of 6.6 animals/100,000 dogs. These three peer-derived rabies testing thresholds for passive surveillance can be used to facilitate assessment of a country's rabies surveillance capacity.

Knowledge, attitudes, and practices regarding dogs and dog bites in Indigenous northern communities: A mixed methods study.

Daigle L, Ravel A, Rondenay Y, Simon A, Mokoush KN, Aenishaenslin C.

20-02-2023

Front Vet Sci.

<https://pubmed.ncbi.nlm.nih.gov/36891468/>

Introduction: The singular relationship developed over the years between northern Indigenous peoples and dogs has been profoundly changed through historical trauma, settlements and increased use of snowmobiles. Issues related to dogs have become increasingly complex and worrisome with the endemic presence of the rabies virus among Arctic fox populations, and given the fact that northern Indigenous peoples may have a higher risk of dog bites than the general population. This study aimed to investigate factors related to the risk of dog bites in Naskapi and Innu communities located in northern Quebec (Canada) by (1) describing the knowledge, attitudes and practices (KAP) regarding dogs and dog bites in these communities, and (2) analyzing experiences of inhabitants and health professionals with regard to dog bites and their management. **Methods:** A mixed methods study design that combined an observational cross-sectional survey and individual interviews was used. The survey collected data on KAP regarding dogs and dog bites among 122 respondents. Individual interviews ($n = 37$) were then conducted with victims of dog bites, owners of dogs that have bitten a person before, and health professionals. Descriptive and inferential analysis (quantitative data) and thematic analysis (qualitative data) were performed. **Results and discussion:** Results highlighted that 21% of respondents have had a dog bite

in their lifetime. Most respondents were not aware of the risk of contracting rabies following a dog bite, although rabies risk perception was associated with risk perception of dogs (linear regression: coefficient = 0.69, 95% CI = 0.36-1.02). The odds of being more knowledgeable on rabies were higher (logistic regression: OR = 2.92, 95% CI = 1.07-7.98) among young adults. Dogs were perceived as both threats and protectors by community members. When the fear of dogs was present, it affected the quality of life of some inhabitants. There was confusion about responsibilities in the management of biting dogs, although protocols to follow after a bite were clear for health care professionals. This study revealed a lack of awareness and knowledge about dog bites and rabies risks in both communities. Results provide important knowledge for the development of interventions adapted to northern Indigenous communities.

Rabies surveillance in the United States during 2021.

Ma X, Bonaparte S, Corbett P, Orciari LA, Gigante CM, Kirby JD, Chipman RB, Fehlner-Gardiner C, Thang C, Cedillo VG, Aréchiga-Ceballos N, Rao A, Wallace RM.

08-03-2023

J Am Vet Med Assoc.

<https://pubmed.ncbi.nlm.nih.gov/36884381/>

It's a small world for parasites: evidence supporting the North American invasion of European *Echinococcus multilocularis*.

Santa MA, Umhang G, Klein C, Grant DM, Ruckstuhl KE, Musiani M, Gilleard JS, Massolo A.

08-03-2023

Proc Biol Sci.

<https://pubmed.ncbi.nlm.nih.gov/36883278/>

Echinococcus multilocularis (*Em*), the causative agent of human alveolar echinococcosis (AE), is present in the Holarctic region, and several genetic variants seem to have differential infectivity and pathogenicity. An unprecedented outbreak of human AE cases in Western Canada infected with a European-like strain circulating in wild hosts warranted assessment of whether this strain was derived from a recent invasion or was endemic but undetected. Using nuclear and mitochondrial markers, we investigated the genetic diversity of *Em* in wild coyotes and red foxes from Western Canada, compared the genetic variants identified to global isolates and assessed their spatial distribution to infer possible invasion dynamics. Genetic variants from Western Canada were closely related to the original European clade, with lesser genetic diversity than that expected for a long-established strain and spatial genetic discontinuities within the study area, supporting the hypothesis of a relatively recent invasion with various founder events.

International Travel Vaccine Recommendations for Children.

Machicao MF, Yashar-Gershman S, Romero JR, Bernstein HH.

Mar-2023

Comparison of Rabies Cases Received by the Shomal Pasteur Institute in Northern Iran: A 2-Year Study.

Kavoosian S, Behzadi R, Asouri M, Ahmadi AA, Nasirikenari M, Salehi A.

25-02-2023

Glob Health Epidemiol Genom.

<https://pubmed.ncbi.nlm.nih.gov/36879889/>

The rabies virus, which belongs to the genus *Lyssavirus*, the family *Rhabdoviridae*, is the causative agent of rabies, a contagious, deadly, and progressive neurological infection. This illness is commonly distributed worldwide and affects all warm-blooded animals. Regarding the zoonotic aspects of rabies, the prevalence of rabies was investigated in this study. Over 2 years, 188 samples were examined via the direct fluorescent antibody test (DFAT) and mouse inoculation test (MIT) techniques by using brain tissue samples. Our findings showed that 73.94% of samples were rabies positive. The highest number of samples belonged to cows and dogs, respectively. The positivity rate in cows was 71.88%, followed by dogs with a 57.78% infection rate. These findings suggested that despite the heavy monitoring protocols in Iran, rabies is still a prevalent disease, and it is advised that vaccinations and screening programs should be carried out more frequently with heavier observation.

Inferring the disruption of rabies circulation in vampire bat populations using a betaherpesvirus-vectored transmissible vaccine.

Griffiths ME, Meza DK, Haydon DT, Streicker DG.

14-03-2023

Proc Natl Acad Sci U S A.

<https://pubmed.ncbi.nlm.nih.gov/36877838/>

Transmissible vaccines are an emerging biotechnology that hold prospects to eliminate pathogens from wildlife populations. Such vaccines would genetically modify naturally occurring, nonpathogenic viruses ("viral vectors") to express pathogen antigens while retaining their capacity to transmit. The epidemiology of candidate viral vectors within the target wildlife population has been notoriously challenging to resolve but underpins the selection of effective vectors prior to major investments in vaccine development. Here, we used spatiotemporally replicated deep sequencing to parameterize competing epidemiological mechanistic models of *Desmodus rotundus* betaherpesvirus (DrBHV), a proposed vector for a transmissible vaccine targeting vampire bat-transmitted rabies. Using 36 strain- and location-specific time series of prevalence collected over 6 y, we found that lifelong infections with cycles of latency and reactivation, combined with a high R_0 (6.9; CI: 4.39 to 7.85), are necessary to explain patterns of DrBHV infection observed in wild bats. These epidemiological properties suggest that DrBHV may be suited to vector a lifelong, self-boosting, and transmissible vaccine. Simulations showed that inoculating a single bat with a DrBHV-vectored rabies

vaccine could immunize >80% of a bat population, reducing the size, frequency, and duration of rabies outbreaks by 50 to 95%. Gradual loss of infectious vaccine from vaccinated individuals is expected but can be countered by inoculating larger but practically achievable proportions of bat populations. Parameterizing epidemiological models using accessible genomic data brings transmissible vaccines one step closer to implementation.

Trachome

Trachoma Prevention Practice and Associated Factors in Rural Lemo District, Southern Ethiopia, 2021.

Shobiso MG, Hussien MS, Munaw MB, Tilahun MM.

Jan-2023

Ethiop J Health Sci.

<https://pubmed.ncbi.nlm.nih.gov/36890944/>

Background: Trachoma is a leading cause of preventable blindness. It is more prevalent in areas where there is poor personal and environmental sanitation. Implementing a SAFE strategy will reduce the incidence of trachoma. The purpose of this study was to look into trachoma prevention practices and associated factors in rural Lemo, South Ethiopian communities. **Methods:** We conducted a community-based cross-sectional study in the rural Lemo district of south Ethiopia, covering 552 households, from July 1 - July 30, 2021. We used a multistage sampling technique. Seven Kebeles were selected using a simple random sampling method. Then, a systematic random sampling procedure with a five-interval size was applied to select the households. Our study assessed the association between the outcome variable and explanatory variables using binary and multivariate logistic regressions. The adjusted odds ratio was calculated, and variables with a p-value below 0.05 at the 95% confidence interval (CI) were considered statistically significant. **Results:** The study found that 59.6% (95% CI: 55.5%-63.7%) of participants had good trachoma prevention practices. Having a favorable attitude (odds ratio [AOR]: 1.91, 95% CI: 1.26-2.89), receiving health education (AOR: 2.16, 95% CI: 1.46-3.21), and obtaining water from a public pipe (AOR: 2.48, 95% CI: 1.09-5.66) were significantly associated with good trachoma prevention practice. **Conclusions:** Fifty-nine percent of the participants had good prevention practices for trachoma. Health education, a favorable attitude, and a water source from public pipes were variables associated with good trachoma prevention practice. Improving water sources and disseminating health information are vital to increasing trachoma prevention practices.

Longitudinal Analysis of Eye Health Disparities Due to Trachoma Using Country-Level Data from the Global Burden of Disease Study 2019.

Ono K, Umeiya R.

Mar-2023

Ophthalmic Epidemiol.

<https://pubmed.ncbi.nlm.nih.gov/36882966/>

The prevention and management of postoperative trichomatous trichiasis: A systematic review.

Kreis AJ, Gower EW, Kropp M, Kello AB, Nouhoum G, Resnikoff S, Talero SL, Solomon AW.

04-03-2023

Surv Ophthalmol.

<https://pubmed.ncbi.nlm.nih.gov/36878359/>

Among ocular infections, trachoma is the main cause of blindness. Repeated conjunctival Chlamydia trachomatis infections lead to trichiasis, corneal opacification, and visual impairment. Surgery is often needed to relieve discomfort and preserve vision; however, a high post-operative trichomatous trichiasis (PTT) rate has been observed in various settings. We wanted to know why, whether PTT rates could be reduced, and how to manage the PTT that occurs. We performed a search of the literature. Of 217 papers screened, 59 studies were identified for inclusion as potentially relevant, the majority having been excluded for not directly concerning PTT in humans. Preventing PTT is a major challenge. Only one published trial, the STAR trial in Ethiopia, has reported a cumulative PTT rate <10% one year after surgery. The literature on the management of PTT is sparse. Though no PTT management guidelines are available, high-quality surgery with a low rate of unfavorable outcomes for PTT patients is likely to require enhanced surgical training of a smaller group of highly skilled surgeons. Based on the surgical complexity and the authors' own experience, the pathway for patients suffering from PTT should be studied further for improvement.

Combined Surgical Strategies Adjusted to Clinical Evaluations for Severe Upper Eyelid Cicatricial Entropion and Trichiasis.

Zhang L, Hou Z, Li Y, Li D.

Mar-Apr 2023

J Craniofac Surg.

<https://pubmed.ncbi.nlm.nih.gov/36635852/>

Ulcère de Buruli

Mycolactone causes catastrophic Sec61-dependent loss of the endothelial glycocalyx and basement membrane: a new indirect mechanism driving tissue necrosis in Mycobacterium ulcerans infection.

Hsieh LT, Hall BS, Newcombe J, Mendum TA, Umrana Y, Deery MJ, Shi WQ, Salguero FJ, Simmonds RE.

21-02-2023

bioRxiv.

<https://pubmed.ncbi.nlm.nih.gov/36865118/>

Lèpre

International Dermoscopy Society (IDS) Criteria for Skin Tumors: Validation for

Skin of Color Through a Delphi Expert Consensus by the "Imaging in Skin of Color" IDS Task Force.

Ankad BS, Behera B, Lallas A, Akay BN, Bhat YJ, Chauhan P, Enechukwu NA, Geller S, Jha AK, Kaliyadan F, Kayitenkore K, Kelati A, Vinay K, Stein J, Traoré I, Usatine RP, Errichetti E.

01-01-2023

Dermatol Pract Concept.

<https://pubmed.ncbi.nlm.nih.gov/36892378/>

Introduction: A structured set of eight basic dermoscopic parameters (lines, clods, dots, circles, pseudopods, structureless, else, and vessels) including a total of 77 variables with corresponding descriptive and metaphoric vocabulary has been released for evaluation of skin tumors by the International Dermoscopy Society (IDS). **Objectives:** To validate the aforementioned criteria for the use in darker phototypes (phototypes IV-VI) via an expert consensus. **Methods:** The two-round "Delphi method" was adopted, with an iterative process including two rounds of email questionnaires. Potential panelists were asked to take part in the procedure via email on the basis of their expertise in the dermoscopy of skin tumors in dark phototypes. **Results:** A total of 17 participants were involved. All the original variables of the eight basic parameters reached agreement during the first round, except for "pink small clods" ("milky red globules") and "structureless pink zone" ("milky red areas"). Moreover, during the first round, panelists proposed a change of three existing items and the introduction of four new items, i.e., "black, small clods" ("black globules"), "follicular plugs", "erosions/ulcerations", and "white color around vessels" ("perivascular white halo"). All such proposals achieved agreement, thus being included in the final list, for a total of 79 items. There was consistency between the descriptive and metaphoric approaches in terms of scoring. **Conclusions:** Albeit most of the original items were considered applicable even for skin of color, there are some points of differences that physicians need to know. No significant preference was found between descriptive and metaphoric terminology among panelists.

Various Colors of Presentation of Pseudochromhidrosis - A Case Series.

Sahu P, Chakraborty D, Dayal S, Sachdeva M.

01-01-2023

Dermatol Pract Concept.

<https://pubmed.ncbi.nlm.nih.gov/36892368/>

ML Flow serological test: complementary tool in leprosy.

Montanha JOM, Nardi SMT, Binhardi FMT, Pedro HDSP, Santi MP, Paschoal VDA.

06-03-2023

An Bras Dermatol.

<https://pubmed.ncbi.nlm.nih.gov/36890048/>

Background: The evaluation of household contacts of leprosy cases allows the early diagnosis of new cases. **Objective:** To associate the results of the ML Flow test with the clinical characteristics of leprosy cases and to verify

their positivity in household contacts, in addition to describing the epidemiological profile of both. **Methods:** Prospective study with patients diagnosed over the course of one year (n = 26), without prior treatment, and their household contacts (n = 44) in six municipalities in northwestern São Paulo, Brazil. **Results:** There was a predominance of men among the leprosy cases, of 61.5% (16/26); 77% (20/26) were over 35 years old; 86.4% (22/26) were multibacillary; 61.5% (16/26) had a positive bacilloscopy; and 65.4% (17/26) had no physical disability. The ML Flow test was positive in 53.8% (14/26) of the leprosy cases and was associated with those who had a positive bacilloscopy and were diagnosed as multibacillary (p-value <0.05). Among the household contacts, 52.3% (23/44) were women and aged over 35 years; 81.8% (36/44) had been vaccinated with BCG – Bacillus Calmette-Guérin. The ML Flow test was positive in 27.3% (12/44) of household contacts, all of whom lived with multibacillary cases; seven lived with positive bacilloscopy cases and six with consanguineous cases. **Study limitations:** Difficulty in convincing the contacts to undergo the evaluation and collection of the clinical sample. **Conclusion:** The ML Flow test, when positive in household contacts, can help the identification of cases that require more attention by the health team, as it indicates a predisposition to disease development, especially when they are household contacts of multibacillary cases, with positive bacilloscopy and consanguineous. The ML Flow test also helps in the correct clinical classification of the leprosy cases.

Be aware: "Leprosy"! Not for nothing an NTD.

Naafs B.

08-03-2023

J Eur Acad Dermatol Venereol.

<https://pubmed.ncbi.nlm.nih.gov/36883806/>

A Gamified Real-time Video Observed Therapies (GRVOTS) Mobile App via the Modified Nominal Group Technique: Development and Validation Study.

Abas SA, Ismail N, Zakaria Y, Ismail I, Mat Zain NH, Yasin SM, Ibrahim K, Razali A, Mohd Yusoff MAS, Ahmad N, Chinnayah T.

07-03-2023

JMIR Serious Games.

<https://pubmed.ncbi.nlm.nih.gov/36881449/>

Background: The success rate of tuberculosis (TB) treatment in Malaysia remains below the recommended World Health Organization target of 90% despite the implementation of directly observed therapy, short-course, a physical drug monitoring system, since 1994. With increasing numbers of patients with TB in Malaysia defaulting on treatment, exploring another method to improve TB treatment adherence is vital. The use of gamification and real-time elements via video-observed therapies in mobile apps is one such method expected to induce motivation toward TB treatment adherence. **Objective:** This study aimed to document the process of designing, developing, and validating the gamification, motivation, and real-time elements in the Gamified Real-

time Video Observed Therapies (GRVOTS) mobile app. **Methods:** The modified nominal group technique via a panel of 11 experts was used to validate the presence of the gamification and motivation elements inside the app, which were assessed based on the percentage of agreement among the experts. **Results:** The GRVOTS mobile app, which can be used by patients, supervisors, and administrators, was successfully developed. For validation purposes, the gamification and motivation features of the app were validated as they achieved a total mean percentage of agreement of 97.95% (SD 2.51%), which was significantly higher than the minimum agreement score of 70% (P<.001). Further, each component of gamification, motivation, and technology was also rated at 70% or more. Among the gamification elements, fun received the lowest scores, possibly because the nature of serious games does not prioritize the fun element and because the perception of fun varies by personality. The least popular element in motivation was relatedness, as stigma and discrimination hinder interaction features, such as leaderboards and chats, in the mobile app. **Conclusions:** It has been validated that the GRVOTS mobile app contains gamification and motivation elements, which are intended to encourage medication adherence to TB treatment.

Association of the rs2111234, rs3135499, rs8057341 polymorphisms in the NOD2 gene with leprosy: A case-control study in the Norte de Santander, Colombia population.

Bustos MA, Castañeda-Castañeda LD, Acosta CR, García D, Bohada DP, Rodríguez R, Guerrero MI.

06-03-2023

PLoS One

<https://pubmed.ncbi.nlm.nih.gov/36877680/>

Altered levels of lymphocyte enhancer-binding factor-1 modulates the pigmentation in acral and non-acral lesions of non-segmental vitiligo patients: a follow-up-based study in North India.

Nayak D, Srivastava N, Dev A, Bishnoi A, Kumaran MS, Vinay K, Parsad D.

06-03-2023

Arch Dermatol Res.

<https://pubmed.ncbi.nlm.nih.gov/36877308/>

Background: Lymphocyte enhancer-binding factor-1 (LEF1) is responsible for melanocyte proliferation, migration and differentiation and its downregulation may result in depigmentation in vitiligo. Narrowband UVB (NB-UVB) phototherapy is known to enhance melanocyte migration from hair follicles to lesional epidermis; hence, it may have a role in the upregulation of LEF1. **Objectives:** We intended to assess the expression of LEF1 both before and after NB-UVB therapy and correlate it with the extent of re-pigmentation. **Materials and methods:** In this prospective cohort study, 30 patients of unstable non-segmental vitiligo were administered NB-UVB phototherapy for 24 weeks. Skin biopsies were obtained

from acral and non-acral sites in all patients, both prior to initiation and after completion of phototherapy and LEF1 expression was measured. **Results:** Amongst the 16 patients who completed the study, at 24 weeks, all patients achieved > 50% re-pigmentation. However, > 75% re-pigmentation was achieved in only 11.1% of acral patches, whereas it was achieved in a significantly higher number of non-acral patches (66.6%) ($p = 0.05$). A significant increase was observed in the mean fluorescent intensity of the LEF1 gene in both acral as well as non-acral areas at 24 weeks as compared to baseline ($p = 0.0078$). However, no difference was observed between acral and non-acral lesions in the LEF1 expression at 24 weeks or the change in LEF1 expression from baseline. **Conclusion:** LEF1 expression modulates the re-pigmentation of vitiligo lesions after treatment with NB-UVB phototherapy.

Intra-articular osteoid osteoma of the hip mimicking as monoarthritis-A case report.

Chandan N, Paul N, J P, Kaganur R.

Oct-2022

J Orthop Case Rep.

<https://pubmed.ncbi.nlm.nih.gov/36874886/>

Multifocal polymorphous cutaneous tuberculosis with Poncet's disease: A case report.

Verma K, Padmawar G, Madke B, Thakur TS, Gupta K.

23-02-2023

J Clin Tuberc Other Mycobact Dis.

<https://pubmed.ncbi.nlm.nih.gov/36874621/>

The protection quest is a primary key to sharing the neutralizing antibody response to cover against all emerging VOCs based on BIV1-CovIran studies.

Shafaati M, Bagherzadeh K, Lotfinia M, Karimi H, Teimoori A, Razazian M, Meidaninikjeh S, Hosseini H, Jamshidi HR, Jalili H, Abdoli A.

Mar-2023

Heliyon.

<https://pubmed.ncbi.nlm.nih.gov/36873499/>

In-vivo studies on Transitmycin, a potent Mycobacterium tuberculosis inhibitor.

Mondal R, Dusthacker V N A, Kannan P, Singh AK, Thiruvengadam K, Manikkam R, A S S, Balasubramanian M, Elango P, Ebenezer Rajadas S, Bharadwaj D, Arumugam GS, Ganesan S, Kumar A K H, Singh M, Patil S, U C A J, Doble M, R B, Tripathy SP, Kumar V.

03-03-2023

PLoS One

<https://pubmed.ncbi.nlm.nih.gov/36867599/>

This study involves the in-vitro and in-vivo anti-TB potency and in-vivo safety of Transitmycin (TR) (PubChem CID:90659753)- identified to be a novel secondary metabolite derived from *Streptomyces* sp (R2). TR was tested in-vitro against drug resistant TB clinical isolates ($n = 49$). 94% of DR-TB strains ($n = 49$) were inhibited by TR

at 10 μ g ml⁻¹. In-vivo safety and efficacy studies showed that 0.005mg kg⁻¹ of TR is toxic to mice, rats and guinea pigs, while 0.001mg kg⁻¹ is safe, infection load did not reduce. TR is a potent DNA intercalator and also targets RecA and methionine aminopeptidases of *Mycobacterium*. Analogue 47 of TR was designed using in-silico based molecule detoxification approaches and SAR analysis. The multiple targeting nature of the TR brightens the chances of the analogues of TR to be a potent TB therapeutic molecule even though the parental compound is toxic. Analog 47 of TR is proposed to have non-DNA intercalating property and lesser in-vivo toxicity with high functional potency. This study attempts to develop a novel anti-TB molecule from microbial sources. Though the parental compound is toxic, its analogs are designed to be safe through in-silico approaches. However, further laboratory validations on this claim need to be carried out before labelling it as a promising anti-TB molecule.

The Unbreakable Journey: Using photovoice to raise awareness and fight leprosy stigma in Papua, Indonesia.

Dien R, Krismawati H, Ayomi I, Timoria D, Chambers M, Soebono H, Grijsen ML.

03-03-2023

Br J Dermatol.

<https://pubmed.ncbi.nlm.nih.gov/36866652/>

Dermatoscopy of Solitary Keratoacanthoma.

Tandel JJ, Polra RV, Pillai D, Nair PA.

Sep-Oct 2022

Indian J Dermatol.

<https://pubmed.ncbi.nlm.nih.gov/36865879/>

Anti CD-6 Monoclonal Antibodies in the Management of Generalised Pustular Psoriasis.

Kura MM, Sodhi A, Sajjane A, Karande A.

Sep-Oct 2022

Indian J Dermatol.

<https://pubmed.ncbi.nlm.nih.gov/36865872/>

Generalised pustular psoriasis (GPP) is an uncommon, severe, life-threatening variant of psoriasis requiring careful therapeutic approach. Conventional treatment modalities have unsatisfactory outcomes, poor side effect profiles and toxicities that have led to an emerging use of biological therapies. Itolizumab, an anti-CD-6 humanised monoclonal IgG1 antibody, is approved for the management of chronic plaque psoriasis in India. We share our experience of using this drug in three cases of GPP that were failing conventional therapies. Its upstream effect on co-stimulatory pathway in disease pathogenesis is the postulated mechanism. Our experience warrants further large-scale exploration of the role of itolizumab in the management of GPP, which would benefit this severely affected population of patients. Although the definite pathogenesis of GPP is unknown fully, molecules blocking CD-6, which plays a role in the interaction

between T cells and antigen-presenting cells (APCs), are expected as new promising treatment options for GPP.

Nicorandil-Induced Bullous Fixed Drug Eruption on the Glans Penis.

Ghosh SK, Majumder B, Mondal S.

Sep-Oct 2022

Indian J Dermatol.

<https://pubmed.ncbi.nlm.nih.gov/36865868/>

Patterns and Trends of Tribal Leprosy: An Overview from a Tertiary Care Leprosy Clinic of Choto Nagpur Plateau of Eastern India.

Sarkar S, Sarkar T, Patra AC, Ghosh A, Gorai H, Mondal S.

Sep-Oct 2022

Indian J Dermatol.

<https://pubmed.ncbi.nlm.nih.gov/36865846/>

Serum Soluble Intercellular Adhesion Molecule-1 (sICAM-1): A Novel Potential Biomarker in Severe Acne Vulgaris.

Mustafa AI, Ebrahim AA, Abel Halim WAL, Fawzy E, Abdou AF.

Sep-Oct 2022

Indian J Dermatol.

<https://pubmed.ncbi.nlm.nih.gov/36865840/>

Background: Acne vulgaris (AV) is a chronic inflammatory disorder. Intercellular adhesion molecule-1 (ICAM-1) is a vital adhesion molecule mediating cellular adhesion during the inflammatory process. **Aims and objectives:** To evaluate serum soluble intercellular adhesion molecule-1 (sICAM-1) level in AV patients as an attempt to elucidate its role in acne pathogenesis and to relate with studied clinical parameters. **Materials and methods:** Serum sICAM-1 level was measured using ELISA technique in 60 patients and 60 controls. **Results:** Serum sICAM-1 level was significantly elevated in studied patients than controls ($P < 0.001$). Additionally, its level increased significantly with increased acne severity ($P < 0.001$) but not in patients with post acne scars ($P > 0.05$). **Conclusion:** Serum sICAM-1 could be a marker for acne etiopathogenesis. Furthermore, it might be considered as a predictor for disease severity.

Congenital Varicella Syndrome with Isolated Limb Hypoplasia and Scarring: A Rare Fascinating Case.

Sethumadhavan S, Maalik Babu ANM, Palanivel N, Baskar A.

Sep-Oct 2022

Indian J Dermatol.

<https://pubmed.ncbi.nlm.nih.gov/36865830/>

A Need to Focus on the Atypical Features and Pronounced STD Transmission of Monkey Pox and the Emergent Role of Dermatologists in Breaking its Transmission.

Sardana K, Sachdeva S, Thole A.

Sep-Oct 2022

Indian J Dermatol.

<https://pubmed.ncbi.nlm.nih.gov/36865823/>

Loeffler's Syndrome and Multifocal Cutaneous Larva Migrans: Case report of an uncommon occurrence and review of the literature.

Sil A, Bhanja DB, Chandra A, Biswas SK.

Feb-2023

Sultan Qaboos Univ Med J.

<https://pubmed.ncbi.nlm.nih.gov/36865421/>

Cutaneous larva migrans (CLM) is a zoonotic skin disease that is frequently diagnosed in tropical and subtropical countries. Loeffler's syndrome (LS) is a transient respiratory ailment characterised by pulmonary infiltration along with peripheral eosinophilia and commonly follows parasitic infestation. We report a 33-year-old male patient who presented to a tertiary care hospital in eastern India in 2019 with LS that was attributed secondary to multifocal CLM. Treatment with seven-day course of oral albendazole (400 mg daily) coupled with nebulisation (levosalbutamol and budesonide) led to complete resolution of cutaneous lesions and respiratory complaints within two weeks. There was complete resolution of pulmonary pathology at four-weeks follow-up.

Leprosy (Hansen's disease): An Update and Review.

Gilmore A, Roller J, Dyer JA.

Jan-Feb-2023

Mo Med.

<https://pubmed.ncbi.nlm.nih.gov/36860602/>

The pipeline for drugs for control and elimination of neglected tropical diseases: 1. Anti-infective drugs for regulatory registration.

Pfarr KM, Krome AK, Al-Obaidi I, Batchelor H, Vaillant M, Hoerauf A, Opoku NO, Kuesel AC.

01-03-2023

Parasit Vectors.

<https://pubmed.ncbi.nlm.nih.gov/36859332/>

Leprosy among new child cases in China: Epidemiological and clinical analysis from 2011 to 2020.

Peng J, Sun P, Wang L, Wang H, Long S, Yu MW.

17-02-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/36800375/>

Linear focal elastosis.

Palaniappan V, Selvaarasan J, Murthy AB, Karthikeyan K.

01-03-2023

Clin Exp Dermatol.

<https://pubmed.ncbi.nlm.nih.gov/36763712/>

Linear focal elastosis (LFE) is an uncommon, benign, acquired elastotic condition with uncertain pathogenesis. It is characterized clinically by asymptomatic, multiple, yellowish, elevated, irregularly indurated, striae-like lines or bands distributed horizontally across the lower and middle part of the posterior trunk. The histopathological hallmark of LFE is a focal increase of elastic fibres in the dermis. The differential diagnosis is varied, and striae distensae is the closest mimic of LFE. Response of LFE to treatment is often poor. The focus of this article is to provide insights into this condition for dermatologists.

Whole transcriptome-based skin virome profiling in typical epidermodysplasia verruciformis reveals α -, β -, and γ -HPV infections.

Saeidian AH, Youssefian L, Naji M, Mahmoudi H, Barnada SM, Huang C, Naghipoor K, Hozhabrpour A, Park JS, Manzo Margiotta F, Vahidnezhad F, Saffarian Z, Kamyab-Hesari K, Tolouei M, Faraji N, Azimi SZ, Namdari G, Mansouri P, Casanova JL, Béziat V, Jouanguy E, Uitto J, Vahidnezhad H.

08-03-2023

JCI Insight.

<https://pubmed.ncbi.nlm.nih.gov/36602881/>

Trypanosomes (trypanosomiasis et maladie de Chagas)

Intranasal Trans-sialidase-based vaccine against *Trypanosoma cruzi* triggers a mixed cytokine profile in the nasopharynx-associated lymphoid tissue and confers local and systemic immunogenicity.

Pacini MF, Camila BB, Brenda D, González FB, Estefania P, de Hernández MA, Pamela C, Cecilia F, Martín E, Blancato VS, Christian M, Iván M, Pérez AR.

07-03-2023

Acta Trop.

<https://pubmed.ncbi.nlm.nih.gov/36893830/>

Trypanosoma cruzi, the agent of Chagas disease, can infect through conjunctive or oral mucosae. Therefore, the induction of mucosal immunity by vaccination is relevant not only to trigger local protection but also to stimulate both humoral and cell-mediated responses in systemic sites to control parasite dissemination. In a previous study, we demonstrated that a nasal vaccine based on a Trans-sialidase (TS) fragment plus the mucosal STING agonist c-di-AMP, was highly immunogenic and elicited prophylactic capacity. However, the immune profile induced by TS-based nasal vaccines at the nasopharyngeal-associated lymphoid tissue (NALT), the target site of nasal immunization, remains unknown. Hence, we analyzed the NALT cytokine expression generated by a TS-based vaccine plus c-di-AMP (TSdA+c-di-AMP) and their association with mucosal and systemic immunogenicity. The vaccine was administered intranasally, in 3 doses separated by 15 days

each other. Control groups received TSdA, c-di-AMP, or the vehicle in a similar schedule. We demonstrated that female BALB/c mice immunized intranasally with TSdA+c-di-AMP boosted NALT expression of IFN- γ and IL-6, as well as IFN- β and TGF- β . TSdA+c-di-AMP increased TSdA-specific IgA secretion in the nasal passages and also in the distal intestinal mucosa. Moreover, T and B-lymphocytes from NALT-draining cervical lymph nodes and spleen showed an intense proliferation after ex-vivo stimulation with TSdA. Intranasal administration of TSdA+c-di-AMP provokes an enhancement of TSdA-specific IgG_{2a} and IgG₁ plasma antibodies, accompanied by an increase IgG_{2a}/IgG₁ ratio, indicative of a Th1-biased profile. In addition, immune plasma derived from TSdA+c-di-AMP vaccinated mice exhibit in-vivo and ex-vivo protective capacity. Lastly, TSdA+c-di-AMP nasal vaccine also promotes intense footpad swelling after local TSdA challenge. Our data support that TSdA+c-di-AMP nasal vaccine triggers a NALT mixed pattern of cytokines that were clearly associated with an evident mucosal and systemic immunogenicity. These data are useful for further understanding the immune responses elicited by the NALT following intranasal immunization and the rational design of TS-based vaccination strategies for prophylaxis against *T. cruzi*.

Chagas disease-induced ventricular tachycardia: A case report.

Alhassani Z, Hennawi HA, Sevelia P, Mena CS, Coppola K.

30-01-2023

Glob Cardiol Sci Pract.

<https://pubmed.ncbi.nlm.nih.gov/36890840/>

Chagas disease is a protozoal infection caused by *Trypanosoma cruzi* (*T. cruzi*) that can affect many organ systems. Chagas cardiomyopathy tends to affect 30% of infected individuals. Cardiac manifestations include myocardial fibrosis, conduction defects, cardiomyopathy, ventricular tachycardia, and sudden cardiac death. In this report, we discuss a 51-year-old male who presented with recurrent episodes of non-sustained ventricular tachycardia refractory to medical therapy.

Indigenous people from Amazon show genetic signatures of pathogen-driven selection.

Couto-Silva CM, Nunes K, Venturini G, Araújo Castro E Silva M, Pereira LV, Comas D, Pereira A, Hünemeier T.

10-03-2023

Sci Adv.

<https://pubmed.ncbi.nlm.nih.gov/36888716/>

Taxonomic re-evaluation of African anuran trypanosomes with the redescription and molecular diagnosis of *Trypanosoma nelspruitense* (Trypanosoma) Laveran, 1904 and *Trypanosoma grandicolor* (Haematomonas) Pienaar, 1962.

Jordaan BJ, du Preez LH, Netherlands EC.

08-03-2023

Parasitology.

<https://pubmed.ncbi.nlm.nih.gov/36883296/>

Analysis of the Chagas disease situation in Japan: a cross sectional study and cost-effectiveness analysis of a Chagas disease screening program.

Iglesias Rodríguez IM, Miura S, Maeda T, Imai K, Smith C, Vasquez Velasquez C, Honda S, Hirayama K.

05-02-2023

Lancet Reg Health West Pac.

<https://pubmed.ncbi.nlm.nih.gov/36879788/>

Background: Japan is estimated to host 3000 cases of Chagas disease (CD). However, there are no epidemiological data and policies for prevention and care. We aimed to analyze the current situation of CD in Japan and identify possible barriers to seeking care. **Methods:** This cross-sectional study included Latin American (LA) migrants living in Japan from March 2019 to October 2020. We obtained blood samples to identify participants infected with *Trypanosoma cruzi*, and data about sociodemographic information, CD risk factors, and barriers to access to the Japanese national health care system (JNHS). We used the observed prevalence to calculate the cost-effectiveness analysis of the screening of CD in the JNHS. **Findings:** The study included 428 participants, most of them were from Brazil, Bolivia and Peru. The observed prevalence was 1.6% (expected prevalence= 0.75%) and 5.3% among Bolivians. Factors associated with seropositivity were being born in Bolivia, having previously taken a CD test, witnessing the triatome bug at home, and having a relative with CD. The screening model was more cost-effective than the non-screening model from a health care perspective (ICER=200,320 JPY). Factors associated with access to JNHS were being female, length of stay in Japan, Japanese communication skills, source of information, and satisfaction about the JNHS. **Interpretation:** Screening of asymptomatic adults at risk of CD may be a cost-effective strategy in Japan. However, its implementation should consider the barriers that affect LA migrants in access to the JNHS. **Funding:** Nagasaki University and Infectious Diseases Japanese Association.

Pfizer-BioNTech vaccine induces the production of cross-reactive antibodies against *Trypanosoma cruzi* proteins: A preliminary study.

López-Monteon A, Balderas-Caballero AE, Domínguez-Guillén JA, Romero-Ramírez H, Baltierra-Uribe SL, Ramos-Ligonio A.

06-03-2023

Trop Med Int Health.

<https://pubmed.ncbi.nlm.nih.gov/36879355/>

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

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

04-03-2023

Exp Parasitol.

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

Trypanosoma cruzi is an obligate parasite that uses glucose as one of the main resources to maintain its survival and proliferation. In eukaryotic cells glucose transport across membranes is mediated by facilitated transport through a variety of transporters. Herein, genes from the recently described SWEET family of carbohydrate transporters were identified in trypanosomatid parasites, including the medically important species *T. cruzi* and *Leishmania* spp. The identified genes have sequences with the typical attributes of known SWEET transporters. The expression of TcSWEET, the gene for the SWEET transporter found in the *T. cruzi* genome, was evidenced by immunohistochemistry using a polyclonal serum raised against peptides selected from the deduced TcSWEET protein sequence. In Western blot analysis, this α -TcSWEET serum detected proteins within the theoretical molecular mass for TcSWEET (25.8 kDa) in total epimastigote lysates, suggesting its expression at this parasite stage. Additionally, this serum stained epimastigotes at localizations consistent with the cell body and the flagellum. Together, these data suggests that SWEET transporters may contribute to glucose transport in trypanosomatid parasites.

The Use of the Antigenically Variable Major Surface Protein 2 in the Establishment of Superinfection during Natural Tick Transmission of *Anaplasma marginale* in Southern Ghana.

Koku R, Futse JE, Morrison J, Brayton KA, Palmer GH, Noh SM.

06-03-2023

Infect Immun.

<https://pubmed.ncbi.nlm.nih.gov/36877065/>

Metallopeptidases as Key Virulence Attributes of Clinically Relevant Protozoa: New Discoveries, Perspectives, and Frontiers of Knowledge.

Vargas Rigo G, Gomes Cardoso F, Bongiorno Galego G, da Rosa DF, Souza Dos Santos AL, Tasca T.

06-03-2023

Curr Protein Pept Sci.

<https://pubmed.ncbi.nlm.nih.gov/36876838/>

Synthesis of urea and thiourea derivatives of C20-epi-aminosalinomycin and their activity against *Trypanosoma brucei*.

Antoszczak M, Gadsby-Davis K, Steverding D, Huczyński A.

25-02-2023

Eur J Med Chem.

<https://pubmed.ncbi.nlm.nih.gov/36870272/>

Salinomycin (SAL) is a natural polyether ionophore that exhibits a very broad spectrum of biological effects, ranging from anticancer to antiparasitic activities. Our recent studies have shown that the chemical modification

of the SAL biomolecule is a fruitful strategy for generating lead compounds for the development of novel antitrypanosomal agents. As a continuation of our program to develop trypanocidal active lead structures, we synthesized a series of 14 novel urea and thiourea analogs of C20-epi-aminosalinomycin (compound 2b). The trypanocidal and cytotoxic activities of the derivatives were assessed with the mammalian life cycle stage of *Trypanosoma brucei* and human leukemic HL-60 cells, respectively. The most antitrypanosomal compounds were the two thiourea derivatives 4b (C20-n-butylthiourea) and 4d (C20-phenylthiourea) with 50% growth inhibition (GI₅₀) values of 0.18 and 0.22 μ M and selectivity indices of 47 and 41, respectively. As potent SAL derivatives have been shown to induce strong cell swelling in bloodstream forms of *T. brucei*, the effect of compounds 4b and 4d to increase the cell volume of the parasite was also investigated. Interestingly, both derivatives were capable to induce faster cell swelling in bloodstream-form trypanosomes than the reference compound SAL. These findings support the suggestion that C20-epi-aminosalinomycin derivatives are suitable leads in the rational development of new and improved trypanocidal drugs.

mt-LAF3 is a pseudouridine synthase ortholog required for mitochondrial rRNA and mRNA gene expression in *Trypanosoma brucei*.

McDermott SM, Pham V, Lewis I, Tracy M, Stuart K.
23-02-2023

bioRxiv.

<https://pubmed.ncbi.nlm.nih.gov/36865177/>

Trypanosoma brucei and related kinetoplastid parasites possess unique RNA processing pathways, including in their mitochondria, that regulate metabolism and development. Altering RNA composition or conformation through nucleotide modifications is one such pathway, and modifications including pseudouridine regulate RNA fate and function in many organisms. We surveyed pseudouridine synthase (PUS) orthologs in Trypanosomatids, with a particular interest in mitochondrial enzymes due to their potential importance for mitochondrial function and metabolism. *T. brucei* mt-LAF3 is an ortholog of human and yeast mitochondrial PUS enzymes, and a mitoribosome assembly factor, but structural studies differ in their conclusion as to whether it has PUS catalytic activity. Here, we generated *T. brucei* cells that are conditionally null for mt-LAF3 and showed that mt-LAF3 loss is lethal and disrupts mitochondrial membrane potential ($\Delta\Psi$ m). Addition of a mutant gamma-ATP synthase allele to the conditionally null cells permitted $\Delta\Psi$ m maintenance and cell survival, allowing us to assess primary effects on mitochondrial RNAs. As expected, these studies showed that loss of mt-LAF3 dramatically decreases levels of mitochondrial 12S and 9S rRNAs. Notably, we also observed decreases in mitochondrial mRNA levels, including differential effects on edited vs. pre-edited mRNAs, indicating that mt-LAF3 is required for mitochondrial rRNA and mRNA processing, including of edited transcripts. To assess the importance of PUS catalytic activity in mt-LAF3 we mutated a conserved

aspartate that is necessary for catalysis in other PUS enzymes and showed it is not essential for cell growth, or maintenance of $\Delta\Psi$ m and mitochondrial RNA levels. Together, these results indicate that mt-LAF3 is required for normal expression of mitochondrial mRNAs in addition to rRNAs, but that PUS catalytic activity is not required for these functions. Instead, our work, combined with previous structural studies, suggests that *T. brucei* mt-LAF3 acts as a mitochondrial RNA-stabilizing scaffold.

Metabolic insights into phosphofructokinase inhibition in bloodstream-form trypanosomes.

Nare Z, Moses T, Burgess K, Schnauffer A, Walkinshaw MD, Michels PAM.

14-02-2023

Front Cell Infect Microbiol.

<https://pubmed.ncbi.nlm.nih.gov/36864883/>

Leishmaniose

Detection of asymptomatic Leishmania infection in blood donors at two blood banks in Ethiopia.

Mohammed R, Melkamu R, Pareyn M, Abdellati S, Bogale T, Engidaw A, Kinfu A, Girma T, van Griensven J.

09-03-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/36893183/>

Visceral leishmaniasis (VL) is a disease caused by *Leishmania* parasites. While predominantly transmitted by sandflies, cases of VL transmitted through blood transfusion have been reported, particularly in immunocompromised recipients. Although *Leishmania* parasites have been found in blood donors in some VL endemic areas, this has never been studied in East-Africa, where HIV prevalence is relatively high. We established the prevalence of asymptomatic *Leishmania* infection and associated socio-demographic factors among blood donors presenting at two blood bank sites (Metema and Gondar) in northwest Ethiopia between June and December 2020. Metema is located in a VL-endemic area; Gondar has historically been considered VL non-endemic but as an outbreak of VL has occurred around Gondar, it was defined as previously VL non-endemic. Blood samples were tested by the rK39 rapid diagnostic test (RDT), rK39 ELISA, direct agglutination test (DAT) and qPCR targeting kinetoplast DNA (kDNA). Asymptomatic infection was defined as positive by any of these tests in a healthy person. A total of 426 voluntary blood donors were included. The median age was 22 years (IQR, 19-28 years); 59% were male and 81% resided in urban areas. Only one participant had a history of VL and three had a family history of VL. Asymptomatic infection was detected in 15.0% (n = 32/213) in Metema and 4.2% (n = 9/213) in Gondar. The rK39 ELISA was positive in 5.4% (n = 23/426), the rK39 RDT in 2.6% (11/426), PCR in 2.6% (11/420) and DAT in 0.5% (2/426). There were six individuals with two positive tests: one positive on rK39 RDT and PCR and five positive on rK39 RDT and ELISA. The prevalence of asymptomatic infection was higher in Metema (VL-

endemic) and males but was not associated with age, a history of VL amongst family members or living in a rural area. Antibodies against Leishmania and parasite DNA was detected in a substantial number of blood donors. Future research should be directed at better defining the risk to recipients, including parasite viability studies and longitudinal studies amongst recipients.

In-vitro and in-vivo anti-leishmanial activity of the hanging sedge flavonoids based on bio- guided fractionation assay.

Moradian N, Hatam G, Hamed A, Pasdaran A.

09-03-2023

Chem Biol Drug Des.

<https://pubmed.ncbi.nlm.nih.gov/36892494/>

MCP-1/IL-12 ratio expressions correlated with adventitial collagen depositions in renal vessels and IL-4/IFN- γ expression correlated with interstitial collagen depositions in the kidneys of dogs with canine leishmaniasis.

Verçosa BLA, Muniz-Junqueira MI, Menezes-Souza D, Fujiwara RT, Borges LF, Melo MN, Vasconcelos AC.

06-03-2023

Mol Immunol.

<https://pubmed.ncbi.nlm.nih.gov/36889187/>

Polyunsaturated fatty acids alter the formation of lipid droplets and eicosanoid production in Leishmania promastigotes.

Andrade YMFS, Castro MV, Tavares VS, Souza RDSO, Faccioli LH, Lima JB, Sorgi CA, Borges VM, Araújo-Santos T.

06-03-2023

Mem Inst Oswaldo Cruz.

<https://pubmed.ncbi.nlm.nih.gov/36888851/>

Background: The knowledge about eicosanoid metabolism and lipid droplet (LD) formation in the Leishmania is very limited and new approaches are needed to identify which bioactive molecules are produced of them. **Objectives:** Herein, we compared LDs and eicosanoids biogenesis in distinct Leishmania species which are etiologic agents of different clinical forms of leishmaniasis. **Methods:** For this, promastigotes of Leishmania amazonensis, L. braziliensis and L. infantum were stimulated with polyunsaturated fatty acids (PUFA) and LD and eicosanoid production was evaluated. We also compared mutations in structural models of human-like cyclooxygenase-2 (GP63) and prostaglandin F synthase (PGFS) proteins, as well as the levels of these enzymes in parasite cell extracts. **Findings:** PUFAs modulate the LD formation in L. braziliensis and L. infantum. Leishmania spp with equivalent tissue tropism had same protein mutations in GP63 and PGFS. No differences in GP63 production were observed among Leishmania spp, however PGFS production increased during the parasite differentiation. Stimulation with arachidonic acid resulted in elevated production of

hydroxyeicosatetraenoic acids compared to prostaglandins. **Main conclusions:** Our data suggest LD formation and eicosanoid production are distinctly modulated by PUFAS dependent of Leishmania species. In addition, eicosanoid-enzyme mutations are more similar between Leishmania species with same host tropism.

Cutaneous leishmaniasis by a needlestick injury, an occupational infection?

Perales-González A, Pérez-Garza DM, Garza-Dávila VF, Ocampo-Candiani J.

08-03-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/36888575/>

Zinc and Manganese Imbalances in BALB/c Mice Experimentally Infected with Leishmania (Leishmania) amazonensis.

Sobotyk C, Baldissera FG, Rodrigues Junior LC, Romão PRT, de Oliveira JS, Dornelles GL, de Andrade CM, Maciel RM, Danesi CC, de Padua Ferreira RV, Bellini MH, de Avila Botton S, Vogel FSF, Sangioni LA.

08-03-2023

Acta Parasitol.

<https://pubmed.ncbi.nlm.nih.gov/36884141/>

Purpose: The clinical progression of Leishmania (Leishmania) amazonensis infection depends on multiple factors, including immunological status of the host and their genotypic interaction. Several immunological processes depend directly on minerals for an efficient performance. Therefore, this study used an experimental model to investigate the alterations of trace metals in L. amazonensis infection associate with clinical outcome, parasite load, and histopathological lesions, and the effect of CD4 + T cells depletion on these parameters. **Methods:** A total of 28 BALB/c mice were divided into 4 groups: 1- non-infected; 2-treated with anti-CD4 antibody; 3- infected with L. amazonensis; and 4-treated with anti-CD4 antibody and infected with L. amazonensis. After 24 weeks post-infection, levels of calcium (Ca), iron (Fe), magnesium (Mg), manganese (Mn), Cu, and Zn were determined by inductively coupled plasma optical emission spectroscopy using tissue samples of the spleen, liver, and kidneys. Additionally, parasite burdens were determined in the infected footpad (inoculation site) and samples of inguinal lymph node, spleen, liver, and kidneys were submitted to histopathological analysis. **Results:** Despite no significant difference was observed between groups 3 and 4, L. amazonensis-infected mice had a significant reduction of Zn (65.68-68.32%) and Mn (65.98 to 82.17%) levels. Presence of L. amazonensis amastigotes was also detected in the inguinal lymph node, spleen, and liver samples in all infected animals. **Conclusion:** The results showed that significant alterations in micro-elements levels occur in BALB/c mice experimentally infected with L. amazonensis and may increase the susceptibility of individuals to the infection.

Determination of the effect of collars containing 10% w/w imidacloprid and 4.5% w/w flumethrin (Seresto®) on the incidence of Leishmania and other canine vector-borne pathogen infections in Greece.

Ligda P, Gizzarelli M, Kostopoulou D, Foglia Manzillo V, Saratsis A, Saratsi K, Michler S, Ringeisen H, Boegel A, Schunack B, Pollmeier M, Kontrafouris M, Tsatsaki O, Oliva G, Sotiraki S.

07-03-2023

Parasit Vectors.

<https://pubmed.ncbi.nlm.nih.gov/36882870/>

NLRP12-expressing dendritic cells mediate both dissemination of infection and adaptive immune responses in visceral leishmaniasis.

Valadares DG, Clay OS, Chen Y, Scorza BM, Cassel SL, Sutterwala FS, Wilson ME.

08-02-2023

iScience.

<https://pubmed.ncbi.nlm.nih.gov/36879824/>

Investigation of comorbidities in dogs with leishmaniosis due to Leishmania infantum.

Apostolidis KN, Chatzis MK, Kasabalis D, Mataragka A, Ikononopoulos J, Skampardonis V, Athanasiou LV, Mylonakis ME, Leontides LS, Saridomichelakis MN.

Apr-2023

Vet Parasitol Reg Stud Reports.

<https://pubmed.ncbi.nlm.nih.gov/36878629/>

In endemic areas, dogs with leishmaniosis due to *Leishmania infantum* frequently have comorbidities, including mostly neoplastic, infectious, and parasitic diseases. The aim of this study was to compare the prevalence of comorbidities among dogs that are not infected by *L. infantum*, dogs that are infected but do not present leishmaniosis, and dogs with leishmaniosis, and to examine if certain comorbidities are independent risk factors for the infection by *L. infantum* and/or for the development of canine leishmaniosis (CanL). A total of 111 dogs, older than 1-year and non-vaccinated against CanL, were allocated into three groups: group A (n = 18) included dogs that were not infected by *L. infantum*, group B (n = 52) included dogs that were infected by *L. infantum* but did not present CanL, and group C (n = 41) included dogs with CanL. Signalment and historical data were obtained using a structured questionnaire. Laboratory examinations included complete blood count, serum biochemistry, urinalysis, fecal parasitology, modified Knott's test, microscopic examination of capillary blood, buffy coat, lymph node, bone marrow and conjunctival smears, qualitative serology for *Dirofilaria immitis*, *Anaplasma phagocytophilum*/*A. platys*, *Borrelia burgdorferi* and *E. canis*, IFAT for *L. infantum*, ELISA for *Babesia* spp. and *Neospora caninum*, and real-time PCR for *L. infantum* in bone marrow, skin biopsies and conjunctival swabs. A variety of comorbidities were found in all three groups. No independent risk factors for infection by *L. infantum* were

found. On the contrary, among dogs infected by *L. infantum*, being a mongrel [odds ratio (OR): 11.2], not receiving prevention for dirofilariosis (OR: 26.5) and being seropositive to *N. caninum* (OR: 17.1) or to *Babesia* spp. (OR: 37.6), were independent risk factors for presenting CanL. Although no comorbidities influence the probability of canine infection by *L. infantum*, certain comorbidities may be precipitating factors for the transition from the subclinical infection by *L. infantum* to the overt CanL.

Exposure to and infection by Leishmania infantum among domestic dogs in an area of the Cerrado biome, Maranhão, Brazil.

Dos Reis AT, do Carmo Silva CF, Rocha TB, Coutinho DJB, da Costa AP, Costa FB, Souza FA, de Maria Seabra Nogueira R.

Apr-2023

Vet Parasitol Reg Stud Reports.

<https://pubmed.ncbi.nlm.nih.gov/36878628/>

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

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

04-03-2023

Exp Parasitol.

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

Trypanosoma cruzi is an obligate parasite that uses glucose as one of the main resources to maintain its survival and proliferation. In eukaryotic cells glucose transport across membranes is mediated by facilitated transport through a variety of transporters. Herein, genes from the recently described SWEET family of carbohydrate transporters were identified in trypanosomatid parasites, including the medically important species *T. cruzi* and *Leishmania* spp. The identified genes have sequences with the typical attributes of known SWEET transporters. The expression of TcSWEET, the gene for the SWEET transporter found in the *T. cruzi* genome, was evidenced by immunohistochemistry using a polyclonal serum raised against peptides selected from the deduced TcSWEET protein sequence. In Western blot analysis, this α -TcSWEET serum detected proteins within the theoretical molecular mass for TcSWEET (25.8 kDa) in total epimastigote lysates, suggesting its expression at this parasite stage. Additionally, this serum stained epimastigotes at localizations consistent with the cell body and the flagellum. Together, these data suggests that SWEET transporters may contribute to glucose transport in trypanosomatid parasites.

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

Kushwaha V, Capalash N.

04-03-2023

Acta Trop.

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

Genomic analysis of *Leishmania turanica* strains from different regions of Central Asia.

Novozhilova TS, Chistyakov DS, Akhmadishina LV, Lukashev AN, Gerasimov ES, Yurchenko V.

06-03-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/36877735/>

Chromosome-Scale Assembly of the Complete Genome Sequence of *Leishmania (Mundinia) procaviensis* Isolate 253, Strain LV425.

Almutairi H, Urbaniak MD, Bates MD, Kwakye-Nuako G, Al-Salem WS, Dillon RJ, Bates PA, Gatherer D.

06-03-2023

Microbiol Resour Announc.

<https://pubmed.ncbi.nlm.nih.gov/36877038/>

Leishmania (Mundinia) procaviensis is a parasitic kinetoplastid that was first isolated from a rock hyrax in Namibia in 1975. We present the complete genome sequence of *Leishmania (Mundinia) procaviensis* isolate 253, strain LV425, sequenced using combined short- and long-read technologies. This genome will contribute to our understanding of hyraxes as a *Leishmania* reservoir.

Metallopeptidases as Key Virulence Attributes of Clinically Relevant Protozoa: New Discoveries, Perspectives, and Frontiers of Knowledge.

Vargas Rigo G, Gomes Cardoso F, Bongiorno Galego G, da Rosa DF, Souza Dos Santos AL, Tasca T.

06-03-2023

Curr Protein Pept Sci.

<https://pubmed.ncbi.nlm.nih.gov/36876838/>

Genome sequence of *Leishmania mexicana* MNYC/BZ/62/M379 expressing Cas9 and T7 RNA polymerase.

Beneke T, Dobramysl U, Catta-Preta CMC, Mottram JC, Gluenz E, Wheeler RJ.

Dec-2022

Wellcome Open Res.

<https://pubmed.ncbi.nlm.nih.gov/36874584/>

Long-term follow-up of a case of feline leishmaniosis treated with a combination of allopurinol and meglumine antimoniate.

Tiozzo AA, Masserdotti C, Becattini L, Ottaiano P, Ferrari F, Tamborini A.

Mar-2023

Can Vet J.

<https://pubmed.ncbi.nlm.nih.gov/36874537/>

A 9-year-old domestic cat, positive for antibodies to feline immunodeficiency virus (FIV), was brought to a veterinary clinic with alopecia, ulcerative skin lesions, and upper respiratory tract (URT) signs. This was after being treated for suspected allergic dermatitis, without clinical improvement, for 2 y. Biopsy of the skin and fine-needle aspirates of the spleen and of the lymph nodes were taken which detected the presence of *Leishmania* amastigotes. *Leishmania* infection was further confirmed by detection of a high titer of anti-*Leishmania* antibodies (≥ 3200) with an indirect fluorescent antibody technique (IFAT) serology. After the diagnosis of feline leishmaniosis (FeL) was made, allopurinol and meglumine antimoniate were started and led to quick and complete clinical improvement. After 7 mo, allopurinol administration was briefly interrupted but was resumed following relapse of the skin lesions. One month later, the cat was treated for suspected acute kidney injury, which prompted reduction of the total daily dose of allopurinol by 50%. The cat remained clinically well, with complete resolution of the cutaneous and URT signs, for nearly 24 mo after the diagnosis of FeL; at which point it was euthanized for worsening cardiac disease. To our knowledge, this represents a rare case of successful treatment of FeL with a suspected nephrotoxic effect associated with long-term use of allopurinol. Further studies are required to clarify the relationship, if any, between leishmaniosis and congestive heart failure in cats.

***Leishmania* species: A narrative review on surface proteins with structural aspects involved in host-pathogen interaction.**

Kaushal RS, Naik N, Prajapati M, Rane S, Raulji H, Ngo FA, Upadhyay TK, Saeed M.

05-03-2023

Chem Biol Drug Des.

<https://pubmed.ncbi.nlm.nih.gov/36872849/>

An anti-leishmanial compound 4',7-dihydroxyflavone elicits ROS-mediated apoptosis-like death in *Leishmania* parasite.

Sasidharan S, Saudagar P.

04-03-2023

FEBS J.

<https://pubmed.ncbi.nlm.nih.gov/36871140/>

The treatment for leishmaniasis is currently plagued by side effects such as toxicity, and the emergence of drug resistance to the available repertoire of drugs, as well as the expense of these drugs. Considering the rising concerns, we report here, the anti-leishmanial activity and mechanism of a flavone compound 4',7-dihydroxyflavone (TI 4). Four flavanoids were initially screened for anti-leishmanial activity and cytotoxicity. The results showed that the compound TI 4 exhibited higher activity and selectivity index while maintaining low cytotoxicity. Preliminary microscopic studies and FACS analysis reported that the parasite underwent apoptosis on TI 4 treatment. Further in-depth studies revealed high ROS production and thiol levels in the parasites suggesting ROS mediated apoptosis in the parasites upon TI 4 treatment.

Other apoptotic indicators like intracellular Ca^{2+} and mitochondrial membrane potential also indicated the onset of apoptosis in the treated parasites. The mRNA expression levels signified that the redox metabolism genes were upregulated by 2-fold along with the apoptotic genes. In summary, the use of T1 4 on Leishmania parasites induces ROS-mediated apoptosis, therefore the compound has immense potential to be an anti-leishmanial drug. However, in vivo studies would be required to ascertain its safety and efficacy before we can exploit the compound against the growing leishmaniasis crisis.

Identification of Leishmania species and frequency distribution of LRV1 and LRV2 viruses on cutaneous leishmaniasis patients in Isfahan Province, Iran.

Zolfaghari A, Beheshti-Maal K, Ahadi AM, Monajemi R.
Jan-Feb 2023

Indian J Med Microbiol.

<https://pubmed.ncbi.nlm.nih.gov/36870742/>

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

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

23-02-2023

Cell Immunol.

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

Compliance of Primary Healthcare Workers in Saudi Arabia With the National Surveillance System of Tropical and Non-tropical Dermatological Diseases.

Almugti HS, AlMarei S, Jurebi RM, Almutiri MK, Alghamdi B, Alghamdi AS, Alhajry HH, Al-Helali SM, Alzaidi AH, Alzahrani YS, Al-Mutairy MH, Jurebi A, Alshareef A, Almarzooq A, Alsaedi MQ.

28-01-2023

Cureus.

<https://pubmed.ncbi.nlm.nih.gov/36865961/>

Background: Control and prevention of infectious diseases has been a primary health mandate. The reporting system is a vital step in preventing and controlling of these diseases. Most important, healthcare workers who have a responsibility to report must be aware of this responsibility. The present study aimed to improve the compliance of primary healthcare workers against reportable tropical and non-tropical dermatological diseases. **Objective of the study:** The objective was to assess the knowledge, skills, and practice of primary healthcare workers in Saudi Arabia regarding the surveillance system of reportable tropical and non-tropical dermatological diseases using an assessment tool featuring closed-ended questions. As a secondary objective, this study assessed the satisfaction of primary healthcare workers with the surveillance system. **Subjects and methods:** Through a cross-sectional design, the study

used an electronic self-administered questionnaire targeting the primary healthcare workers who met the inclusion criteria through a non-probability sampling technique. **Results:** By the end of the study period, data had been collected from 377 primary healthcare workers. Slightly more than half of them worked for the ministry of health facilities. In the last year, the vast majority (88%) of participants did not report any infectious diseases. Poor or low knowledge was reported by almost half of the participants concerning which dermatological diseases should be notified immediately on clinical suspicion or routinely on a weekly basis. Clinically and in response to the skills assessment, 57% of the participants had lower skills scores in detecting and identifying the skin ulcer of leishmania. Half of the participants were less satisfied with the feedback after their notification and considered the notification forms complicated and time-consuming, especially with the usual high workload in primary healthcare centers. Furthermore, the observed significant differences ($p < 0.001$) in knowledge and skill scores were demonstrated with female healthcare workers, older participants, employees from the Ministry of National Guard Health Affairs, and workers with more than ten years of experience. **Conclusion:** The present study has shown the limitations of public health surveillance due to underreporting and lack of timeliness. The dissatisfaction of study participants with feedback after the notification step is another finding that demonstrates the need for collaboration among public health authorities and healthcare workers. Fortunately, health departments can implement measures to improve practitioners' awareness through continuous medical education and providing frequent feedback to overcome these hurdles.

Recombinant protein KR95 as an alternative for serological diagnosis of human visceral leishmaniasis in the Americas.

Fujimori M, Valencia-Portillo RT, Lindoso JAL, Celeste BJ, de Almeida RP, Costa CHN, da Cruz AM, Druzian AF, Duthie MS, Fortaleza CMCB, Oliveira ALL, Paniago AMM, Queiroz IT, Reed S, Vallur AC, Goto H, Sanchez MCA.

02-03-2023

PLoS One

<https://pubmed.ncbi.nlm.nih.gov/36862710/>

In the Americas, visceral leishmaniasis (VL) is caused by the protozoan Leishmania infantum, leading to death if not promptly diagnosed and treated. In Brazil, the disease reaches all regions, and in 2020, 1,933 VL cases were reported with 9.5% lethality. Thus, an accurate diagnosis is essential to provide the appropriate treatment. Serological VL diagnosis is based mainly on immunochromatographic tests, but their performance may vary by location, and evaluation of diagnostic alternatives is necessary. In this study, we aimed to evaluate the performance of ELISA with the scantily studied recombinant antigens, K18 and KR95, comparing their performance with the already known rK28 and rK39. Sera from parasitologically confirmed symptomatic VL patients ($n = 90$) and healthy endemic controls ($n = 90$) were submitted to ELISA with rK18 and rKR95. Sensitivity (95% CI) was, respectively, 83.3% (74.2-89.7) and 95.6%

(88.8-98.6), and specificity (95% CI) was 93.3% (85.9-97.2) and 97.8% (91.8-99.9). For validation of ELISA with the recombinant antigens, we included samples from 122 VL patients and 83 healthy controls collected in three regions in Brazil (Northeast, Southeast, and Midwest). When comparing the results obtained with the VL patients' samples, significantly lower sensitivity was obtained by rK18-ELISA (88.5%, 95% CI: 81.5-93.2) compared with rK28-ELISA (95.9%, 95% CI: 90.5-98.5), but the sensitivity was similar comparing rKR95-ELISA (95.1%, 95% CI: 89.5-98.0), rK28-ELISA (95.9%, 95% CI: 90.5-98.5), and rK39-ELISA (94.3%, 95% CI: 88.4-97.4). Analyzing the specificity, it was lowest with rK18-ELISA (62.7%, 95% CI: 51.9-72.3) with 83 healthy control samples. Conversely, higher and similar specificity was obtained by rKR95-ELISA (96.4%, 95% CI: 89.5-99.2), rK28-ELISA (95.2%, 95% CI: 87.9-98.5), and rK39-ELISA (95.2%, 95% CI: 87.9-98.5). There was no difference in sensitivity and specificity across localities. Cross-reactivity assessment, performed with sera of patients diagnosed with inflammatory disorders and other infectious diseases, was 34.2% with rK18-ELISA and 3.1% with rKR95-ELISA. Based on these data, we suggest using recombinant antigen KR95 in serological assays for VL diagnosis.

Leaf hydroalcoholic extract and oleoresin from *Copaifera multijuga* control *Toxoplasma gondii* infection in human trophoblast cells and placental explants from third-trimester pregnancy.

Martínez AFF, Teixeira SC, de Souza G, Rosini AM, Júnior JPL, Melo GN, Blandón KOE, Gomes AO, Ambrósio SR, Veneziani RCS, Bastos JK, Martins CHG, Ferro EAV, Barbosa BF.

13-02-2023

Front Cell Infect Microbiol.

<https://pubmed.ncbi.nlm.nih.gov/36860986/>

Data-driven predictions of potential *Leishmania* vectors in the Americas.

Vadmal GM, Glidden CK, Han BA, Carvalho BM, Castellanos AA, Mordecai EA.

21-02-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/36809249/>

The incidence of vector-borne diseases is rising as deforestation, climate change, and globalization bring humans in contact with arthropods that can transmit pathogens. In particular, incidence of American Cutaneous Leishmaniasis (ACL), a disease caused by parasites transmitted by sandflies, is increasing as previously intact habitats are cleared for agriculture and urban areas, potentially bringing people into contact with vectors and reservoir hosts. Previous evidence has identified dozens of sandfly species that have been infected with and/or transmit *Leishmania* parasites. However, there is an incomplete understanding of which sandfly species transmit the parasite, complicating efforts to limit disease spread. Here, we apply machine learning models (boosted regression trees) to leverage biological and geographical

traits of known sandfly vectors to predict potential vectors. Additionally, we generate trait profiles of confirmed vectors and identify important factors in transmission. Our model performed well with an average out of sample accuracy of 86%. The models predict that synanthropic sandflies living in areas with greater canopy height, less human modification, and within an optimal range of rainfall are more likely to be *Leishmania* vectors. We also observed that generalist sandflies that are able to inhabit many different ecoregions are more likely to transmit the parasites. Our results suggest that *Psychodopygus amazonensis* and *Nyssomia antunesi* are unidentified potential vectors, and should be the focus of sampling and research efforts. Overall, we found that our machine learning approach provides valuable information for *Leishmania* surveillance and management in an otherwise complex and data sparse system.

Cysticercose

Pre-slaughter, slaughter and post-slaughter practices of slaughterhouse workers in Southeast, Nigeria: Animal welfare, meat quality, food safety and public health implications.

Njoga EO, Ilo SU, Nwobi OC, Onwumere-Idolor OS, Ajibo FE, Okoli CE, Jaja IF, Oguttu JW.

03-03-2023

PLoS One

<https://pubmed.ncbi.nlm.nih.gov/36867613/>

The pipeline for drugs for control and elimination of neglected tropical diseases: 1. Anti-infective drugs for regulatory registration.

Pfarr KM, Krome AK, Al-Obaidi I, Batchelor H, Vaillant M, Hoerauf A, Opoku NO, Kuesel AC.

01-03-2023

Parasit Vectors.

<https://pubmed.ncbi.nlm.nih.gov/36859332/>

The World Health Organization 'Ending the neglect to attain the Sustainable Development Goals: A road map for neglected tropical diseases 2021-2030' outlines the targets for control and elimination of neglected tropical diseases (NTDs). New drugs are needed to achieve some of them. We are providing an overview of the pipeline for new anti-infective drugs for regulatory registration and steps to effective use for NTD control and elimination. Considering drugs approved for an NTD by at least one stringent regulatory authority: fexinidazole, included in WHO guidelines for *Trypanosoma brucei* gambiense African trypanosomiasis, is in development for Chagas disease. Moxidectin, registered in 2018 for treatment of individuals ≥ 12 years old with onchocerciasis, is undergoing studies to extend the indication to 4-11-year-old children and obtain additional data to inform WHO and endemic countries' decisions on moxidectin inclusion in guidelines and policies. Moxidectin is also being evaluated for other NTDs. Considering drugs in at least Phase 2 clinical development, a submission is being prepared for

registration of acoziborole as an oral treatment for first and second stage T.b. gambiense African trypanosomiasis. Bedaquiline, registered for tuberculosis, is being evaluated for multibacillary leprosy. Phase 2 studies of emodepside and flubentylol in *O. volvulus*-infected individuals are ongoing; studies for *Trichuris trichuria* and hookworm are planned. A trial of fosravuconazole in *Madurella mycetomatis*-infected patients is ongoing. JNJ-64281802 is undergoing Phase 2 trials for reducing dengue viral load. Studies are ongoing or planned to evaluate oxantel pamoate for onchocerciasis and soil-transmitted helminths, including *Trichuris*, and oxfendazole for onchocerciasis, *Fasciola hepatica*, *Taenia solium* cysticercosis, *Echinococcus granulosus* and soil-transmitted helminths, including *Trichuris*. Additional steps from first registration to effective use for NTD control and elimination include country registrations, possibly additional studies to inform WHO guidelines and country policies, and implementation research to address barriers to effective use of new drugs. Relative to the number of people suffering from NTDs, the pipeline is small. Close collaboration and exchange of experience among all stakeholders developing drugs for NTDs may increase the probability that the current pipeline will translate into new drugs effectively implemented in affected countries.

A Rapid Point-of-Care Assay for Cysticercosis Antigen Detection in Urine Samples.

Toribio L, Handali S, Marin Y, Perez E, Castillo Y, Bustos JA, O'Neal SE, Garcia HH.

06-02-2023

Am J Trop Med Hyg.

<https://pubmed.ncbi.nlm.nih.gov/36746658/>

Role of Treg, Breg and other cytokine sets in host protection and immunopathology during human leishmaniasis: Are they potential valuable markers in clinical settings and vaccine evaluation?

Divenuto F, Pavia G, Marascio N, Barreca GS, Quirino A, Matera G.

Apr-2023

Acta Trop.

<https://pubmed.ncbi.nlm.nih.gov/36731621/>

Leishmaniasis is a vector-borne disease caused by obligate intracellular protozoan parasites that can infect humans and other mammals. Pro- and anti-inflammatory cytokines are important regulators of innate and specific responses in Leishmania infection. Resistance to leishmaniasis is related to T helper 1 (Th1) response with the production of pro-inflammatory cytokines: IL-12, IL-1 β , IFN- γ , TNF- α , IL-2 leading to activation of macrophages and parasite killing. Instead, a more intense Th2 (IL-4, IL-5, IL-13), Treg (IL-10 and TGF- β) and Breg response (IL-10 and IL-35) are related to parasite persistence through the inhibition of macrophage activation, which promotes the escape from host immune system. Interestingly, a cytokine involved in the parasite killing in one form of leishmaniasis may be

"pathogen friendly" in another form of the disease. To date, few studies are focusing on the role of Treg and Breg cytokines in human models of leishmaniasis; therefore, further investigations are needed to clarify their potential role in the diagnosis and prognosis of such protozoan infections, as well as in the development of vaccines against leishmaniasis. This review summarizes the current knowledge about the role of cytokines produced by Th1, Th2, Treg, and Breg cells involved in Leishmania disease progression and host protection. Some cytokines might play a role as diagnostic and prognostic clinical markers, or they could represent a novel approach leading to new anti-leishmaniasis therapies. Overall, advances in knowledge of the complex network of cytokines secreted by immune cells could help to better understand signaling pathways and host immune responses during Leishmania infection. This approach would allow these mediators to be used as therapeutic strategies against leishmaniasis.

Recombinant endonuclease III protein from Leishmania infantum associated with Th1-type adjuvants is immunogenic and induces protection against visceral leishmaniasis.

Lage DP, Machado AS, Freitas CS, Vale DL, Linhares FP, Cardoso JMO, Oliveira-da-Silva JA, Ramos FF, Pereira IAG, Ludolf F, Tavares GSV, Bandeira RS, Oliveira JS, Menezes-Souza D, Duarte MC, Galdino AS, Christodoulides M, Chávez-Fumagalli MA, Roatt BM, Martins VT, Coelho EAF.

Mar-2023

Mol Immunol.

<https://pubmed.ncbi.nlm.nih.gov/36731193/>

Vaccination against visceral leishmaniasis (VL) should be considered as a safe and effective measure to disease control; however, few vaccines are available against canine VL and there is no an approved human vaccine. In this context, in the present study, we evaluated the endonuclease III (ENDO) protein, which was recently showed to be antigenic for human disease, as a vaccine candidate against Leishmania infantum infection. The recombinant protein (rENDO) was administered in BALB/c mice alone or associated with saponin (rENDO/Sap) or micelles (rENDO/Mic) as adjuvants. Controls received saline, saponin or empty micelles. Results showed that both rENDO/Sap and rENDO/Mic compositions induced higher levels of IFN- γ , IL-12, TNF- α , and GM-CSF cytokines, besides nitrite and IgG2a isotype antibodies, before and after challenge infection, which were related to both CD4 $^{+}$ and CD8 $^{+}$ T cell subtypes. The immunological results contributed to significant reductions in the parasite load found in the spleens, livers, bone marrows and draining lymph nodes of the vaccinated animals. In general, mice immunized with rENDO/Mic presented a slightly higher Th1-type cellular and humoral immune response, as compared to those receiving rENDO/Sap. In addition, saponin caused a slight to moderate inflammatory edema in their vaccinated footpads, which was not observed when micelles were used with rENDO. In addition, a preliminary analysis showed that the recombinant protein was immunogenic to human cells cultures, since PBMCs from treated VL patients and healthy subjects showed

higher lymphoproliferation and IFN- γ production in the culture supernatants. In conclusion, data suggest that rENDO could be considered as a candidate to be evaluated in future studies as vaccine to protect against VL.

A review on new natural and synthetic anti-leishmanial chemotherapeutic agents and current perspective of treatment approaches.

Majumder N, Banerjee A, Saha S.

Apr-2023

Acta Trop.

<https://pubmed.ncbi.nlm.nih.gov/36720335/>

Leishmania RNA Virus Is Not Detected in All Species of the Leishmania Viannia Subgenus: The Case of L. (V.) panamensis in Colombia.

Rosales-Chilama M, Y Oviedo M, K Quintero Y, L Fernández O, Gómez MA.

30-01-2023

Am J Trop Med Hyg.

<https://pubmed.ncbi.nlm.nih.gov/36716739/>

The endosymbiotic *Leishmania* RNA virus 1 (LRV1) has been associated with severity and clinical manifestations of American tegumentary leishmaniasis caused by species of the *Leishmania* (*Viannia*) subgenus. Between and within *Leishmania* species, and among endemic countries, the prevalence of LRV is highly variable. The LRV virus has not been detected in *L. (V.) panamensis*, the second-most prevalent species in Central America and Colombia. However, no systematic screening of LRV has been conducted in *L. (V.) panamensis*, and thus it is still controversial whether this virus is truly absent from the species. We sought to determine the prevalence of LRV1 in *L. (V.) panamensis* clinical strains isolated from patients with cutaneous leishmaniasis (CL), from different geographic areas of Colombia. We analyzed 219 clinical strains; 78% were *L. (V.) panamensis*, 18% were *L. (V.) braziliensis*, and 4% were *L. (V.) guyanensis*. Screening for LRV1 was performed by quantitative reverse transcription-polymerase chain reaction. The LRV1 was detected in 18% (7 of 40) of *L. (V.) braziliensis* strains, and was not detected in any of the *L. (V.) guyanensis* or *L. (V.) panamensis* strains. The LRV1-positive *L. (V.) braziliensis* strains came from the Amazon Basin. Of the seven LRV1-positive strains, two were isolated from patients with mucocutaneous leishmaniasis, and the remaining from patients with CL. Our results confirm the absence of LRV1 in *L. (V.) panamensis* in Colombia.

Integrated computational and experimental approach for novel anti-leishmanial molecules by targeting Dephospho-coenzyme A kinase.

Menpadi N, Prakash J, Kundu D, Chandra P, Dubey VK.

31-03-2023

Int J Biol Macromol.

<https://pubmed.ncbi.nlm.nih.gov/36708902/>

Coenzyme A acts as a necessary cofactor for many enzymes and is a part of many biochemical processes. One of the critical enzymes involved in Coenzyme A synthesis is Dephospho-coenzyme A-kinase (DPCK). In this study, we have used integrated computational and experimental approaches for promising inhibitors of DPCK using the natural products available in the ZINC database for anti-leishmanial drug development. The top hit compounds chosen after molecular docking were Veratramine, Azulene, Hupehenine, and Hederagenin. The free binding energy of Veratramine, Azulene, Hupehenine, and Hederagenin was estimated. Besides the favourable binding point, the ligands also showed good hydrogen bonding and other interactions with key residues of the enzyme's active site. The natural compounds were also experimentally investigated for their effect on the *L. donovani* promastigotes and murine macrophage (J774A.1). A good antileishmanial activity by the compounds on the promastigotes was observed as estimated by the MTT assay. The in-vitro experiments revealed that Hupehenine ($IC_{50} = 7.34 \pm 0.37 \mu M$) and Veratramine ($IC_{50} = 12.46 \pm 2.28 \mu M$) exhibited better inhibition than Hederagenin ($IC_{50} = 23.36 \pm 0.54 \mu M$) and Azulene ($IC_{50} = 24.42 \pm 3.28 \mu M$). This work has identified novel anti-leishmanial molecules possibly acting through the inhibition of DPCK.

Comparison of Sampling Procedures for the Molecular Diagnosis of Leishmaniasis.

Andrade Zampieri R, Ide Aoki J, Müller KE, Jon Shaw J, Maria Floeter-Winter L.

30-01-2023

Am J Trop Med Hyg.

<https://pubmed.ncbi.nlm.nih.gov/36689945/>

Membrane-acting biomimetic peptoids against visceral leishmaniasis.

Kumar V, Lin JS, Molchanova N, Fortkort JA, Reckmann C, Bräse S, Jenssen H, Barron AE, Chugh A.

Mar-2023

FEBS Open Bio.

<https://pubmed.ncbi.nlm.nih.gov/36683396/>

Population Genetic Structure of Phlebotomus sergenti (Diptera: Psychodidae) Collected in Four Regions of Morocco Based on the Analysis of Cyt b and EF-1 α Genes.

El Kacem S, Ait Kbaich M, Mhaidi I, Daoui O, Bennani H, Dvořák V, Lemrani M.

06-03-2023

J Med Entomol.

<https://pubmed.ncbi.nlm.nih.gov/36610984/>

Phlebotomus (Ph.) *sergenti* is the main vector of *Leishmania* (L.) *tropica* (Trypanosomatida: Trypanosomatidae), the causative agent of anthroponotic cutaneous leishmaniasis in Morocco. This species has an extended geographical distribution, wider than that of the parasite. The main objective of our study was to analyze the genetic diversity of Ph. *sergenti* collected in four foci

in Morocco: Taza, Fom Jemâa, El Hanchane, and Ouarzazate. We studied a set of diversity and population structure indices by sequencing two markers; nuclear EF-1 α and mitochondrial Cyt b from 175 individual sand flies. Our results showed a considerable degree of intraspecific polymorphism with a high number of haplotypes identified in both genes. Many polymorphic sites detected in the Cyt b sequences (SCyt b = 45) indicate that it is the most polymorphic marker showing a distinct distribution of haplotypes according to their geographical origin, whereas the EF-1 α marker showed no geographical isolation. Analysis by Tajima's D and Fu's Fs tests revealed a possible recent expansion of the populations, especially with the EF-1 α marker, showing significant values in Taza and Ouarzazate sequences. The present study revealed significant genetic diversity within *Ph. sergenti* populations in Morocco. The results warrant further research using a combination of more than two markers including mitochondrial and non-mitochondrial markers, which may provide more information to clarify the genetic status of *Ph. sergenti*.

Phlebotominae Fauna (Diptera: Psychodidae) and the Spatial Distribution of Species in Sergipe, Brazil.

Andrade DC, Lima AFVA, Jeraldo VLS, de Melo CM, Pinto MC, Madi RR.

06-03-2023

J Med Entomol.

<https://pubmed.ncbi.nlm.nih.gov/36462189/>

Dracunculose

Chemical Characterization and Multidirectional Biological Effects of Different Solvent Extracts of *Arum elongatum*: in vitro and in silico Approaches.

Mahomoodally MF, Zengin G, Roumita SS, Caprioli G, Mustafa AM, Piatti D, Yildiztugay E, Ak G, Karadağ AE, Khalid A, Abdalla AN, Uba AI, Demirci F.

09-03-2023

Chem Biodivers.

<https://pubmed.ncbi.nlm.nih.gov/36891864/>

Arum elongatum (Araceae) is widely used traditionally for the treatment of abdominal pain, arterial hypertension, diabetes mellitus, rheumatism and hemorrhoids. This study investigated the antioxidant properties, individual phenolic compounds, total phenolic and total flavonoid contents (HPLC-MS analysis), reducing power and metal chelating effects of four extracts obtained from *A. elongatum* (ethyl acetate (EA), methanol (MeOH), methanol/water (MeOH/water) and infusion). The inhibitory activity of the extracts were also determined against acetylcholinesterase, butyrylcholinesterase, tyrosinase, amylase and glucosidase enzymes. The MeOH/water extracts contained the highest amount of phenolic contents (28.85 mg GAE/g) while the highest total flavonoid content was obtained with MeOH extract (36.77 mg RE/g). MeOH/water demonstrated highest antioxidant activity against DPPH \cdot radical at 38.90 mg

Trolox equivalent per gram. The infusion extract was the most active against ABTS $\cdot+$ (133.08 mg TE/g). MeOH/water extract showed the highest reducing abilities with the CUPRAC value of 102.22 mg TE/g and the FRAP value of 68.50 mg TE/g. A strong metal chelating effect was observed with MeOH/water extract (35.72 mg EDTAE/g). The PBD values of the extracts ranged from 1.01 to 2.17 mmol TE/g. EA extract displayed the highest inhibitory activity against AChE (2.32 mg GALAE/g), BChE (3.80 mg GALAE/g), α -amylase (0.56 mmol ACAE/g) and α -glucosidase (9.16 mmol ACAE/g) enzymes. Infusion extract was the most active against tyrosinase enzyme with a value of 83.33 mg KAE/g. A total of 28 compounds were identified from the different extracts. The compounds present in the highest concentration were chlorogenic acids, 4-hydroxy benzoic acid, caffeic acid, p-coumaric acid, ferulic acid, isoquercitrin, delphinidin 3,5 diglucoside, kaempferol-3-glucoside and hyperoside. The biological activities of *A. elongatum* extracts could be due to the presence of compounds such as gallic acid, chlorogenic acids, ellagic acid, epicatechin, catechin, kaempferol, 4-hydroxy benzoic acid, caffeic acid, p-coumaric acid, ferulic acid, quercetin, isoquercitrin, and hyperoside. Extracts of *A. elongatum* showed promising biological activities which warrants further investigations in an endeavour to develop biopharmaceuticals.

First Report of Anthracnose Caused by *Colletotrichum camelliae* on *Amorphophallus konjac* in Hunan Province of China.

Sun L, Wu S, Lu Y, Wu F, Chen X.

07-03-2023

Plant Dis.

<https://pubmed.ncbi.nlm.nih.gov/36880860/>

[Effect of lime water processing of *Pinelliae Rhizoma Praeparatum* on toxic component lectin protein].

Tao XB, Wu H.

Feb-2023

Zhongguo Zhong Yao Za Zhi.

<https://pubmed.ncbi.nlm.nih.gov/36872265/>

The present study investigated the effect of immersion in the excipient lime water on the toxic component lectin protein and explained the scientific connotation of lime water detoxication during the processing of *Pinelliae Rhizoma Praeparatum*. Western blot was used to investigate the effects of immersion in lime water with different pH (pH 10, 11, and 12.4), saturated sodium hydroxide, and sodium bicarbonate solution on the content of lectin protein. The protein compositions of the supernatant and the precipitate after immersing lectin protein in lime water of different pH were determined by the SDS-PAGE method combined with the silver staining technique. The MALDI-TOF-MS/MS technique was used to detect the molecular weight distribution of peptide fragments in the supernatant and precipitate after immersing lectin protein in lime water of different pH, and circular dichroism spectroscopy was used to detect the ratio changes in the secondary structure of lectin protein

during the immersion. The results showed that immersion in lime water at pH>12 and saturated sodium hydroxide solution could significantly reduce the content of lectin protein, while immersion in lime water at pH<12 and sodium bicarbonate solution had no significant effect on lectin protein content. The corresponding lectin protein bands and molecular ion peaks were not detected at the 12 kDa position in the supernatant and precipitate after immersing the lectin protein in lime water at pH>12, which was attributed to the fact that lime water immersion at pH>12 could significantly change the ratio of the secondary structure of lectin protein, resulting in irreversible denaturation, while lime water immersion at pH<12 did not change the ratio of the secondary structure of lectin protein. Therefore, pH>12 was the key condition for the detoxication of lime water during the processing of *Pinelliae Rhizoma Praeparatum*. Lime water immersion at pH>12 could cause irreversible denaturation of lectin protein, resulting in a significant decrease in the inflammatory toxicity of *Pinelliae Rhizoma Praeparatum*, which played a key role in detoxification.

Conformational changes and physicochemical attributes of texturized pea protein isolate-konjac gum: With a new perspective of residence time during extrusion.

Sun D, Wu M, Zhang T, Wei D, Zhou C, Shang N.

Mar-2023

Food Res Int.

<https://pubmed.ncbi.nlm.nih.gov/36869508/>

The intervention effects of konjac glucomannan with different molecular weights on high-fat and high-fructose diet-fed obese mice based on the regulation of gut microbiota.

Liu Q, Fang J, Huang W, Liu S, Zhang X, Gong G, Huang L, Lin X, Wang Z.

Mar-2023

Food Res Int.

<https://pubmed.ncbi.nlm.nih.gov/36869507/>

Performance evaluation of developed macrophyte-assisted vermifiltration system designed with varied macrophytes and earthworm species for domestic wastewater treatment.

Nsiah-Gyambibi R, Acheampong E, Von-Kiti E, Larbi Ayisi C.

01-03-2023

PLoS One

<https://pubmed.ncbi.nlm.nih.gov/36857364/>

Development of sustainable technology to treat domestic wastewater with added advantages of cost reduction and improved handling efficiency is crucial in developing countries. This is because, domestic wastewater from households are stored in septic tanks and are poorly treated prior discharge. This study developed a macrophyte-assisted vermifiltration (MAV) system to treat

domestic wastewater. The MAV system is an integrated approach of macrophytes and earthworms in a vermifiltration and complex physicochemical mechanism processes. The use of different macrophyte and earthworm species was hypothesized by the study to affect and vary the treatment performance of the developed MAV. The study therefore aimed to evaluate the treatment performance of the developed MAV when three varied macrophyte species (*Eichhornia crassipes*, *Pistia stratiotes* and *Spirodela* sp.) and two varied earthworm species (*Eisenia fetida* and *Eudrilus eugeniae*) were used to design the treatment system. Treated effluents were collected every 48 hours within two weeks for physico-chemical, pathogen and helminth analysis. The contaminants (N_{tot}, NH₃, NO₃-N and P_{tot}) in the wastewater were high (>50 mgL⁻¹, >5 mgL⁻¹, >1 mgL⁻¹ and >20 mgL⁻¹ respectively). Results revealed that the developed MAV systems were effective in the removal of solids (>60%), nutrients (>60%) and pathogens (>90%). In most cases, there were no significant differences between the selected varied macrophytes and earthworms in the treatment performances. Results therefore demonstrated that the selected macrophytes combined with the earthworm species were suitable when used in the development of the MAV system. Developing the MAV with the selected varied macrophyte and earthworm species did not only contribute to the treatment of the wastewater, but also improved the vermiculture. *Eudrilus eugeniae* however demonstrated higher biomass gain (5-10% more) compared to *Eisenia fetida*.

Phytotoxicity of microplastics to the floating plant *Spirodela polyrrhiza* (L.): Plant functional traits and metabolomics.

Wang Y, Bai J, Wen L, Wang W, Zhang L, Liu Z, Liu H.

01-04-2023

Environ Pollut.

<https://pubmed.ncbi.nlm.nih.gov/36738884/>

Toxicological effects resulting from co-exposure to nanomaterials and to a β -blocker pharmaceutical drug in the non-target macrophyte species *Lemna minor*.

Silva PMMD, Alkimin GD, Camparotto NG, Prediger P, Nunes B.

01-04-2023

Environ Pollut.

<https://pubmed.ncbi.nlm.nih.gov/36738879/>

Phytoremediation of nickel and chromium-containing industrial wastewaters by water lettuce (*Pistia stratiotes*).

Şentürk İ, Eyceyurt Divarç NS, Öztürk M.

2023

Int J Phytoremediation.

<https://pubmed.ncbi.nlm.nih.gov/35786212/>

This study was conducted to assess the phytoremediation potential of *Pistia stratiotes* for post-treatment of Ni(II) and Cr(III)-containing industrial wastewater effluents in

mono (synthetic wastewater) and bimetallic systems (real wastewater). Differences were seen in metal uptake, growth performance, and metal accumulation of the plants. In the monometallic system, the highest removal efficiency was calculated as 77.50% for Cr(III) and 70.79% for Ni(II) at 5 mg L⁻¹ concentration. At 1.25 mg L⁻¹ concentration, the bioconcentration factor of *P. stratiotes* was calculated as 734.2 for Ni(II) and 799.0 for Cr(III). To assess the effects of metal stress on plants, photosynthetic pigments and percent growth rates were also investigated. The percent growth rate increased from 38.22 to 81.74% for Ni and decreased from 87.53 to 43.18% for Cr(III) when the metal concentrations increased from 1.25 to 5 mg L⁻¹. Toxicity symptoms were less severe in plants exposed to low Ni concentrations. The greatest reduction in chlorophyll was observed at 5 mg L⁻¹ Ni concentration. *P. stratiotes* showed better performance in the monometallic system. It was concluded based on present findings that *P. stratiotes* could potentially be used for the post-treatment of wastewaters containing Ni and Cr. **Novelty Statement** Previous phytoremediation studies were mostly conducted only in either mono- or multi-metallic systems. In this study, mono- and bimetallic systems were assessed together and the feasibility of research findings on a large scale was investigated in detail. Present findings may also aid in the development of phyto-remedial strategies and the identification of Ni and Cr toxicity in macrophytes. *Pistia stratiotes* are already known for its incredible potential in removing metals and other contaminants from wastewater effluents. However, most studies only present data regarding the plant performance in laboratory studies (synthetic wastewater), while this study provides some important additional information on natural effluent conditions, which transform the presented data more interesting from a practical point of view.

Echinococcose

Primary Pelvic Hydatid Cyst Mimicking an Ovarian Neoplasm: a Diagnostic Dilemma.

Neethu PK, Nanda S, Mohapatra J.

Mar-2023

Indian J Surg Oncol.

<https://pubmed.ncbi.nlm.nih.gov/36891413/>

Primary giant splenic hydatid disease in a pregnant woman: case report.

Segura-Gago GP, Estela-Reynel R, Calisaya-Sánchez M, Flores-Rodríguez M.

Oct-Dec 2023

Rev Peru Med Exp Salud Publica.

<https://pubmed.ncbi.nlm.nih.gov/36888814/>

Hydatidosis is currently considered a public health problem in Peru. It is a parasitic infection transmitted by the ingestion of eggs of *Echinococcus granulosus*. The most involved organs are the liver and lungs, with spleen involvement being rare. We present the case of a young pregnant woman with abdominal pain and a sensation of

mass in the left hypochondrium. The ultrasound study revealed a multiloculated cystic image in the left hemiabdomen, and a viable fetus. She underwent cesarean section, followed by exploratory laparotomy, which revealed a giant spleen tumor that, according to the anatomopathological study, corresponded to multicystic splenic hydatid disease. Likewise, intrauterine growth restriction was found as a fetal complication. The patient progressed favorably without recurrence of hydatid foci and the neonate had an adequate growth pattern.

It's a small world for parasites: evidence supporting the North American invasion of European *Echinococcus multilocularis*.

Santa MA, Umhang G, Klein C, Grant DM, Ruckstuhl KE, Musiani M, Gilleard JS, Massolo A.

08-03-2023

Proc Biol Sci.

<https://pubmed.ncbi.nlm.nih.gov/36883278/>

Echinococcus multilocularis (*Em*), the causative agent of human alveolar echinococcosis (AE), is present in the Holarctic region, and several genetic variants seem to have differential infectivity and pathogenicity. An unprecedented outbreak of human AE cases in Western Canada infected with a European-like strain circulating in wild hosts warranted assessment of whether this strain was derived from a recent invasion or was endemic but undetected. Using nuclear and mitochondrial markers, we investigated the genetic diversity of *Em* in wild coyotes and red foxes from Western Canada, compared the genetic variants identified to global isolates and assessed their spatial distribution to infer possible invasion dynamics. Genetic variants from Western Canada were closely related to the original European clade, with lesser genetic diversity than that expected for a long-established strain and spatial genetic discontinuities within the study area, supporting the hypothesis of a relatively recent invasion with various founder events.

Giant Hydatid Cyst with Diaphragmatic, Pericardial, and Hepatic Involvement: Use of Extracorporeal Circulation for Major Liver Resection: A Case Report and Literature Review.

Galvis V, Rey Chaves CE, Conde D, Peláez M, Sabogal Olarte JC.

06-03-2023

Am J Case Rep.

<https://pubmed.ncbi.nlm.nih.gov/36876895/>

Differential Activity of Human Leukocyte Extract on Systemic Immune Response and Cyst Growth in Mice with *Echinococcus Multilocularis* Infection After Oral, Subcutaneous and Intraperitoneal Routes of Administration.

Ciglanová D, Jurčáková Z, Mudroňová D, Dvorožňáková E, Hřčková G.

30-12-2023

Helminthologia.

<https://pubmed.ncbi.nlm.nih.gov/36875680/>

Alveolar echinococcosis (AE) caused by the larval stage of *Echinococcus multilocularis* is serious parasitic diseases associated with the host's immunosuppression. The effects of human non-immune dialyzable leukocyte extract (DLE) on immune cells in blood and spleen and parasitic cysts weight in Balb/c mice after oral (PO), subcutaneous (SC) and intraperitoneal administration (IP) were compared. The reduction in cysts weight ($p < 0.01$) was recorded after PO route, whereas moderate reduction was found after SC and IP routes. The elevation of lymphoid populations in blood and spleen was found after PO administration ($p < 0.01$) in parallel with reduced myeloid population. Infection-elicited decline in B220+B cells was partially abolished by PO route, but DLE routes did not influence the CD3+ T cells. The proportions of CD3+CD4+Th lymphocytes were moderately upregulated, whereas CD3+CD8+Tc populations were reduced after all DLE routes ($p < 0.01$). PO administration increased CD11b+MHCII^{high} blood monocytes, CD11b-SigleF+ cell, but not CD11b+Si-glecF+ eosinophils in the blood, stimulated after SC and IP routes. DLE induced downregulation of NO production by LPS-stimulated adherent splenocytes *ex vivo*. Con A-triggered T lymphocyte proliferation was associated with the elevated IFN- γ production and transcription factor Tbet mRNA expression. The alleviation of Th2 (IL-4) and Treg (TGF- β) cytokine production by lymphocytes *ex vivo* paralleled with downregulation of gene transcription for cytokines, GATA and FoxP3. Reduction of myeloid cells with suppressive activity was found. The SC and IP routes affected partially the cysts weights, diminished significantly gene transcription, NO levels and Th2 and Treg cytokines production. Results showed that PO route of DLE administration was the most effective in ameliorating immunosuppression via stimulation of Th1 type, reducing Th2 and Treg type of immunity and CD3+CD8+Tc lymphocytes in the blood and spleens during *E. multilocularis* infection in mice.

Liver Hydatid Cyst Masquerading as a Liver Abscess.

Magacha HM, Vedantam V, Vedantam N, Jagadish A.

29-01-2023

Cureus.

<https://pubmed.ncbi.nlm.nih.gov/36865972/>

Hydatid cyst of the liver is a rare zoonotic disease in the United States. It is caused by *Echinococcus granulosus*. This disease is mainly seen among immigrants from countries where this parasite is endemic. Differential diagnoses of such lesions can include pyogenic or amebic abscesses, in addition to other benign or malignant lesions. We report the case of a 47-year-old woman who presented with symptoms of abdominal pain and was diagnosed with a hydatid cyst of the liver masquerading as a liver abscess. Microscopic and parasitological tests confirmed this diagnosis. The patient was treated and discharged without further complications during follow-up.

The pipeline for drugs for control and elimination of neglected tropical diseases: 1. Anti-infective drugs for regulatory registration.

Pfarr KM, Krome AK, Al-Obaidi I, Batchelor H, Vaillant M, Hoerauf A, Opoku NO, Kuesel AC.

01-03-2023

Parasit Vectors.

<https://pubmed.ncbi.nlm.nih.gov/36859332/>

Case Report: Amphotericin B and Mefloquine as a Salvage Treatment of Alveolar Echinococcosis

Jelicic K, Papic N, Viskovic K, Vince A.

30-01-2023

Am J Trop Med Hyg.

<https://pubmed.ncbi.nlm.nih.gov/36716742/>

Alveolar echinococcosis is an emerging zoonotic disease caused by the parasite *Echinococcus multilocularis*. Most patients are diagnosed at a late stage, when lifelong treatment with benzimidazoles is required to stop disease progression. However, for patients who do not tolerate benzimidazole therapy, there are no alternatives. Here, we present a patient with advanced alveolar echinococcosis who was successfully treated with amphotericin B deoxycholate and mefloquine as a rescue therapy after he developed albendazole intolerance.

Trématodoses d'origine alimentaire (clonorchiose, opisthorchiase, fasciolase et paragonimose)

The Importance of Antioxidant Enzymes and Oxidative Stress in Human Fascioliasis.

Taş Cengiz Z, Yılmaz H, Beyhan YE, Ekici A, Çiçek M, Aydemir S.

02-03-2023

Türkiye Parazitol Derg.

<https://pubmed.ncbi.nlm.nih.gov/36872484/>

Objective: The aim of this study was to determine the levels of superoxide dismutase (SOD), glutathione peroxidase (GPx), catalase (CAT), and malondialdehyde (MDA) in the patients infected with *Fasciola hepatica* and establish whether these parameters differ among the patients with fascioliasis. **Methods:** The patient group consisted of 140 individuals with *F. hepatica* seropositive; the control group consisted of 140 healthy individuals who tested negative for this parasite and had no other diseases. The patient group consisted of individuals with no chronic diseases other than fascioliasis; in both the patient and the control groups, the subjects had no unhealthy habits such as smoking and alcohol

consumption, etc. The blood samples taken to diagnose fascioliasis were evaluated by the ELISA method. The samples were studied according to the kit procedures for SOD, CAT, GPx and MDA markers. **Results:** In this study, 43.6% of 140 individuals in the patient group infected with *F. hepatica* had CAT ($p=0.001$), 35% had GPx ($p=0.001$), 12.9% had SOD ($p=0.002$), 90.7% had MDA ($p=0.001$). There was found a statistically significant difference between the patient and the control group in terms of the positivity of these four parameters. **Conclusion:** As a result, a statistically significant relationship was found between the increase in the SOD, GPx, CAT, and MDA levels and fascioliasis. The high rate of MDA revealed that oxidative stress occurred in patients with fascioliasis, resulting in an increased activity of SOD, GPx, and CAT.

Molecular Prevalence of Larval Stages of *Fasciola hepatica* in *Lymnaea stagnalis* Species Snails in the Vicinity of the Ağrı Province.

Ünlü AH, Yıldız R, Aydemir S, Ekici A.

02-03-2023

Türkiye Parazitol Derg.

<https://pubmed.ncbi.nlm.nih.gov/36872483/>

Global prevalence of 4 neglected foodborne trematodes targeted for control by WHO: A scoping review to highlight the gaps.

Tidman R, Kanankege KST, Bangert M, Abela-Ridder B.

02-03-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/36862635/>

The pipeline for drugs for control and elimination of neglected tropical diseases: 1. Anti-infective drugs for regulatory registration.

Pfarr KM, Krome AK, Al-Obaidi I, Batchelor H, Vaillant M, Hoerauf A, Opoku NO, Kuesel AC.

01-03-2023

Parasit Vectors.

<https://pubmed.ncbi.nlm.nih.gov/36859332/>

The World Health Organization 'Ending the neglect to attain the Sustainable Development Goals: A road map for neglected tropical diseases 2021-2030' outlines the targets for control and elimination of neglected tropical diseases (NTDs). New drugs are needed to achieve some of them. We are providing an overview of the pipeline for new anti-infective drugs for regulatory registration and steps to effective use for NTD control and elimination. Considering drugs approved for an NTD by at least one stringent regulatory authority: fexinidazole, included in WHO guidelines for *Trypanosoma brucei* gambiense African trypanosomiasis, is in development for Chagas disease. Moxidectin, registered in 2018 for treatment of individuals ≥ 12 years old with onchocerciasis, is undergoing studies to extend the indication to 4-11-year-old children and obtain additional data to inform WHO and endemic countries' decisions on moxidectin inclusion in guidelines and policies. Moxidectin is also being evaluated

for other NTDs. Considering drugs in at least Phase 2 clinical development, a submission is being prepared for registration of acoziborole as an oral treatment for first and second stage T.b. gambiense African trypanosomiasis. Bedaquiline, registered for tuberculosis, is being evaluated for multibacillary leprosy. Phase 2 studies of emodepside and flubentylol in *O. volvulus*-infected individuals are ongoing; studies for *Trichuris trichuria* and hookworm are planned. A trial of fosravuconazole in *Madurella mycetomatis*-infected patients is ongoing. JNJ-64281802 is undergoing Phase 2 trials for reducing dengue viral load. Studies are ongoing or planned to evaluate oxantel pamoate for onchocerciasis and soil-transmitted helminths, including *Trichuris*, and oxfendazole for onchocerciasis, *Fasciola hepatica*, *Taenia solium* cysticercosis, *Echinococcus granulosus* and soil-transmitted helminths, including *Trichuris*. Additional steps from first registration to effective use for NTD control and elimination include country registrations, possibly additional studies to inform WHO guidelines and country policies, and implementation research to address barriers to effective use of new drugs. Relative to the number of people suffering from NTDs, the pipeline is small. Close collaboration and exchange of experience among all stakeholders developing drugs for NTDs may increase the probability that the current pipeline will translate into new drugs effectively implemented in affected countries.

Differentiating paramphistome species in cattle using DNA barcoding coupled with high-resolution melting analysis (Bar-HRM).

Buddhachat K, Sriuan S, Nak-On S, Chontanarath T.

Mar-2023

Parasitol Res.

<https://pubmed.ncbi.nlm.nih.gov/36604333/>

Filariose lymphatique

A Case of Tropical Pulmonary Eosinophilia With Incomplete Response to Diethylcarbamazine Therapy.

Datta A, Chhotray P, Jena B, Sivasankar R.

29-01-2023

Cureus.

<https://pubmed.ncbi.nlm.nih.gov/36874679/>

Tropical pulmonary eosinophilia (TPE) is a specific pulmonary manifestation of lymphatic filariasis. There is overwhelming infiltration of eosinophils in the lung parenchyma in response to microfilaria. The characteristic features include paroxysmal respiratory symptoms, strikingly high blood eosinophil count, elevated level of immunoglobulin (Ig) E along with high titer of anti-filarial antibody. Treatment with diethylcarbamazine (DEC) has an excellent favorable response. However, recovery may often be incomplete. We present a case of a 36-year-old man with TPE who had complete symptomatic improvement after a three-week course of DEC, but only a partial response in radiological and pulmonary function abnormalities.

Pharmacoinformatics-based screening of active compounds from *Vitex negundo* against lymphatic filariasis by targeting asparaginyl-tRNA synthetase.

Kabilan SJ, Kunjiappan S, Sundar K, Pavadai P, Sathishkumar N, Velayuthaperumal H.

06-03-2023

J Mol Model.

<https://pubmed.ncbi.nlm.nih.gov/36872402/>

Context: Lymphatic filariasis, generally called as elephantiasis, is a vector-borne infectious disease caused by the filarial nematodes, mainly *Wuchereria bancrofti*, *Brugia malayi*, and *Brugia timori*, which are transmitted through mosquitoes. The infection affects the normal flow of lymph leading to abnormal enlargement of body parts, severe pain, permanent disability, and social stigma. Due to the development of resistance as well as toxic effects, existing medicines for lymphatic filariasis are becoming ineffective in killing the adult worms. It is essential to search novel filaricidal drugs with new molecular targets. Asparaginyl-tRNA synthetase (PDB ID: 2XGT) belongs to the group of aminoacyl-tRNA synthetases that catalyze specific attachment of amino acids to their tRNA during protein biosynthesis. Plants and their extracts are well-known medicinal practice for the management of several parasitic infectious diseases including filarial infections. **Methods:** In this study, asparaginyl-tRNA synthetase of *Brugia malayi* was used as a target to perform virtual screening of plant phytoconstituents of *Vitex negundo* from IMPPAT database, which exhibits anti-filarial and anti-helminthic properties. A total of sixty-eight compounds from *Vitex negundo* were docked against asparaginyl-tRNA synthetase using Autodock module of PyRx tool. Among the 68 compounds screened, 3 compounds, negundoside, myricetin, and nishindaside, exhibited a higher binding affinity compared to standard drugs. The pharmacokinetic and physicochemical prediction, stability of ligand-receptor complexes via molecular dynamics simulation, and density functionality theory were done further for the top-scored ligands with receptor.

Mycétome

Deforming vegetative nodules in a woman from Amazon.

Lobo LE, João FM, Frota MZM, Santos M.

25-01-2023

JAAD Case Rep.

<https://pubmed.ncbi.nlm.nih.gov/36876038/>

An unusual presentation of mycetoma around knee joint as a subcutaneous mass - A case report.

Singh B, Gehlot R, Saxena M, Bharwani N, Raichandani K, Bhati M.

Oct-2022

J Orthop Case Rep.

<https://pubmed.ncbi.nlm.nih.gov/36874900/>

Introduction: Mycetoma is a form of chronic granulomatous disease which involves subcutaneous tissues and causes bone destruction in advanced stages. The characteristic features are sinus formation, granules formation, and mass in subcutaneous region. **Case report:** A 19-year-old male presented to our out-patient clinic with complaint of a painless swelling around the medial aspect of the right knee joint for 8 months with no sinus or discharge of granules. *Pes anserinus* bursitis was thought of as differential diagnosis for the present condition. "Staging-classification of mycetoma" is commonly used for classifying mycetoma and as per classification, the present case had Stage-A. **Conclusion:** Single-stage local excision was performed and supplemented with anti-fungal agent for 6 months, which showed good outcome at the final follow-up of 13 months.

Onchocercose

Potential of *Onchocerca ochengi* inosine-5'-monophosphate dehydrogenase (IMPDH) and guanosine-5'-monophosphate oxidoreductase (GMPR) as druggable and vaccine candidates: immunoinformatics screening.

Gaiya DD, Muhammad A, Aimola IA, Udu SK, Balarabe SA, Auta R, Ekpa E, Sheyin A.

03-03-2023

J Biomol Struct Dyn.

<https://pubmed.ncbi.nlm.nih.gov/36866624/>

Geospatial distribution and predictive modeling of onchocerciasis in Ogun State, Nigeria.

Surakat OA, Babalola AS, Adeleke MA, Adeogun AO, Idowu OA, Sam-Wobo SO.

01-03-2023

PLoS One.

<https://pubmed.ncbi.nlm.nih.gov/36857325/>

Onchocerciasis caused by infection with *Onchocerca volvulus* is a disease of public health importance and is highly associated with disability. As Nigeria is aiming at eliminating onchocerciasis by 2030, there is a need to develop newer tools to map disease prevalence and identify environmental factors driving disease prevalence, even in places that have not been previously targeted for preventive chemotherapy. This study produced predictive risk-maps of onchocerciasis in Ogun State. Georeferenced onchocerciasis infection data obtained from a cross-sectional survey at 32 locations between March and July 2015 together with remotely-sensed environmental data were analyzed using Ecological Niche Models (ENM). A total of 107 field occurrence points for *O. volvulus* infection were recorded. A total of 43 positive occurrence points were used for modelling. ENMs were used to estimate the current geographic distribution of *O. volvulus* in Ogun State. Maximum Entropy distribution modeling (MaxEnt) was used for predicting the potential suitable habitats, using a portion of the occurrence records. A total of 19 environmental variables were used to model the

potential geographical distribution area under current climatic conditions. Empirical prevalence of 9.3% was recorded in this study. The geospatial distribution of infection revealed that all communities in Odeda Local Government Area (a peri-urban LGA) showed remarkably high prevalence compared with other LGAs. The predicted high-risk areas (probability > 0.8) of *O. volvulus* infection were all parts of Odeda, Abeokuta South, and Abeokuta North, southern part of Imeko-Afon, a large part of Yewa North, some parts of Ewekoro and Obafemi-Owode LGAs. The estimated prevalence for these regions were >60% (between 61% and 100%). As predicted, *O. volvulus* occurrence showed a positive association with variables reflecting precipitation in Ogun State. Our predictive risk-maps has provided useful information for the elimination of onchocerciasis, by identifying priority areas for delivery of intervention in Ogun State, Nigeria.

Genomic analysis, immunomodulation and deep phenotyping of patients with nodding syndrome.

Soldatos A, Nutman TB, Johnson T, Dowell SF, Sejvar JJ, Wilson MR, DeRisi JL, Inati SK, Groden C, Evans C, O'Connell EM, Toliva BO, Aceng JR, Aryek-Kwe J, Toro C, Stratakis CA, Buckler AG, Cantilena C, Palmore TN, Thurm A, Baker EH, Chang R, Fauni H, Adams D, Macnamara EF, Lau CC, Malicdan MCV, Pusey-Swerdzewski B, Downing R, Bunga S, Thomas JD, Gahl WA, Nath A.

01-03-2032

Brain.

<https://pubmed.ncbi.nlm.nih.gov/36181424/>

The aetiology of nodding syndrome remains unclear, and comprehensive genotyping and phenotyping data from patients remain sparse. Our objectives were to characterize the phenotype of patients with nodding syndrome, investigate potential contributors to disease aetiology, and evaluate response to immunotherapy. This cohort study investigated members of a single-family unit from Lamwo District, Uganda. The participants for this study were selected by the Ugandan Ministry of Health as representative for nodding syndrome and with a conducive family structure for genomic analyses. Of the eight family members who participated in the study at the National Institutes of Health (NIH) Clinical Center, three had nodding syndrome. The three affected patients were extensively evaluated with metagenomic sequencing for infectious pathogens, exome sequencing, spinal fluid immune analyses, neurometabolic and toxicology testing, continuous electroencephalography and neuroimaging. Five unaffected family members underwent a subset of testing for comparison. A distinctive interictal pattern of sleep-activated bursts of generalized and multifocal epileptiform discharges and slowing was observed in two patients. Brain imaging showed two patients had mild generalized cerebral atrophy, and both patients and unaffected family members had excessive metal deposition in the basal ganglia. Trace metal biochemical evaluation was normal. CSF was non-inflammatory and one patient had CSF-restricted oligoclonal bands. *Onchocerca volvulus*-specific antibodies were present in all patients and skin snips were negative for active

onchocerciasis. Metagenomic sequencing of serum and CSF revealed hepatitis B virus in the serum of one patient. Vitamin B6 metabolites were borderline low in all family members and CSF pyridoxine metabolites were normal. Mitochondrial DNA testing was normal. Exome sequencing did not identify potentially causal candidate gene variants. Nodding syndrome is characterized by a distinctive pattern of sleep-activated epileptiform activity. The associated growth stunting may be due to hypothalamic dysfunction. Extensive testing years after disease onset did not clarify a causal aetiology. A trial of immunomodulation (plasmapheresis in two patients and intravenous immunoglobulin in one patient) was given without short-term effect, but longer-term follow-up was not possible to fully assess any benefit of this intervention.

Schistosomiasis

Efficacy, safety, and palatability of arpraziquantel (L-praziquantel) orodispersible tablets in children aged 3 months to 6 years infected with *Schistosoma* in Côte d'Ivoire and Kenya: an open-label, partly randomised, phase 3 trial.

N'Goran EK, Odiere MR, Assandé Aka R, Ouattara M, Aka NAD, Ogutu B, Rawago F, Bagchus WM, Bödding M, Kourany-Lefoll E, Tappert A, Yin X, Bezuidenhout D, Badenhorst H, Huber E, Dälken B, Haj-Ali Saflo O.

06-03-2023

Lancet Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/36893784/>

Association between polymorphisms of IL4, IL13, IL10, STAT6 and IFNG genes, cytokines and immunoglobulin E levels with high burden of *Schistosoma mansoni* in children from schistosomiasis endemic areas of Cameroon.

Mewamba EM, Noyes H, Tiofack AAZ, Kanga RMN, Kamdem CN, Mengoue LET, Ofon E, Ngassam RIK, Nyangiri O, Bucheton B, Njiokou F, Womeni MH, Matovu E, MacLeod A, Simo G; TrypanoGEN+ research group of the H3Africa consortium.

06-03-2023

Infect Genet Evol.

<https://pubmed.ncbi.nlm.nih.gov/36889485/>

Eliminating schistosomiasis as a public health problem by 2030 requires a better understanding of the disease transmission, especially the asymmetric distribution of worm burden in individuals living and sharing the same environment. It is in this light that this study was designed to identify human genetic determinants associated with high burden of *S. mansoni* and also with the plasma concentrations of IgE and four cytokines in children from two schistosomiasis endemic areas of Cameroon. In school-aged children of schistosomiasis endemic areas of Makenene and Nom-Kandi of Cameroon, *S. mansoni* infections and their infection intensities were evaluated in

urine and stool samples using respectively the Point-of-care Circulating Cathodic Antigen test (POC-CCA) and the Kato Katz (KK) test. Thereafter, blood samples were collected in children harbouring high burden of schistosome infections as well as in their parents and siblings. DNA extracts and plasma were obtained from blood. Polymorphisms at 14 loci of five genes were assessed using PCR-restriction fragment length polymorphism and amplification-refractory mutation system. The ELISA test enabled to determine the plasma concentrations of IgE, IL-13, IL-10, IL-4 and IFN- γ . The prevalence of *S. mansoni* infections was significantly higher ($P < 0.0001$ for POC-CCA; $P = 0.001$ for KK) in Makenene (48.6% for POC-CCA and 7.9% for KK) compared to Nom-Kandi (31% for POC-CCA and 4.3% for KK). The infection intensities were also higher ($P < 0.0001$ for POC-CCA; $P = 0.001$ for KK) in children from Makenene than those from Nom-Kandi. The allele C of SNP rs3024974 of STAT6 was associated with an increased risk of bearing high burden of *S. mansoni* both in the additive ($p = 0.009$) and recessive model ($p = 0.01$) while the allele C of SNP rs1800871 of IL10 was protective ($p = 0.0009$) against high burden of *S. mansoni*. The alleles A of SNP rs2069739 of IL13 and G of SNP rs2243283 of IL4 were associated with an increased risk of having low plasma concentrations of IL-13 ($P = 0.04$) and IL-10 ($P = 0.04$), respectively. This study showed that host genetic polymorphisms may influence the outcome (high or low worm burden) of *S. mansoni* infections and also the plasma concentrations of some cytokines.

Schistosoma mansoni infection alters the host pre-vaccination environment resulting in blunted Hepatitis B vaccination immune responses.

Muir R, Metcalf T, Fourati S, Bartsch Y, Lugemwa JK, Canderan G, Alter G, Muyanja E, Okech B, Namatovu T, Namara I, Namuniina A, Ssetaala A, Mpendo J, Nanvubya A, Kitandwe PK, Bagaya BS, Kiwanuka N, Nassuna J, Biribawa VM, Elliott AM, de Dood CJ, Senyonga W, Balungi P, Kaleebu P, Mayanja Y, Odongo M, Fast P, Price MA, Corstjens PLAM, van Dam GJ, Kamali A, Sekaly RP, Haddad EK.

26-02-2023

medRxiv.

<https://pubmed.ncbi.nlm.nih.gov/36865336/>

Visual diagnosis of female genital schistosomiasis in Zambian women from hand-held colposcopy: agreement of expert image review.

Sturt A, Bristowe H, Webb E, Hansingo I, Phiri C, Mudenda M, Mapani J, Mweene T, Levecke B, Cools P, van Dam G, Corstjens P, Ayles H, Hayes R, Francis S, van Lieshout L, Vwalika B, Kjetland E, Bustinduy A.

10-01-2023

Wellcome Open Res.

<https://pubmed.ncbi.nlm.nih.gov/36864924/>

Female genital schistosomiasis (FGS) can occur in *S. haematobium* infection and is caused by parasite egg deposition in the genital tract. Confirming a diagnosis of

FGS is challenging due to the lack of a diagnostic reference standard. A 2010 expert-led consensus meeting proposed visual inspection of the cervicovaginal mucosa as an adequate reference standard for FGS diagnosis. The agreement of expert human reviewers for visual-FGS has not been previously described. Methods: In two Zambian communities, non-menstruating, non-pregnant, sexually-active women aged 18-31 years participating in the HPTN 071 (PopART) Population-Cohort were enrolled in a cross-sectional study. Self-collected genital swabs and a urine specimen were collected at a home visit; trained midwives performed CVL and hand-held colposcopy at a clinic visit. *S. haematobium* eggs and circulating anodic antigen (CAA) were detected from urine. Two expert reviewers independently diagnosed visual-FGS as the presence of sandy patches, rubbery papules or abnormal blood vessels in digital cervicovaginal images obtained by hand-held colposcopy. PCR-FGS was defined as *Schistosoma* DNA detected by real-time PCR in any genital specimen (CVL or genital swab). Results: Of 527 women with cervicovaginal colposcopic images, 468/527 (88.8%) were deemed interpretable by Reviewer 1 and 417/527 (79.1%) by Reviewer 2. Visual-FGS was detected in 35.3% (165/468) of participants by expert review of colposcopic images by Reviewer 1 and in 63.6% (265/417) by Reviewer 2. Cohen's kappa statistic for agreement between the two expert reviewers was 0.16, corresponding to "slight" agreement. The reviewers made concordant diagnoses in 38.7% (204/527) participants (100 negative, 104 positive) and discordant diagnoses in 31.8% (168/527) participants. **Conclusions:** The unexpectedly low level of correlation between expert reviewers highlights the imperfect nature of visual diagnosis for FGS based on cervicovaginal images obtained with a hand-held colposcope. This finding is a call to action for improved point-of-care diagnostics for female genital schistosomiasis.

Diagnostic performances of Schistosoma haematobium and Schistosoma mansoni recombinant proteins, peptides and chimeric proteins antibody based tests. Systematic scoping review.

Vengesai A, Muleya V, Midzi H, Tinago TV, Chipako I, Manuwa M, Naicker T, Mduluzi T.

02-03-2023

PLoS One

<https://pubmed.ncbi.nlm.nih.gov/36862712/>

The Idiosyncratic Efficacy of Spironolactone-Loaded PLGA Nanoparticles Against Murine Intestinal Schistosomiasis.

Abd El Hady WE, El-Emam GA, Saleh NE, Hamouda MM, Motawea A.

22-02-2032

Int J Nanomedicine.

<https://pubmed.ncbi.nlm.nih.gov/36860210/>

Background: Schistosomiasis is a chronic debilitating parasitic disease accompanied with severe mortality rates. Although praziquantel (PZQ) acts as the sole drug for the management of this disease, it has many limitations that

restrict the use of this treatment approach. Repurposing of spironolactone (SPL) and nanomedicine represents a promising approach to improve anti-schistosomal therapy. We have developed SPL-loaded poly(lactic-co-glycolic acid) (PLGA) nanoparticles (NPs) to enhance the solubility, efficacy, and drug delivery and hence decrease the frequency of administration, which is of great clinical value. **Methods:** The physico-chemical assessment was performed starting with particle size analysis and confirmed using TEM, FT-IR, DSC, and XRD. The antischistosomal effect of the SPL-loaded PLGA NPs against *Schistosoma mansoni* (*S. mansoni*)-induced infection in mice was also estimated. **Results:** Our results manifested that the optimized prepared NPs had particle size of 238.00 ± 7.21 nm, and the zeta potential was -19.66 ± 0.98 nm, effective encapsulation $90.43 \pm 8.81\%$. Other physico-chemical features emphasized that nanoparticles were completely encapsulated inside the polymer matrix. The in vitro dissolution studies revealed that SPL-loaded PLGA NPs showed sustained biphasic release pattern and followed Korsmeyer-Peppas kinetics corresponding to Fickian diffusion ($n < 0.45$). The used regimen was efficient against *S. mansoni* infection and induced significant reduction in spleen, liver indices, and total worm count ($p < 0.05$). Besides, when targeting the adult stages, it induced decline in the hepatic egg load and the small intestinal egg load by 57.75% and 54.17%, respectively, when compared to the control group. SPL-loaded PLGA NPs caused extensive damage to adult worms on tegument and suckers, leading to the death of the parasites in less time, plus marked improvement in liver pathology. **Conclusion:** Collectively, these findings provided proof-of-evidence that the developed SPL-loaded PLGA NPs could be potentially used as a promising candidate for new antischistosomal drug development.

Impact of the COVID-19 pandemic on the actions of the Schistosomiasis Control Program in an endemic area in Northeastern Brazil.

Dantas NM, Andrade LA, Paz WSD, Borges WN, Barbosa VGB, Hora DPGD, Silva CED, do Carmo RF, Souza CDF, Santos ADD, Wanderley FS, Negrão-Corrêa DA, Fujiwara RT, Bezerra-Santos M, Porto WJN.

Apr-2023

Acta Trop.

<https://pubmed.ncbi.nlm.nih.gov/36781094/>

Schistosomiasis remains a serious public health concern in Brazil and the Schistosomiasis Control Program (PCE) was elaborated to assist in the control of the disease. Nevertheless, the irruption of the COVID-19 pandemic may have impacted the program. Herein, we assessed the impact of the pandemic on PCE actions in an endemic area in the region with the highest positivity rate for schistosomiasis in Brazil. We conducted an ecological, population-based study using data from the PCE of the state of Alagoas, between 2015 and 2021, to calculate the percentage of change. The temporal trend analysis was performed using the segmented log-linear regression model. To evaluate the spatial distribution of the data, choropleth maps were made showing the values of the % of change. Moran maps were elaborated to indicate the

critical areas. Our analysis showed a decrease in the population surveyed in 2020 (-41.00%) and 2021 (-18.42%). Likewise, there was a reduction in the number of Kato-Katz tests performed (2020 = -43.45%; and in 2021 = -19.63%) and, consequently, a drop in the rate of positive tests (-37.98% in 2020 and -26.14% in 2021). Importantly, treatment of positive cases was lower than 80% (77.44% in 2020 and 77.38% in 2021). Additionally, spatial clusters with negative percentage values of up to -100% of the PCE indicators were identified mostly in the municipalities of the coastal areas that are historically most affected by schistosomiasis. Taken together, our analyzes corroborate that PCE actions in endemic municipalities of Alagoas were impacted by the COVID-19 pandemic.

Time series analysis of tegument ultrastructure of in vitro transformed miracidium to mother sporocyst of the human parasite Schistosoma mansoni.

Poteaux P, Gourbal B, Duval D.

Apr-2023

Acta Trop.

<https://pubmed.ncbi.nlm.nih.gov/36681315/>

Experimental water hyacinth invasion and destructive management increase human schistosome transmission potential.

Desautels DJ, Hartman RB, Weber ME, Jacob N, Sun A, Civitello DJ.

Mar-2023

Ecol Appl.

<https://pubmed.ncbi.nlm.nih.gov/36268601/>

Invasive species cause environmental degradation, decrease biodiversity, and alter ecosystem function. Invasions can also drive changes in vector-borne and zoonotic diseases by altering important traits of wildlife hosts or disease vectors. Managing invasive species can restore biodiversity and ecosystem function, but it may have cascading effects on hosts, parasites, and human risk of infection. Water hyacinth, *Eichhornia crassipes*, is an extremely detrimental invader in many sites of human schistosome transmission, especially in Lake Victoria, where hyacinth is correlated with high snail abundance and hotspots of human schistosome infection. Hyacinth is often managed via removal or in situ destruction, but the effects of these strategies on snail intermediate hosts and schistosomes are not known. We evaluated the effects of water hyacinth invasion and these management strategies on the dynamics of human schistosomes, *Schistosoma mansoni*, and snails, *Biomphalaria glabrata*, in experimental mesocosms over 17 weeks. We hypothesized that hyacinth, which is inedible to snails, would affect snail growth, reproduction, and cercariae production through the balance of its competitive effects on edible algae and its production of edible detritus. We predicted that destruction would create a pulse of edible detrital resources, thereby increasing snail growth, reproduction, and parasite production. Conversely, we predicted that removal would have small or negligible effects on snails and schistosomes, because it would

alleviate competition on edible algae without generating a resource pulse. We found that hyacinth invasion suppressed algae, changed the timing of peak snail abundance, and increased total production of human-infectious cercariae ~6-fold relative to uninvaded controls. Hyacinth management had complex effects on algae, snails, and schistosomes. Removal increased algal growth and snail abundance (but not biomass), and slightly reduced schistosome production. In contrast, destruction increased snail biomass (but not abundance), indicating increases in body size. Destruction caused the greatest schistosome production (10-fold more than the control), consistent with evidence that larger snails with greater access to food are most infectious. Our results highlight the dynamic effects of invasion and management on a globally impactful human parasite and its intermediate host. Ultimately, preventing or removing hyacinth invasions would simultaneously benefit human and environmental health outcomes.

Helminthiasis transmitted by soil (ascariasis, trichuriasis, ankylostomiasis)

Comparative transcriptomics from intestinal cells of permissive and non-permissive hosts during *Ancylostoma ceylanicum* infection reveals unique signatures of protection and host specificity.

Langeland A, Grill E, Shetty AC, O'Halloran DM, Hawdon JM.

08-03-2023

Parasitology.

<https://pubmed.ncbi.nlm.nih.gov/36883013/>

Soil-transmitted helminth infection among school-age children in Ogoja, Nigeria: implication for control.

Imalele EE, Braide EI, Emanghe UE, Effanga EO, Usang AU.

08-03-2023

Parasitol Res.

<https://pubmed.ncbi.nlm.nih.gov/36882536/>

The study aimed at assessing the prevalence and risk factors of soil-transmitted helminthiasis among school-aged children in Ogoja Local Government Area, Cross River State. Fecal samples were collected from 504 participants and analyzed using the Kato-Katz technique and modified Baermann technique for identifying larvae of *Strongyloides*. A total of 232 (46.0%) samples were positive for soil-transmitted helminths. The overall prevalence of *Ascaris lumbricoides*, hookworm, *Trichuris trichiura*, and *Strongyloides stercoralis* were 14.1%, 16.5%, 2.6%, and 12.9% respectively. The prevalence of infections were higher among males (46.6%) than females (45.4%). Overall, parasitic infection was higher in the 5-7-year age group (65.6%) than in the other age groups ($p = 0.000$).

Infection intensities of *A. lumbricoides* (84.00 EPG) ($p = 0.044$) and *T. trichiura* (96.00 EPG) ($p = 0.041$) were higher in school-age children aged 14-16 years. *A. lumbricoides* and hookworm co-infection (8.7%) was the most common mixed infection and was significantly higher in males than females. School-aged children who did not have prior knowledge about soil-transmitted helminth infections, the habit of drinking water without boiling, open defecation, use of pit latrine, and children who did not have toilet facilities in school were significantly associated with soil-transmitted helminthiasis. There was a significant relationship between washing hands after using the toilet, the habit of putting on footwear outside the house, and soil-transmitted helminth infection. In addition to preventive chemotherapy, control measures should focus on health education, providing clean drinking water, proper disposal of human excreta and sewage, and environmental hygiene.

Advantages and Limitations of Microscopy and Molecular Detections for Diagnosis of Soil-transmitted Helminths: An Overview.

Miswan N, Singham GV, Othman N.

30-12-2023

Helminthologia.

<https://pubmed.ncbi.nlm.nih.gov/36875683/>

World Health Organization (WHO) reported that over 1.5 billion people are infected by soil-transmitted helminths (STH) worldwide in sub-Saharan Africa, the United States of America, China, and East Asia. Heavy infections and polyparasitism are associated with higher morbidity rates, and the patients are exposed to increased vulnerability to other diseases. Therefore, accurate diagnosis followed by mass treatment for morbidity control is necessary. STH diagnosis commonly involves the microscopic observation of the presence of the STH eggs and larvae in the faecal samples. Furthermore, molecular approaches are increasingly utilised in monitoring and surveillance as they show higher sensitivity. Their capability to differentiate hookworm species is an advantage over the Kato-Katz technique. This review discusses the advantages and limitations of microscopy and various molecular tools used for STH detection.

Perceptions and practices of urban slum-dwelling women concerning soil-transmitted helminths infections in Bangladesh: A cross-sectional study.

Mukutmoni M, Liza FT, Parvin RA, Nath TC.

17-02-2023

Parasite Epidemiol Control.

<https://pubmed.ncbi.nlm.nih.gov/36875174/>

Red palm olein-enriched biscuit supplementation lowers *Ascaris lumbricoides* reinfection at 6-month after anthelmintic treatment among schoolchildren with vitamin A deficiency (VAD).

Tan PY, Loganathan R, Teng KT, Lee SC, Mohd Johari SN, Selvaduray KR, Ngui R, Lim YA.

Apr-2023

Acta Trop.

<https://pubmed.ncbi.nlm.nih.gov/36775004/>

Gale

Crusted Hyperkeratotic Scabies: A Case Report.

Meraz Soto JM, Alvarado Motte RA, Ramírez Carrillo P, Meraz Soto AA, Bayón Villaseñor V, Cheirif Wolosky O.

01-02-2023

Cureus.

<https://pubmed.ncbi.nlm.nih.gov/36879685/>

Crusted scabies is a rare form of classic scabies characterized by severe symptoms, mainly observed in immunosuppressed patients. This disease has been associated with a variety of health problems, such as delayed diagnosis, infection risk, and high mortality, mainly from sepsis. We report the case of a patient with hyperkeratotic scabies in the context of immunosuppression associated with malnutrition and the use of topical corticosteroids. Ivermectin is critical for successfully treating crusted scabies. However, a higher cure rate has been reported with the combination of oral ivermectin and topical permethrin. In our study, we chose to use a plan suitable for grade two scabies, resulting in a subtotal regression of the lesions. Crusted scabies is a highly contagious parasitic cutaneous disease, and there are few reports in the national and international literature. It is necessary to suspect this presentation form in order to establish a timely diagnosis and detect and treat associated comorbidities.

Oral ivermectin treatment for an infant with crusted scabies.

Bourkas AN, Pope E.

06-03-2023

CMAJ.

<https://pubmed.ncbi.nlm.nih.gov/36878546/>

Commentary: Transcriptome analysis of host inflammatory responses to the ectoparasitic mite *Sarcoptes scabiei* var. *hominis*.

Mounsey KE.

15-02-2023

Front Immunol.

<https://pubmed.ncbi.nlm.nih.gov/36875118/>

Sight the Mite: A Meta-Analysis on the Diagnosis of Scabies.

Shoukat Q, Rizvi A, Wahood W, Coetzee S, Wrench A.

30-01-2023

Cureus.

<https://pubmed.ncbi.nlm.nih.gov/36874720/>

[Modern research progress in external application of traditional Chinese medicine to acupoints].

Zhu WF, Wang YQ, Wu WT, Li Z, Liu LL, Guan ZY, Chen LH, Guan YM.

Feb-2023

Zhongguo Zhong Yao Za Zhi.

<https://pubmed.ncbi.nlm.nih.gov/36872220/>

Traditional Chinese medicine (TCM) has a long history and abundant experience in external therapy, which marks human wisdom. In the early history of human, people found that fumigation, coating, and sticking of some tree branches and herb stems can help alleviate scabies and remove parasites in productive labor, which indicates the emergence of external therapy. Pathogen usually enters the body through the surface, so external therapy can be used to treat the disease. External therapy is among the major characteristic of surgery of TCM. As one of the external therapies in TCM, external application to acupoints smooths the zang-fu organs through meridians and collaterals, thereby harmonizing yin and yang. This therapy emerged in the early society, formed the Spring and Autumn Period and the Warring States Period, improved in the Song and Ming dynasties, and matured in the Qing dynasty. With the efforts of experts in history, it has had a mature theory. According to modern research, it can avoid the first-pass effect of liver and the gastrointestinal irritation and improve the bioavailability of Chinese medicine. Based on the effect of Chinese medicine and the theory of meridian and collateral, it can stimulate the acupoints, exert regulatory effect on acupoints, and give full play to the efficacy of TCM and the interaction of the two. Thereby, it can regulate qi and blood and balance yin and yang, thus being widely used in the treatment of diseases. In this paper, the use of external application to acupoints, the effect on skin immunity, the regulation of neuro-inflammatory mechanism, the relationship between acupoint application and human circulation network, and the development of its dosage form were summarized through literature review. On this basis, this study is expected to lay a foundation for further research.

Severe Scabies: A French Multi-centre Study Involving 95 Patients with Crusted and Profuse Disease and Review of the Literature.

Skayem C, Majda A, Gary C, Hemery F, Mahé E, Caux F, Dupin N, Senet P, Greder-Belan A, Hillion B, Meni C, Saiag P, Bellaud G, Bleibtreu A, Lariven S, Bollens D, Descamps V, Molina JM, Bouchaud O, Vittecoq D, Do-Pham G, Foulet F, Botterel F, Chosidow O, Bernigaud C.

02-03-2023

Acta Derm Venereol.

<https://pubmed.ncbi.nlm.nih.gov/36861856/>

Beliefs, attitudes and practices towards scabies in central Ghana.

Amoako YA, van Rietschoten LS, Oppong MN, Amoako KO, Abass KM, Anim BA, Laryea DO, Phillips RO, Stienstra Y.

22-02-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/36812249/>

Oral ivermectin to treat scabies: a comparison of two different regimens.

Balestri R, Magnano M, Infusino SD, Girardelli CR, Ioris T, Rech G.

01-03-2023

Clin Exp Dermatol.

<https://pubmed.ncbi.nlm.nih.gov/36702573/>

As *Sarcoptes scabiei* is becoming less sensitive to permethrin, clinicians have started to prescribe oral ivermectin (OI) as a first-line treatment. Guidelines suggest OI 200 µg kg⁻¹ as two doses, 1 week apart. However, the black box of the ivermectin registered in Italy recommends a single dose. To compare these two regimens, we collected 71 cases of scabies and treated them according to this protocol [single-dose group (SDG)]. This population was compared to 68 patients who received two doses 1 week apart [double-dose group (DDG)]. Clearance of the disease was achieved in 98% of DDG patients. In the SDG, treatment was successful in only 58% of patients. This study confirms that the absence of a second intake of OI is one of the main predictors of treatment failure ($P < 0.001$), which may also increase the likelihood of emerging resistance in *S. scabiei*.

Morsures de serpent

Protein-protein interaction of LDH and CRP-1 with hematoxin snake venom proteins of all species of snake: An in silico approach.

Honutagi RM, Sunil R, Patil SM, Bhosale S, Das SN, Parvatikar PP, Das KK.

Mar-Apr 2023

Int J Health Sci (Qassim).

<https://pubmed.ncbi.nlm.nih.gov/36891039/>

Epidemiology of secondary infection after snakebites in center-west Brazil.

Soares Coriolano Coutinho JV, Fraga Guimarães T, Borges Valente B, Gomes Martins de Moura Tomich L.

06-03-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/36877732/>

Background: Snakebites represent a significant health problem in tropical countries, with an annual incidence of 2.7 million cases worldwide. The incidence of secondary infections after snake bites is also high and is usually caused by bacteria from the oral cavity of snakes. *Morganella morganii* has been identified as an important cause of infections and has been guiding antibiotic therapy in several regions of Brazil and the world.

Methodology/principal findings: We performed a retrospective cross-sectional evaluation of snakebites in hospitalized patients between January 2018 and November 2019 and selected those with secondary

infection in their medical records. During the period, 326 cases of snakebites were treated, and 155 (47.5%) of them eventually had secondary infections. However, only seven patients underwent culture of soft tissue fragments, in which three cases were negative culture results, while *Aeromonas hydrophila* was identified in four cases. Of these, 75% were resistant to ampicillin/sulbactam, 50% had intermediate sensitivity to imipenem, and 25% had intermediate sensitivity to piperacillin/tazobactam. Trimethoprim/sulfamethoxazole (TMP-SMX) was not tested on any strain. Of the 155 cases that progressed to secondary infections, 48.4% (75) were empirically treated with amoxicillin/clavulanate, 41.9% (65) with TMP-SMX, and 32 (22%) of these 144 cases required a change to a second regimen, and 10 of these 32 patients required a third therapeutic regimen. **Conclusion:** Wild animals act as reservoirs of resistant bacteria because their oral cavity favors biofilm formation, which explains the finding of *A. hydrophila* with a reduced sensitivity profile in this study. This fact is essential for the appropriate choice of empirical antibiotic therapy.

Bite-to-needle Time - An Extrapolative Indicator of Repercussion in Patients with Snakebite.

Jayaraman T, Dhanasinghu R, Kuppusamy S, Gaur A, Sakthivadivel V.

Nov-2022

Indian J Crit Care Med.

<https://pubmed.ncbi.nlm.nih.gov/36873588/>

Phenotypic, functional and plasticity features of human PBMCs induced by venom secreted PLA₂s.

Lopes JA, Boeno CN, Paloschi MV, Silva MDS, Rego CMA, Pires WL, Santana HM, Chaves YO, Rodrigues MMS, Lima AM, Setúbal SDS, Soares AM, Zuliani JP.

Mar-2023

Mol Immunol.

<https://pubmed.ncbi.nlm.nih.gov/36812762/>

Bothrops venom contains a high amount of secreted phospholipase A₂ (sPLA₂s) enzymes responsible for the inflammatory reaction and activation of leukocytes in cases of envenoming. PLA₂s are proteins that have enzymatic activity and can hydrolyze phospholipids at the sn-2 position, thereby releasing fatty acids and lysophospholipids precursors of eicosanoids, which are significant mediators of inflammatory conditions. Whether these enzymes have a role in the activation and function of peripheral blood mononuclear cells (PBMCs) is not known. Here we show for the first time how two secreted PLA₂s (BthTX-I and BthTX-II) isolated from the venom of *Bothrops jararacussu* affect the function and polarization of PBMCs. Neither BthTX-I nor BthTX-II exhibited significant cytotoxicity to isolated PBMCs compared with the control at any of the time points studied. RT-qPCR and enzyme-linked immunosorbent assays were used to determine changes in gene expression and the release of pro-inflammatory (TNF-α, IL-6, and IL-12) and anti-inflammatory (TGF-β and IL-10) cytokines, respectively, during the cell differentiation process. Lipid

droplets formation and phagocytosis were also investigated. Monocytes/macrophages were labeled with anti-CD14, -CD163, and -CD206 antibodies to assay cell polarization. Both toxins caused a heterogeneous morphology (M1 and M2) on days 1 and 7 based on immunofluorescence analysis, revealing the considerable flexibility of these cells even in the presence of typical polarization stimuli. Thus, these findings indicate that the two sPLA₂s trigger both immune response profiles in PBMCs indicating a significant degree of cell plasticity, which may be crucial for understanding the consequences of snake envenoming.

The use of serum protein analysis in the diagnosis of fatal envenomation via *Crotalus horridus* (timber rattlesnake).

Gallagher T, Roberts S, Silva-Sanchez C, Sutton L, Laventure K.

Mar-2023

J Forensic Sci.

<https://pubmed.ncbi.nlm.nih.gov/36715131/>

Deaths occurring due to rattlesnake envenomization are extremely rare and must be thoroughly investigated in the same manner as any other type of death. Our research presents the case of an adult white male who suffered a fatal timber rattlesnake (*Crotalus horridus*) envenomation in northwest Florida in 2018. Blood samples were taken from the decedent's heart and vasculature of the chest and sent for serum proteomic analysis. Serum proteomic analysis was utilized in order to identify proteins from timber rattlesnake (*C. horridus*) found within the victim's blood. The confirmation of the presence of timber rattlesnake venom within the victim's blood allows the forensic pathologist to determine the cause of death most accurately and likewise, assists with the manner of death determination. Blood samples were separated into two groups: one with the abundant endogenous proteins depleted to facilitate detection of lower abundant proteins and one undepleted. In the depleted sample, a total of 712 proteins were identified, with 47 of the proteins (6.6%) occurring originating from timber rattlesnake (*C. horridus*). Likewise, a total of 742 proteins were identified in the undepleted sample, with 52 of the proteins (7.0%) occurring in timber rattlesnake (*C. horridus*). No timber rattlesnake (*C. horridus*) proteins were found in control human serum.

Hemodynamic impairment induced by Crotoxin using in vivo and ex vivo approach in a rat model.

Sartim MA, Nogueira RC, Cavalcante TTA, Sousa LO, Monteiro WM, Cintra ACO, Neto-Neves EM, Sampaio SV.

31-03-2032

Int J Biol Macromol.

<https://pubmed.ncbi.nlm.nih.gov/36709813/>

Attitudes, knowledge and practices of traditional snakebite healers in Nepal: implications for prevention and control of snakebite.

Pandey DP, Subedi Pandey G, Sapkota S, Dangol DR, Devkota NR.

01-03-2022

Trans R Soc Trop Med Hyg.

<https://pubmed.ncbi.nlm.nih.gov/36366978/>

Background: Traditional healers are a valuable source of information about community-level treatment of snakebite. Snakebite victims in Nepal depend on traditional healers for treatment, but their practices have not been well-documented. **Methods:** This was a cross-sectional study of 50 traditional snakebite healers (TSHs) who were selected using a snowball sampling method representing eight districts and four provinces of Nepal. Data were collected using face-to-face-interviews and semi-structured questionnaires. **Results:** About half of the respondents liked to gain knowledge on modern care for snakebite management and nearly all respondents (94%) wished to cooperate closely with the local healthcare system to support snakebite management. People's ingrained faith in traditional healing of snakebite (84%), unaffordable modern care of snakebite (60%) and wishes for early treatment of snakebites (44-48%) were the main causes of their dependency on TSHs. *Rauvolfia serpentina*, *Piper nigrum*, *Momordica charantia* and *Tinospora cordifolia* were commonly used plants in traditional treatment of snakebite. **Conclusions:** Easily accessible and affordable healthcare facilities provided by TSHs, public beliefs in traditional healing and inadequate knowledge of antivenom therapy caused dependency on TSHs. The introduction of snakebite treatment centres in snakebite-prone regions and educational interventions are essential to minimize this kind of dependency and associated deaths and disabilities.

The Amazonian Tropical Bites Research Initiative, a hope for resolving zoonotic neglected tropical diseases in the One Health era.

Taylor E, Aguilar-Ancori EG, Banyard AC, Abel I, Mantini-Briggs C, Briggs CL, Carrillo C, Gavidia CM, Castillo-Neyra R, Parola AD, Villena FE, Prada JM, Petersen BW, Falcon Perez N, Cabezas Sanchez C, Sihuincha M, Streicker DG, Maguina Vargas C, Navarro Vela AM, Vigilato MAN, Wen Fan H, Willoughby R, Horton DL, Recuenco SE.

01-03-2023

Int Health.

<https://pubmed.ncbi.nlm.nih.gov/35896028/>