



Réseau MTN Francophone

Veille scientifique Maladies tropicales négligées

Semaine 26

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DENGUE, CHIKUNGUNYA ET MALADIE A VIRUS ZIKA

Clinical Profile and Lab Findings of Dengue Fever in Children Admitted in a Tertiary Care Hospital.

Mutanabbi, M., Shova, S., Kibtiar, M., Mosleh, T.

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Mymensingh Med J

<https://pubmed.ncbi.nlm.nih.gov/35780359>

Dengue is an arboviral infection dengue virus (DENV 1-4) transmitted by Aedes mosquito. It shows a wide range of clinical presentation from asymptomatic cases to undifferentiated fever, dengue hemorrhagic fever (DHF) or dengue shock syndrome (DSS) or non-severe and severe dengue. Most cases of dengue are self-limiting; however, severe dengue has high mortality if not diagnosed and managed early during the disease. Dengue virus (DENV) infection is a serious global public health challenge resulting approximately 200 million cases of morbidity and 50,000 cases of mortality annually. Management is based on clinical and lab parameters with certain lab tests aiding in the early forecast of severe dengue. While serological tests (detection of nonstructural protein 1 [NS1] antigen, immunoglobulin IgM and IgG antibodies aid in diagnosis of dengue, simple, cost-effective, easy tests such as hematocrit and platelet counts have great utility in resource-poor healthcare systems for predicting onset of severe dengue. To determine the clinical profile and lab findings of different varieties of Dengue fever in children admitted in a tertiary care hospital. This retrospective observational study was designed to collect data from the medical records of children of both sexes, aged up to 12 years old. The study was conducted from April 2019 to September 2019 in pediatrics department of BSMMU, Dhaka. A total of 50 children who were admitted with the complaints of fever and were found positive for either NS1 antigen or dengue IgM or IgG antibodies were included in the study. Patients with chronic diseases or any concurrent infections were excluded. Samples were collected from hospital record and kept in a separate management system only for dengue patients. The demographics, clinical and laboratory findings were recorded via structured data collection sheet. Among 50 cases, 22 were dengue fever, 17 were dengue hemorrhagic fever and 11 were dengue shock syndrome. The mean age of study participant was 6.95. Out of 50 patients, Male 62.0% were predominant over the female 38.0% and majority 74.0% came from urban area. Fever (95.5%) was mostly the presenting feature in dengue fever. Bleeding (29.4%) and tourniquet test positive (47.0%) were most in DHF. Hypotension (90.0%), tachycardia (90.9%), edema (18.2%), shock (90.9%) and hepatomegaly (72.7%) were mostly present in DSS. Neutropenia (72.7%) was significant in DSS. Platelet count (32,588.24±22,335.67) was significantly low in DHF. Albumin count (27.82±5.25) and TCO2 (18.27±1.8) were significantly low in DSS. Statistical analysis was done by Kuskalwallis test for categorical data analysis and one way ANOVA test for comparison of continuous data. P value <0.05

is considered as significant. This time it was seen that bleeding, tourniquet test positivity with low platelet count is seen in DHF. But DSS was marked by hepatomegaly and hypalbuminaemia.

A fatal case of dengue hemorrhagic fever associated with dengue virus 4 (DENV-4) in Brazil: genomic and histopathological findings.

Cunha, M., de Moura Coletti, T., Guerra, J., Ponce, C., Fernandes, N., Rézio, R., Claro, I., Salles, F., Lima Neto, D., Sabino, E.

02-07-2022

Braz J Microbiol

<https://doi.org/10.1007/s42770-022-00784-4>

Dengue infection is the most prevalent arthropod-borne viral disease in subtropical and tropical regions, whose primary vector is Aedes aegypti mosquitoes. The mechanisms of dengue virus (DENV) pathogenesis are little understood because we have no good disease models. Only humans develop symptoms (dengue fever, DF, or dengue hemorrhagic fever, DHF) and research has been limited to studies involving patients. Samples from serum, brain, cerebellum, heart, lungs, liver, and kidneys from a 13-year-old male patient that died with hemorrhagic manifestations were sent for differential diagnosis at Adolfo Lutz, using both classical virological methods (RT-qPCR, virus isolation, ELISA, and hemagglutination inhibition test) and immunohistochemistry (IHQ). A DENV serotype 4 was detected by a DENV multiplex RT-qPCR, and the C6/36 cell supernatant was used for NGS using Minion. Lesions were described in the heart, liver, lung, and kidney with positive IHQ in endothelial cells of the brain, cerebellum, heart, and kidney, and also in hepatocytes and Kupffer cells. A whole genome was obtained, revealing a DENV-4 genotype II, with no evidence of secondary dengue infection.

Visualization of scientific collaboration and themes for arbovirus disease in the caribbean: A forty-year trend analysis with focus on dengue, Zika and Chikungunya.

Contaret, C., Césaire, R., Deloumeaux, J., Joachim, C., Cabié, A., Dramé, M.

28-06-2022

Travel Med Infect Dis

<https://pubmed.ncbi.nlm.nih.gov/35777660>

Background: The (re-)emergence of arboviruses in the Caribbean, and worldwide, is a major public health issue of concern to all scientific research stakeholders. This study aimed to use bibliometric analysis to identify the contribution of Caribbean countries to scientific production regarding the three arboviruses with the greatest impact, namely Zika, chikungunya and dengue. **Method:** Bibliographic data related to arbovirus diseases were collected from three international databases (Web of Science, Pubmed, and Scopus), filtered by Caribbean islands of affiliation. VosViewer was used to identify

scientific connections between countries or institutions and to identify research themes. **Results:** The dataset comprised 1332 indexed articles, with 50% of articles categorized in the top quartile of quality. Cuba was found to lead research on dengue, with a total of 300 articles, and 18 international connections. The USA-Puerto Rico duo was found to be the leader on emerging arboviruses (Zika and Chikungunya), followed by a predominantly French-language cluster (mainland France, Guadeloupe, Martinique). Key research topics were related to clinical presentations, epidemiology, and research on mosquito-borne viruses **CONCLUSIONS:** Co-authorship network analysis on emerging arboviruses revealed the dynamics of collaboration, and provides insights into Caribbean collaborations that deserve to be created and consolidated in case of resurgence of new arbovirus epidemics.

A volatile from the skin microbiota of flavivirus-infected hosts promotes mosquito attractiveness.

Zhang, H., Zhu, Y., Liu, Z., Peng, Y., Peng, W., Tong, L., Wang, J., Liu, Q., Wang, P., Cheng, G.

28-06-2022

Cell

<https://pubmed.ncbi.nlm.nih.gov/35777355>

The host-seeking activity of hematophagous arthropods is essential for arboviral transmission. Here, we demonstrate that mosquito-transmitted flaviviruses can manipulate host skin microbiota to produce a scent that attracts mosquitoes. We observed that *Aedes* mosquitoes preferred to seek and feed on mice infected by dengue and Zika viruses. Acetophenone, a volatile compound that is predominantly produced by the skin microbiota, was enriched in the volatiles from the infected hosts to potently stimulate mosquito olfaction for attractiveness. Of note, acetophenone emission was higher in dengue patients than in healthy people. Mechanistically, flaviviruses infection suppressed the expression of RELM α , an essential antimicrobial protein on host skin, thereby leading to the expansion of acetophenone-producing commensal bacteria and, consequently, a high acetophenone level. Given that RELM α can be specifically induced by a vitamin A derivative, the dietary administration of isotretinoin to flavivirus-infected animals interrupted flavivirus life cycle by reducing mosquito host-seeking activity, thus providing a strategy of arboviral control.

Small-scale field assessment against the dengue vector *Aedes aegypti* using the auto-dissemination approach in an urban area of Vientiane, Lao PDR.

Thammavong, P., Boyer, S., Luangamath, P., Phommavanh, N., Vungkyly, V., Nilaxay, S., Lakeomany, K., Brey, P., Grandadam, M., Marcombe, S.

01-07-2022

PLoS One

<https://doi.org/10.1371/journal.pone.0270987>

Background: In Lao PDR, dengue fever is the most important

vector borne disease and vector control remains the principal method to fight against *Aedes aegypti* the primary transmitter mosquito species. Vector control management programs need new strategies in addition to conventional larviciding and adulticiding interventions in the country. In this study, we examined the In2Care[®] Mosquito Trap's efficacy using insecticide auto-dissemination strategy. The insecticide pyriproxyfen, present in powder form inside the trap station, contaminates the body of gravid female mosquitoes visiting the traps and is later on disseminated via the mosquitoes in breeding sites surrounding the traps. We tested the attractiveness of the Traps, their efficacy to reduce the larval and adult abundance, and the impact on emergence rates. Specifically, we tested if the servicing interval of the In2Care[®] Mosquito Trap could be extended to 12 weeks. **Methods:** Two black plastic ovitrap buckets and two BG[®] sentinel traps were placed in the premises of the Science campus of Vientiane Capital located in an urban area to measure weekly the larval and adult relative abundance of *Aedes* mosquitoes from 2017 to 2019. Twenty-five In2Care[®] Mosquito Traps were evenly distributed in this area and two studies of 12 weeks were implemented during January and April 2018 and, July to October 2018 (dry and rainy season, respectively). Every 2 weeks, water samples from 5 In2Care[®] Traps were randomly selected and tested at the laboratory with *Ae. aegypti* larvae to measure the larval and pupal mortality. The relative abundance of *Aedes* mosquitoes in the BG traps[®] with the presence of In2Care[®] Traps in 2018, was compared with the surveillance results obtained in 2017 and 2019 without In2Care[®] Traps. Every week, water samples from the ovitrap buckets were tested for Emergence Inhibition (EI). **Results:** The In2Care[®] Traps were very attractive to gravid *Ae. aegypti* mosquitoes specifically during the rainy seasons with 96% of the traps colonized with larvae/pupae within four weeks. The bioassays showed 100% mortality in the water samples from the traps during the twelve weeks studies showing the good efficacy over time of the pyriproxyfen without additional servicing in the 12 week period. In addition, the larvicide was successfully disseminated into the ovitrap buckets placed in the treated area where 100% of EI during all weeks of intervention was measured. There was no significant effect of the treatment on adult abundance reduction in the treated area, probably due to recolonization of adult mosquitoes surrounding the field experiment. **Conclusions:** The observed potential of the In2Care[®] Mosquito Trap using the auto-dissemination strategy could lead to the use of this new tool in combination with conventional control methods against Dengue vectors in urban tropical areas. Large scale field trials should be implemented in Lao PDR to prove its efficacy for Public Health programs.

Partial masculinization of *Aedes aegypti* females by conditional expression of Nix.

Kojin, B., Jakes, E., Biedler, J., Tu, Z., Adelman, Z.

01-07-2022

PLoS Negl Trop Dis

<https://doi.org/10.1371/journal.pntd.0010598>

Background: *Aedes aegypti*, the main vector of dengue, yellow fever, and other arboviruses thrives in tropical and subtropical areas around the globe putting half of the world's population at risk. Despite aggressive efforts to control the transmission of those viruses, an unacceptable number of cases occur every year, emphasizing the need to develop new control strategies. Proposals for vector control focused on population suppression could offer a feasible alternative method to reduce disease transmission. The induction of extreme male-biased sex ratios has been hypothesized to be able to suppress or collapse a population, with previous experiments showing that stable expression of the male determining factor Nix in *A. aegypti* is sufficient to convert females into fertile males.

Methodology/Principal findings: Here, we report on the conditional expression of Nix in transgenic *A. aegypti* under the control of the tetracycline-dependent (Tet-off) system, with the goal of establishing repressible sex distortion. A masculinization phenotype was observed in three of the seven transgenic lines with females exhibiting male-like long maxillary palps and most importantly, the masculinized females were unable to blood feed. Doxycycline treatment of the transgenic lines only partially restored the normal phenotype from the masculinized transgenic lines, while RT-qPCR analysis of early embryos or adults showed no correlation between the level of masculinization and ectopic Nix expression. **Conclusions/Significance:** While the conditional expression of Nix produced intersex phenotypes, the level of expression was insufficient to program full conversion. Modifications that increase both the level of activation (no tet) and the level of repression (with tet) will be necessary, as such this study represents one step forward in the development of genetic strategies to control vector-borne diseases via sex ratio distortion.

How scared are Americans of the Zika virus? The role of threat, efficacy, and third-person perception to induce protective behaviors.

Zheng, N., Vilela, A., Deshpande, S.

01-07-2022

Health Mark Q

<https://doi.org/10.1080/07359683.2022.2092376>

This study examines how public perception of threat and efficacy (on self and others) influence their tendency to take preventive action against the Zika virus by surveying 1,152 U.S. adults in Texas and Florida. Findings show that individuals were likely to take protective actions when they: (1) saw a high risk of the disease (high threat) and were confident about their ability to reduce the danger (high efficacy); and (2) perceived *others* as having a high risk (high threat), but lacked the ability to reduce the danger (low efficacy). Further, the study discusses practical implications for the design of public health campaigns.

Chikungunya virus assembly and budding visualized in situ using cryogenic electron tomography.

Chmielewski, D., Schmid, M., Simmons, G., Jin, J., Chiu, W.

30-06-2022

Nat Microbiol

<https://doi.org/10.1038/s41564-022-01164-2>

Chikungunya virus (CHIKV) is a representative alphavirus causing debilitating arthritogenic disease in humans. Alphavirus particles assemble into two icosahedral layers: the glycoprotein spike shell embedded in a lipid envelope and the inner nucleocapsid (NC) core. In contrast to matrix-driven assembly of some enveloped viruses, the assembly/budding process of two-layered icosahedral particles remains poorly understood. Here we used cryogenic electron tomography (cryo-ET) to capture snapshots of the CHIKV assembly in infected human cells. Subvolume classification of the snapshots revealed 12 intermediates representing different stages of assembly at the plasma membrane. Further subtomogram average structures ranging from subnanometre to nanometre resolutions show that immature non-icosahedral NCs function as rough scaffolds to trigger icosahedral assembly of the spike lattice, which in turn progressively transforms the underlying NCs into icosahedral cores during budding. Further, analysis of CHIKV-infected cells treated with budding-inhibiting antibodies revealed wider spaces between spikes than in icosahedral spike lattice, suggesting that spacing spikes apart to prevent their lateral interactions prevents the plasma membrane from bending around the NC, thus blocking virus budding. These findings provide the molecular mechanisms for alphavirus assembly and antibody-mediated budding inhibition that provide valuable insights for the development of broad therapeutics targeting the assembly of icosahedral enveloped viruses.

The polymorphic landscape analysis of GATA1 exons uncovered the genetic variants associated with higher thrombocytopenia in dengue patients.

Al Rimon, R., Sayem, M., Alam, S., Al Saba, A., Sanyal, M., Amin, M., Kabir, A., Chakraborty, S., Nabi, A.

30-06-2022

PLoS Negl Trop Dis

<https://doi.org/10.1371/journal.pntd.0010537>

The current study elucidated an association between gene variants and thrombocytopenia through the investigation of the exonic polymorphic landscape of hematopoietic transcription factor-GATA1 gene in dengue patients. A total of 115 unrelated dengue patients with dengue fever (DF) (N = 91) and dengue hemorrhagic fever (DHF) (N = 24) were included in the study. All dengue patients were confirmed through detection of NS1 antigen, IgM, and IgG antibodies against the dengue virus. Polymerase chain reaction using specific primers amplified the exonic regions of GATA1 while Sanger sequencing and chromatogram analyses facilitated the identification of variants. Variants G>A (at chX: 48792009) and C>A (at chX: 4879118) had higher frequency out of 13 variants identified (3 annotated and 10 newly recognized). Patients carrying either nonsynonymous or synonymous variants had significantly lower mean values of platelets compared to those

harboring the reference nucleotides (NC_000023.11). Further analyses revealed that the change in amino acid residue leads to the altered three-dimensional structure followed by interaction with neighboring residues. Increased stability of the protein due to substitution of serine by asparagine (S129N at chX: 48792009) may cause increased rigidity followed by reduced structural flexibility which may ultimately disturb the dimerization (an important prerequisite for GATA1 to perform its biological activity) process of the GATA1 protein. This, in turn, may affect the function of GATA1 followed by impaired production of mature platelets which may be reflected by the lower platelet counts in individuals with such variation. In summary, we have identified new variants within the GATA1 gene which were found to be clinically relevant to the outcome of dengue patients and thus, have the potential as candidate biomarkers for the determination of severity and prognosis of thrombocytopenia caused by dengue virus. However, further validation of this study in a large number of dengue patients is warranted. Trial Registration: number SLCTR/2019/037.

The effect of weather and climate on dengue outbreak risk in Peru, 2000-2018: A time-series analysis.

Dostal, T., Meisner, J., Munayco, C., García, P., Cárcamo, C., Pérez Lu, J., Morin, C., Frisbie, L., Rabinowitz, P.
30-06-2022

PLoS Negl Trop Dis

<https://doi.org/10.1371/journal.pntd.0010479>

Background: Dengue fever is the most common arboviral disease in humans, with an estimated 50-100 million annual infections worldwide. Dengue fever cases have increased substantially in the past four decades, driven largely by anthropogenic factors including climate change. More than half the population of Peru is at risk of dengue infection and due to its geography, Peru is also particularly sensitive to the effects of El Niño Southern Oscillation (ENSO). Determining the effect of ENSO on the risk for dengue outbreaks is of particular public health relevance and may also be applicable to other Aedes-vector-borne viruses. **Methods:** We conducted a time-series analysis at the level of the district-month, using surveillance data collected from January 2000 to September 2018 from all districts with a mean elevation suitable to survival of the mosquito vector (<2,500m), and ENSO and weather data from publicly-available datasets maintained by national and international agencies. We took a Bayesian hierarchical modeling approach to address correlation in space, and B-splines with four knots per year to address correlation in time. We furthermore conducted subgroup analyses by season and natural region. **Results:** We detected a positive and significant effect of temperature (°C, RR 1.14, 95% CI 1.13, 1.15, adjusted for precipitation) and ENSO (ICEN index: RR 1.17, 95% CI 1.15, 1.20; ONI index: RR 1.04, 95% CI 1.02, 1.07) on outbreak risk, but no evidence of a strong effect for precipitation after adjustment for temperature. Both natural region and season were found to be significant effect modifiers of the ENSO-dengue effect, with the effect of ENSO

being stronger in the summer and the Selva Alta and Costa regions, compared with winter and Selva Baja and Sierra regions. **Conclusions:** Our results provide strong evidence that temperature and ENSO have significant effects on dengue outbreaks in Peru, however these results interact with region and season, and are stronger for local ENSO impacts than remote ENSO impacts. These findings support optimization of a dengue early warning system based on local weather and climate monitoring, including where and when to deploy such a system and parameterization of ENSO events, and provide high-precision effect estimates for future climate and dengue modeling efforts.

Artificial intelligence in differentiating tropical infections: A step ahead.

Shenoy, S., Rajan, A., Rashid, M., Chandran, V., Poojari, P., Kunhikatta, V., Acharya, D., Nair, S., Varma, M., Thunga, G.
30-06-2022

PLoS Negl Trop Dis

<https://doi.org/10.1371/journal.pntd.0010455>

Background and objective: Differentiating tropical infections are difficult due to its homogenous nature of clinical and laboratorial presentations among them. Sophisticated differential tests and prediction tools are better ways to tackle this issue. Here, we aimed to develop a clinician assisted decision making tool to differentiate the common tropical infections. **Methodology:** A cross sectional study through 9 item self-administered questionnaire were performed to understand the need of developing a decision making tool and its parameters. The most significant differential parameters among the identified infections were measured through a retrospective study and decision tree was developed. Based on the parameters identified, a multinomial logistic regression model and a machine learning model were developed which could better differentiate the infection. **Results:** A total of 40 physicians involved in the management of tropical infections were included for need analysis. Dengue, malaria, leptospirosis and scrub typhus were the common tropical infections in our settings. Sodium, total bilirubin, albumin, lymphocytes and platelets were the laboratory parameters; and abdominal pain, arthralgia, myalgia and urine output were the clinical presentation identified as better predictors. In multinomial logistic regression analysis with dengue as a reference revealed a predictability of 60.7%, 62.5% and 66% for dengue, malaria and leptospirosis, respectively, whereas, scrub typhus showed only 38% of predictability. The multi classification machine learning model observed to have an overall predictability of 55-60%, whereas a binary classification machine learning algorithms showed an average of 79-84% for one vs other and 69-88% for one vs one disease category. **Conclusion:** This is a first of its kind study where both statistical and machine learning approaches were explored simultaneously for differentiating tropical infections. Machine learning techniques in healthcare sectors will aid in early detection and better patient care.

Specificity and Breadth of the Neutralizing Antibody Response to a Live Attenuated Tetravalent Dengue Vaccine.

DeMaso, C., Karwal, L., Zahralban-Steele, M., Dominguez, D., Springer, Z., Kaiser, M., Palani, S., Rindfleisch, T., Bohning, K., Hather, G., Das, S., Sharma, M., Dean, H.

30-06-2022

J Infect Dis

<https://pubmed.ncbi.nlm.nih.gov/35771658>

An effective dengue vaccine should ideally induce broadly neutralizing antibody (nAb) responses against all four dengue virus (DENV) serotypes. We characterized the specificity and breadth of the nAb response to TAK-003, a live attenuated tetravalent dengue vaccine, in serum samples from phase 2 and 3 clinical trials. Microneutralization tests using post-vaccination serum showed comparable neutralization against diverse DENV-1-4 genotypes. Reporter virus particle neutralization assays post- depletion of anti-DENV-2 nAbs demonstrated that the nAb response to DENV-1, -3 and -4 comprises both type-specific (TS) and cross-reactive (CR) nAbs. Therefore, TAK-003 induces broad tetravalent TS and CR nAb responses.

Epidemiological and hematological investigation of Dengue Virus infection.

Anwar, F., Ullah, S., Aziz, A., Rehman, A., Khan, J., Tayyab, M., Haq, I., Mahmood, M.

29-06-2022

Microbiol Immunol

<https://doi.org/10.1111/1348-0421.13018>

Dengue is a mosquito-borne viral illness that infects humans. For the last few decades, it has been declared a global public health problem. The current study was conducted at the district headquarter hospital (DHQ) Bannu between June to September 2018 based on the seroprevalence of antibodies against dengue virus serotypes and their hematological parameters among the patients. A total of 1738 suspected individuals were diagnosed through NS1, IgG, and IgM antibodies and RT-PCR techniques. Out of all the samples, 716 (41.19%) were found to be positive for dengue. A higher infection rate was found in males (65.92%) as compared to females (34.07%). The most affected age group was 16-40 years, whereas the most affected tehsil was Bannu, where the DENV-3 serotype was prevalent. The rare serotype (DENV-4) was found in 1% of cases. Symptoms including fever (100%), myalgia (100%), headache (61.31%), vomiting (34.63%), and rashes were common among the dengue patients. However, the mild cases showed fewer clinical signs compared to the severe infected cases. The study also revealed a significant association ($P<0.05$) between hematological parameters and dengue infection, showing a significant decrease in TC, eosinophils, neutrophils, and platelets and a significant increase in monocytes and lymphocytes. Based on the current report, it is concluded that patients with the above symptoms and hematological changes may have increased probability of Dengue and should be kept under observation to separate

dengue positive patients and enhance treatment process. This article is protected by copyright. All rights reserved.

Population-based surveillance for congenital zika virus syndrome: a latent class analysis of recorded cases from 2015-2018.

Paixao, E., Rodrigues, L., Costa, M., de Carvalho-Sauer, R., Oliveira, W., Cardim, L., Schuler-Faccini, L., Andrade, R., Rodrigues, M., Brickley, E., Veiga, R., Costa, L., Carmo, E., Smeeth, L., Barreto, M., Teixeira, M.

29-06-2022

BMC Pregnancy Childbirth

<https://doi.org/10.1186/s12884-022-04860-3>

Objective: This study aims to describe clinical findings and determine the medium-term survival of congenital zika syndrome (CZS) suspected cases. **Methods:** A retrospective cohort study using routine register-based linked data. It included all suspected cases of CZS born in Brazil from January 1, 2015, to December 31, 2018, and followed up from birth until death, 36 months, or December 31, 2018, whichever came first. Latent class analysis was used to cluster unconfirmed cases into classes with similar combinations of anthropometry at birth, imaging findings, maternally reported rash, region, and year of birth. Kaplan-Meier curves were plotted, and Cox proportional hazards models were fitted to determine mortality up to 36 months. **Results:** We followed 11,850 suspected cases of CZS, of which 28.3% were confirmed, 9.3% inconclusive and 62.4% unconfirmed. Confirmed cases had almost two times higher mortality when compared with unconfirmed cases. Among unconfirmed cases, we identified three distinct clusters with different mortality trajectories. The highest mortality risk was observed in those with abnormal imaging findings compatible with congenital infections (HR=12.6; IC95%8.8-18.0) and other abnormalities (HR=11.6; IC95%8.6-15.6) compared with those with normal imaging findings. The risk was high in those with severe microcephaly (HR=8.2; IC95%6.4-10.6) and macrocephaly (HR=6.6; IC95%4.5-9.7) compared with normal head size. **Conclusion:** Abnormal imaging and head circumference appear to be the main drivers of the increased mortality among suspected cases of CZS. We suggest identifying children who are more likely to die and have a greater need to optimise interventions and resource allocation regardless of the final diagnoses.

Antibody Fc characteristics and effector functions correlate with protection from symptomatic dengue virus type 3 infection.

Dias, A., Atyeo, C., Loos, C., Montoya, M., Roy, V., Bos, S., Narvekar, P., Singh, T., Katzelnick, L., Kuan, G., Lauffenburger, D., Balmaseda, A., Alter, G., Harris, E.

29-06-2022

Sci Transl Med

<https://doi.org/10.1126/scitranslmed.abm3151>

Preexisting cross-reactive antibodies have been implicated in both protection and pathogenesis during subsequent

infections with different dengue virus (DENV) serotypes (DENV1-4). Nonetheless, humoral immune correlates and mechanisms of protection have remained elusive. Using a systems serology approach to evaluate humoral responses, we profiled plasma collected before inapparent or symptomatic secondary DENV3 infection from our pediatric cohort in Nicaragua. Children protected from symptomatic infections had more anti-envelope (E) and anti-nonstructural protein 1 (NS1) total immunoglobulin G (IgG), IgG4, and greater Fc effector functions than those with symptoms. Fc effector functions were also associated with protection from hemorrhagic manifestations in the pre-symptomatic group. Furthermore, *in vitro* virological assays using these plasma samples revealed that protection mediated by antibody-dependent complement deposition was associated with both lysis of virions and DENV-infected cells. These data suggest that E- and NS1-specific Fc functions may serve as correlates of protection, which can be potentially applied toward the design and evaluation of dengue vaccines.

Cytokines, CXCL10 and CCL2 and kynurenine metabolites, anthranilic acid accurately predicts patients at risk of developing Dengue with Warning Signs.

Jusof, F., Lim, C., Aziz, F., Soe, H., Raju, C., Sekaran, S., Guillemin, G.
29-06-2022

J Infect Dis

<https://pubmed.ncbi.nlm.nih.gov/35767283>

Introduction: The resolution or aggravation of dengue infection depends on the patient's immune response during the critical phase. Cytokines released by immune cells increase with the worsening severity of dengue infections. Cytokines activate the kynurenine pathway (KP) and the extent of KP activation then influences disease severity. **Methods:** KP metabolites and cytokines in plasma samples of patients with dengue infections (DWS-, DWS+ or SD) were analysed. Cytokines (IFN- γ , TNF, IL-6, CXCL10/IP-10, IL-18, CCL2/MCP-1 and CCL4/MIP-1 β) were assessed by a Human Luminex Screening Assay, while KP metabolites (tryptophan, kynurenine, anthranilic acid, picolinic acid and quinolinic acid) by uHPLC and GCMS assays. **Results:** Patients with DWS+ had increased activation of the KP where kynurenine-tryptophan ratio, anthranilic acid and picolinic acid were elevated. These patients also had higher levels of cytokines, IFN- γ , CXCL10, CCL4 and IL-18 than those with DWS-. Further ROC analysis identified three prognostic biomarker candidates, CXCL10, CCL2 and AA which predicted patients with higher risks of developing DWS+ with an accuracy of 97%. **Conclusion:** The data suggest a unique biochemical signature in patients with DWS+. CXCL10 and CCL2 together with AA are potential prognostic biomarkers that discern patients with higher risks of developing DWS+ at earlier stages of infection.

MBZM-N-IBT, a Novel Small Molecule, Restricts Chikungunya Virus Infection by Targeting nsP2 Protease Activity *In Vitro*, *In Vivo*, and *Ex Vivo*.

De, S., Ghosh, S., Keshry, S., Mahish, C., Mohapatra, C., Guru, A., Mamidi, P., Datey, A., Pani, S., Vasudevan, D., Beuria, T., Chattopadhyay, S., Subudhi, B., Chattopadhyay, S.
29-06-2022

Antimicrob Agents Chemother

<https://doi.org/10.1128/aac.00463-22>

The increase in disease incidences and persistent Chikungunya virus (CHIKV)-induced arthritis have been a huge burden on public health globally. In the absence of specific antivirals or vaccines, it is essential to continue efforts to develop effective anti-CHIKV strategies. Our previous study showing the *in vitro* anti-CHIKV potential of a novel molecule 1-[(2-methylbenzimidazol-1-yl) methyl]-2-oxo-indolin-3-ylidene] amino] thiourea (MBZM-N-IBT) encouraged us to further validate its efficacy. Here, the effect of MBZM-N-IBT was evaluated *in vitro* in RAW 264.7 cells, *in vivo* in C57BL/6 mice, and *ex vivo* in human peripheral blood mononuclear cells (hPBMCs). The study demonstrated that CHIKV infection was efficiently abrogated in RAW 264.7 cells (IC₅₀ = 22.34 μ M) with significant inhibition in viral proteins. The inhibition was effective in the postentry step, and MBZM-N-IBT predominately interfered in the early stages of CHIKV life cycle. It was further supported when the protease activity of CHIKV-nsP2 was hindered by the compound. Moreover, it diminished the CHIKV-induced inflammatory responses *in vitro* through significant downregulation of all the major mitogen-activated protein kinases (MAPKs), NF- κ B, cyclooxygenase (COX)-2, and cytokines. Furthermore, MBZM-N-IBT restricted CHIKV infection and inflammation *in vivo*, leading to reduced clinical scores and complete survival of C57BL/6 mice. Additionally, it has been noticed that the CHIKV infection was reduced remarkably in hPBMC-derived monocyte-macrophage populations *ex vivo* by the compound. In conclusion, it can be suggested that this novel compound MBZM-N-IBT has been demonstrated to be a potential anti-CHIKV molecule *in vitro*, *in vivo*, and *ex vivo* and fulfilled all the criteria to investigate further for successful treatment of CHIKV infection.

Dynamic immune ecosystem of dengue infection revealed by single-cell sequencing.

Xu, G., Gao, Y., Pan, T., Li, S., Zhang, Y., Guo, J., Tian, Z., Xu, J., Li, Y., Li, X.

29-06-2022

J Leukoc Biol

<https://doi.org/10.1002/JLB.6MA0622-738RR>

Dengue is the most common human arboviral disease worldwide, which can result in severe complications. A dysfunctional immune response in dengue infective patients is a recurrent theme impacting symptoms and mortality, but the heterogeneity and dynamics of immune infiltrates during dengue infection remain poorly characterized. Here, we identified the immune cell types in scRNA-seq data from 13127 cells of 10 dengue infective patients and discovered the

dynamic immune ecosystems of dengue infection. Notably, genes that exhibited higher expression in specific cell types play important roles in response to virus infection in a module manner. Transcription factors (TFs) are the major regulators (i.e., PAX5, IRF7, KLF4, and IRF8) that can potentially regulate infection-related genes. We demonstrated that the dynamic rewired regulatory network during dengue infection. Moreover, our data revealed the complex cell-cell communications from control to fever and severe dengue patients and prevalent cell-cell communication rewiring was observed. We further identified the IFN-II and CXCL signaling pathways that mediated the communications and play important roles in dengue infection. Together, our comprehensive analysis of dynamic immune ecosystem of dengue infection provided novel insights for understanding the pathogenesis of and developing effective therapeutic strategies for dengue infection.

Reflections on research ethics in a public health emergency: Experiences of Brazilian women affected by Zika.

Ambrogi, I., Brito, L., Rego, S.

28-06-2022

Dev World Bioeth

<https://doi.org/10.1111/dewb.12361>

In Brazil, the epicenter of the Zika crisis, brown, black, and indigenous poor women living in municipalities with scarce resources were disproportionately affected. The gendered consequences of the epidemic exposed how intersectional lenses are central to understand the impact of public health emergencies in the lives of women and girls. The demand for Zika-affected children and women to be research participants is relevant for an ethical analysis of participant protection procedures during a crisis. We investigated how women experienced research participation by analyzing their narratives. Two-year-long longitudinal qualitative study in Brazilian sites located in the epidemic's epicenter was performed using mixed methods: ethnography with women from two distinct states and individual semi-structured interviews with five women in different Zika-affected states, four of which were community leaders. All women in the study were mothers or grandmothers of Zika-affected children. Thematic analysis was used for data evaluation. Women perceived being pressured to participate in research and a lack of benefit sharing. Structural determinants of gender inequality, such as its effect on power distribution, were found to impact research participant protection. Formal procedures for research protocols approvals were insufficient in protecting participants because these instruments were unable to account for structural aspects. Communitarian mobilization, through WhatsApp groups, was found to be an important mechanism to create conditions to challenge oppressive structures. Strengthening public health, effective community-based participation in research planning and implantation of ethical strategies that promotes gender equality can have transformative effect on unequal power structures and promote participant protection.

Etiology of acute febrile illnesses in Southern China: Findings from a two-year sentinel surveillance project, 2017-2019.

Rainey, J., Siesel, C., Guo, X., Yi, L., Zhang, Y., Wu, S., Cohen, A., Liu, J., Houpt, E., Fields, B., Yang, Z., Ke, C.

28-06-2022

PLoS One

<https://doi.org/10.1371/journal.pone.0270586>

Background: Southern China is at risk for arbovirus disease transmission, including Zika virus and dengue. Patients often present to clinical care with non-specific acute febrile illnesses (AFI). To better describe the etiology of AFI, we implemented a two-year AFI surveillance project at five sentinel hospitals in Yunnan and Guangdong Provinces. **Methods:** Between June 2017 and August 2019, we enrolled patients between 2 and 65 years of age presenting at one sentinel hospital in Mengla County, Yunnan, and four in Jiangmen City, Guangdong, with symptoms of AFI (acute onset of fever $\geq 37.5^{\circ}\text{C}$ within the past 7 days) without respiratory symptoms or diarrhea. Demographic, epidemiologic, and clinical information was obtained and entered into a web-based AFI surveillance database. A custom TaqMan Array card (TAC) was used to test patients' whole blood specimens for 27 different pathogens using real-time polymerase chain reaction assays. **Results:** During the two-year project period, 836 patients were enrolled; 443 patients from Mengla County and 393 patients from Jiangmen City. The median age was 33 years [range: 2-65], and most were hospitalized [641, 77%]. Of 796 patients with valid TAC results, 341 (43%) were positive for at least one of the 10 unique pathogens detected. This included 205 (26%) patients positive for dengue virus, 60 (8%) for *Orientia tsutsugamushi*, and 42 (5%) for *Coxiella burnetii*. Ten patients (1%) in Jiangmen City tested positive for malaria, 8 of whom reported recent travel outside of China. TAC results were negative for 455 (57%) patients. None of the patients had a positive TAC detection for Zika virus. **Conclusions:** The project detected variability in the etiology of AFI in Southern China and highlighted the importance of differential diagnosis. Dengue, *O. tsutsugamushi*, and *C. burnetii* were the most frequently identified pathogens among enrolled AFI patients. As a non-notifiable disease, the frequent detection of *C. burnetii* is noteworthy and warrants additional investigation. The project provided a framework for routine surveillance for persons presenting with AFI.

Interactions between vector competence to chikungunya virus and resistance to deltamethrin in *Aedes aegypti* laboratory lines?

Wang, L., Fontaine, A., Gaborit, P., Guidez, A., Issaly, J., Girod, R., Kazanji, M., Rousset, D., Vignuzzi, M., Epelboin, Y., Dufour, I.

28-06-2022

Med Vet Entomol

<https://doi.org/10.1111/mve.12593>

The urban mosquito species *Aedes aegypti* is the main vector of arboviruses worldwide. Mosquito control with insecticides

is the most prevalent method for preventing transmission in the absence of effective vaccines and available treatments; however, the extensive use of insecticides has led to the development of resistance in mosquito populations throughout the world, and the number of epidemics caused by arboviruses has increased. Three mosquito lines with different resistance profiles to deltamethrin were isolated in French Guiana, including one with the I1016 knock-down resistant allele. Significant differences were observed in the cumulative proportion of mosquitoes with a disseminated chikungunya virus infection over time across these lines. In addition, some genes related to resistance (CYP6BB2, CYP6N12, GST2, trypsin) were variably overexpressed in the midgut at 7 days after an infectious bloodmeal in these three lines. Our work shows that vector competence for chikungunya virus varied between *Ae. aegypti* laboratory lines with different deltamethrin resistance profiles. More accurate verification of the functional association between insecticide resistance and vector competence remains to be demonstrated.

Zika, Nipah and Kala-azar: Emerging lethal infectious diseases amid COVID-19 as an escalating public health threat in South India.

Uday, U., Tadi, L., Islam, Z., Mohanan, P., Ghazanfar, S., Babar, M., Ismail, S.

15-06-2022

Ann Med Surg (Lond)

<https://doi.org/10.1016/j.amsu.2022.103972>

As of 6 June 2022, a sum 25,782 of active cases and 524,701 deaths due to Coronavirus disease-19 (COVID-19) have been recorded in India. Stewing in the flares of the pandemic, Kerala is entwined in the wrath of multiple emerging infectious diseases. India, a home to 1.3 billion people, recently faced a devastating second wave of COVID-19 during May of 2021, with a ruckus of chronic shortage of medicine, oxygen supplies, ventilators, besides, being challenged by secondary infections and chronic health ailments. The state of Kerala, alone contributes to 50% COVID-19 caseload, besides, recent simultaneous outbreaks of Zika Virus Disease (ZVD), Nipah Virus Disease (NiVD) and Kala-azar (black fever) on July 8, September 5 and 8, 2021 respectively. Syndemicity and a high case fatality rates of these highly contagious diseases coupled with post infection sequelae, overwhelm the already fragile healthcare system. Thus, these lethal infectious diseases along with an anticipated third wave of COVID-19 pose a serious public health threat in and around South India. With this narrative review, we aim to discuss the challenges that the emergence of intersecting outbreaks of Zika, Nipah, Kala-azar presents with, in the nation, amidst the global pandemic of COVID-19 and provide recommendations so as to help alleviate the situation. The syndemicity of COVID-19 with other infectious diseases, calls for adequate surveillance and monitoring of diseases' outbreaks. To avoid the worst situations like pandemic, the health ministry, public and private health stakeholders in India should strengthen the public healthcare delivery system and providence of quick

medical facilities to control the rate of mortality and morbidity during outbreaks.

Evaluation of Zika rapid tests as aids for clinical diagnosis and epidemic preparedness.

Boeras, D., Diagne, C., Pelegrino, J., Grandadam, M., Duong, V., Dussart, P., Brey, P., Ruiz, D., Adati, M., Wilder-Smith, A., Falconar, A., Romero, C., Guzman, M., Hasanin, N., Sall, A., Peeling, R.

04-06-2022

EClinicalMedicine

<https://doi.org/10.1016/j.eclim.2022.101478>

Background: Development and evaluation of diagnostics for diseases of epidemic potential are often funded during epidemics, but not afterwards, leaving countries unprepared for the next epidemic. United Nations Children's Emergency Fund (UNICEF) partnered with the United States Agency for International Development (USAID) to address this important gap by investing in an advance purchase commitment (APC) mechanism to accelerate the development and evaluation of Zika rapid diagnostic tests (RDTs) for case detection and surveillance. This paper describes the performance evaluation of five Zika RDTs eligible for procurement. **Methods:** A network of European Union-funded ZikaPLAN sites in Africa, Asia, Latin America with access to relevant serum specimens were selected to evaluate RDTs developed for the UNICEF APC mechanism. A standardised protocol and evaluation panels were developed and a call for specimens for the evaluation panels issued to different sites. Each site contributed specimens to the evaluation from their biobank. Data were collated, analysed and presented to the UNICEF Procurement Review Group for review. **Findings:** Three RDTs met the criteria for UNICEF procurement of sensitivity and specificity of 85% against a reference standard. The sensitivity/specificity of the ChemBio anti-Zika Virus (ZIKV) immunoglobulin M (IgM) test was 86.4%/86.7% and the ChemBio ZCD system for anti-ZIKV IgM was 79.0%/97.1%, anti-dengue virus (DENV) IgM 90.0%/89.2%, anti-Chikungunya virus (CHIKV) IgM 90.6%/97.2%. The sensitivity/specificity of the SD Biosensor anti-ZIKV IgM was 96.8%/90.8%, anti-DENV IgM 71.8%/83.5%, the DENV nonstructural protein 1 (NS1) glycoprotein 90.0%/90.2%, anti-yellow fever virus (YFV) IgM 84.6%/92.4%, anti-CHIKV IgM 86.3%/97.5%. **Interpretation:** Three RDTs fulfilled the performance thresholds set by WHO and were eligible for UNICEF procurement. These tests will improve the diagnosis of ZIKV and other arboviral infections as well as providing countries with better tools for surveillance and response to future epidemics. **Funding:** This work was supported by the USAID grant GHA-G-00-07-00007 and ZikaPLAN (European Union's Horizon 2020 Research and Innovation Programme under Grant Agreement No. 734584).

Comparative overview of emerging RNA viruses: Epidemiology, pathogenesis, diagnosis and current treatment.

Revue de littérature

Chakrabarty, I., Khan, M., Mahanta, S., Chopra, H., Dhawan, M., Choudhary, O., Bibi, S., Mohanta, Y., Emran, T.
11-06-2022

Ann Med Surg (Lond)

<https://doi.org/10.1016/j.amsu.2022.103985>

From many decades, emerging infections have threatened humanity. The pandemics caused by different CoVs have already claimed and will continue to claim millions of lives. The SARS, Ebola, MERS epidemics and the most recent emergence of COVID-19 pandemic have threatened populations across borders. Since a highly pathogenic CoV has been evolved into the human population in the twenty-first century known as SARS, scientific advancements and innovative methods to tackle these viruses have increased in order to improve response preparedness towards the unpredictable threat posed by these rapidly emerging pathogens. Recently published review articles on SARS-CoV-2 have mainly focused on its pathogenesis, epidemiology and available treatments. However, in this review, we have done a systematic comparison of all three CoVs i.e., SARS, MERS and SARS-CoV-2 along with Ebola and Zika in terms of their epidemiology, virology, clinical features and current treatment strategies. This review focuses on important emerging RNA viruses starting from Zika, Ebola and the CoVs which include SARS, MERS and SARS-CoV-2. Each of these viruses has been elaborated on the basis of their epidemiology, virulence, transmission and treatment. However, special attention has been given to SARS-CoV-2 and the disease caused by it i.e., COVID-19 due to current havoc caused worldwide. At the end, insights into the current understanding of the lessons learned from previous epidemics to combat emerging CoVs have been described. The travel-related viral spread, the unprecedented nosocomial outbreaks and the high case-fatality rates associated with these highly transmissible and pathogenic viruses highlight the need for new prophylactic and therapeutic actions which include but are not limited to clinical indicators, contact tracing, and laboratory investigations as important factors that need to be taken into account in order to arrive at the final conclusion.

Simple and Economical Extraction of Viral RNA and Storage at Ambient Temperature.

Hernandez, S., Cardozo, F., Myers, D., Rojas, A., Waggoner, J.
01-06-2022

Microbiol Spectr

<https://doi.org/10.1128/spectrum.00859-22>

RNA extraction is essential for the molecular detection of common viral pathogens. However, available extraction methods and the need for ultra-cold storage limit molecular testing in resource-constrained settings. Herein, we describe the development of an economical RNA Extraction and Storage (RNAES) protocol that eliminates requirements for instrumentation, expensive materials, and preserved cold chain. Through an iterative process, we optimized viral lysis and RNA binding to and elution from glass fiber membranes included in simple RNAES packets. Efficient viral lysis was

achieved with a nontoxic buffer containing sucrose, KCl, proteinase K, and carrier RNA. Viral RNA binding to glass fiber membranes was concentration dependent across seven orders of magnitude (4.0-10.0 log₁₀ copies/μL) and significantly increased with an acidic arginine binding buffer. For the clinical evaluation, 36 dengue virus (DENV)-positive serum samples were extracted in duplicate with the optimized RNAES protocol and once in an EMAG instrument (bioMérieux). DENV RNA was successfully extracted from 71/72 replicates (98.6%) in the RNAES protocol, and real-time RT-PCR cycle threshold (C_T) values correlated between extraction methods. DENV RNA, extracted from clinical samples, was stable when stored on dried RNAES membranes at ambient temperature for up to 35 days, with median eluate RNA concentration decreasing by 0.18 and 0.29 log₁₀ copies/μL between day 0 and days 7 and 35, respectively. At a cost of \$0.08/sample, RNAES packets address key limitations to available protocols and may increase capacity for molecular detection of RNA viruses. **IMPORTANCE** RNA extraction methods and ultra-cold storage requirements limit molecular testing for common viruses. We developed a simple, flexible, and economical method that simultaneously addresses these limitations. At \$0.08/sample, the new RNA Extraction and Storage (RNAES) protocol successfully extracted viral RNA from acute-phase sera and provided stable, ambient-temperature RNA storage for 35 days. Using this approach, we expect to improve RNA virus detection and outbreak response in resource-constrained settings.

Child Neurology Care in Latin America: Challenges and Potential Solutions.

Vidaurre, J., Weisleder, P.

28-04-2022

Pediatr Neurol

<https://pubmed.ncbi.nlm.nih.gov/35598586>

Background: The current practice of child neurology in Latin America has been impacted by the waves of sociopolitical unrest that in the last decades have swept the region. **Methods:** We searched the available literature referring to the situation of child neurology in Latin America and conditions that specifically impact the region. **Results:** In lower-middle-income countries, the number of child neurologists is inadequate. Child neurologists working in large public hospitals can only afford to do so on a part-time basis as these institutions are chronically underfunded. Several circumstances are particularly relevant to Latin America: Spanish is the main language spoken, something that limits the opportunity to keep local child neurologists up to date. The structure of health care systems in Latin America varies significantly. Some countries have fragmented systems with inadequate capacity to offer equitable access to medical care. Latin America has been impacted by epidemics of arthropod-borne viruses: Zika, chikungunya, and dengue. It stands to reason that the COVID-19 pandemic will affect the distribution of resources for chronic neurological conditions. **Conclusions:** The virtual platforms such as Zoom, expanded during the COVID-19 pandemic, are useful not only to improve access to

care through telemedicine but also for educational purposes. Collaborative efforts to support educational courses and symposia in Spanish are ongoing. It is necessary to set short- and long-term priorities to improve child neurology care in the region. Immediate priorities should focus on improving the diagnosis of neurological conditions, making emphasis on locally available resources.

Zika in the MIDST of the COVID-19 Pandemic.

Tangsathapornpong, A., Thisyakorn, U.

20-05-2022

Asia Pac J Public Health

<https://doi.org/10.1177/10105395221100811>

Modulation of Zika virus replication via glycosphingolipids.

Konan, K., Ogbamikaël, S., Yager, E., Yamaji, T., Cerone, J., Monaco-Brown, M., Barroso, M., Hanada, K.

03-05-2022

Virology

<https://pubmed.ncbi.nlm.nih.gov/35550476>

The enveloped positive-sense RNA viruses including Zika virus (ZIKV) need host lipids to successfully replicate. The nature of the lipids and the replication step(s) where lipids are utilized often vary amongst viruses. In this study, we demonstrate that ZIKV particle envelope is significantly enriched in distinct sphingolipid species. To determine the role of sphingolipids in ZIKV replication, we leveraged a panel of sphingolipid-deficient cell lines. Notably, knockout of glucosylceramide and lactosylceramide synthase encoding genes (GCS^{KO}; B4G5^{KO}) resulted in a marked decrease in ZIKV titers. GCS^{KO} or pharmacological inhibition of GCS also led to a significant decrease in ZIKV genome replication. Further analysis indicated that GCS^{KO} reduced intracellular virus titers but had minimal impact on ZIKV binding. Restoration of B4G5 expression in B4G5^{KO} cells or supplementing PDMP-treated cells with glucosylceramide led to a significant rescue of ZIKV replication. Altogether, our findings suggest that ZIKV needs glycosphingolipids to facilitate virus replication.

Molecular organization of dengue fusion peptide in phospholipid monolayers revealed by tensiometry and vibrational spectroscopy.

Schmidt, T., Caseli, L.

23-03-2022

Colloids Surf B Biointerfaces

<https://pubmed.ncbi.nlm.nih.gov/35381500>

The interaction of Dengue fusion peptide (FLAG) in selected lipid Langmuir monolayers was characterized with surface pressure-area isotherms and infrared spectroscopy to investigate the role of the membrane charge and molecular organization in the peptide-lipid binding. Surface pressure-area isotherms were employed to analyze the thermodynamic and mechanical properties of the FLAG-lipid monolayer,

showing that charged lipid monolayers showed different peptide adsorption patterns for an optimized peptide concentration (maximum membrane adsorption). Polarization modulation infrared reflection-absorption spectroscopy pointed out that incorporating FLAG changed the dipole orientations for the lipid polar head groups, as confirmed in PG-containing monolayers. Also, FLAG reorients the lipid film when it interacts with the phosphate and choline groups. Finally, analysis of the 3₁₀-helix bands suggests that FLAG assumes a configuration as a hairpin, an essential premise for the beginning of the membrane fusion process.

Vaginal transmission causes prolonged Zika virus shedding in the vaginal mucosa and delays systemic dissemination.

Balint, E., Somani, A., Giles, E., Feng, E., Vahedi, F., Ashkar, A.

21-04-2022

Immunol Cell Biol

<https://doi.org/10.1111/imcb.12549>

Zika virus (ZIKV) has emerged as a significant health threat worldwide. Although typically mosquito-borne, recent evidence suggests that ZIKV is also a sexually transmitted virus. While persistent ZIKV infections in male reproductive tissues have been identified, little is understood regarding the outcomes of primary sexual transmission in females. We investigated how the route of infection affects vaginal ZIKV shedding and dissemination. In two mouse models, vaginal infection resulted in prolonged ZIKV shedding in the vaginal mucosa with delayed systemic infection. Furthermore, heightened vaginal inflammation did not influence ZIKV replication or dissemination, in contrast to previous studies of mosquito-borne infection. Thus, vaginal infection significantly alters ZIKV infection kinetics and must be considered when developing novel treatments.

Symbionts and gene drive: two strategies to combat vector-borne disease.

Revue de littérature

Wang, G., Du, J., Chu, C., Madhav, M., Hughes, G., Champer, J.

21-03-2022

Trends Genet

<https://pubmed.ncbi.nlm.nih.gov/35314082>

Mosquitoes bring global health problems by transmitting parasites and viruses such as malaria and dengue. Unfortunately, current insecticide-based control strategies are only moderately effective because of high cost and resistance. Thus, scalable, sustainable, and cost-effective strategies are needed for mosquito-borne disease control. Symbiont-based and genome engineering-based approaches provide new tools that show promise for meeting these criteria, enabling modification or suppression approaches. Symbiotic bacteria like *Wolbachia* are maternally inherited and manipulate mosquito host reproduction to enhance their vertical transmission. Genome engineering-based gene drive methods, in which mosquitoes are genetically altered to spread drive

alleles throughout wild populations, are also proving to be a potentially powerful approach in the laboratory. Here, we review the latest developments in both symbionts and gene drive-based methods. We describe some notable similarities, as well as distinctions and obstacles, relating to these promising technologies.

Global prevalence of dengue and chikungunya coinfection: A systematic review and meta-analysis of 43,341 participants.

Irekeola, A., Engku Nur Syafirah, E., Islam, M., Shueb, R.
16-03-2022

Acta Trop

<https://pubmed.ncbi.nlm.nih.gov/35305942>

Dengue and chikungunya virus are important arboviruses of public health concern. In the past decades, they have accounted for numerous outbreaks of dengue and chikungunya in different parts of the world. Several cases of concurrent infection of dengue and chikungunya have been documented. However, the true burden of this concurrent infection is unknown. Here, a systematic review and meta-analysis of published data on the prevalence of dengue and chikungunya coinfection in the human population was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis. Six electronic databases (Web of science, Embase, PubMed, ScienceDirect, Scopus, and Google Scholar) were searched without year or language restrictions for relevant studies. The study protocol was registered with PROSPERO (CRD42020175344). Eighty-three studies involving a total of 43,341 participants were included. The random-effects model was employed to calculate the summary estimates. A pooled global prevalence of 2.5% (95% CI: 1.8-3.4) was obtained for dengue and chikungunya coinfection. Males and females appear to be coinfecting at a fairly similar rate. Among the regions, Asia accounted for the highest prevalence (3.3%, 95% CI: 2.3-4.6) while North America was the least (0.8%, 95% CI: 0.3-2.4). The prevalence estimates varied across different countries. A much higher prevalence rates were obtained for Colombia (37.4%, 95% CI: 9.1-78.1), Madagascar (18.2%, 95% CI: 10.1-30.6), Laos (12.5%, 95% CI: 5.3-26.7), Maldives (4.5%, 95% CI: 1.5-13.0) and Thailand (3.7%, 95% CI: 0.4-26.3). This first extensive systematic review and meta-analysis reveals dengue and chikungunya coinfection as a global problem worthy of consideration. It is therefore pertinent that both infections be assessed during diagnosis, mosquito vector control practices be implemented, and vaccine development strides be supported globally.

Could species-focused suppression of *Aedes aegypti*, the yellow fever mosquito, and *Aedes albopictus*, the tiger mosquito, affect interacting predators? An evidence synthesis from the literature.

Revue de littérature

Bonds, J., Collins, C., Gouagna, L.
07-04-2022

Pest Manag Sci

<https://doi.org/10.1002/ps.6870>

The risks of *Aedes aegypti* and *Aedes albopictus* nuisance and vector-borne diseases are rising and the adverse effects of broad-spectrum insecticide application have promoted species-specific techniques, such as sterile insect technique (SIT) and other genetic strategies, as contenders in their control operations. When specific vector suppression is proposed, potential effects on predators and wider ecosystem are some of the first stakeholder questions. These are not the only *Aedes* vectors of human diseases, but are those for which SIT and genetic strategies are of most interest. They vary ecologically and in habitat origin, but both have behaviorally human-adapted forms with expanding ranges. The aquatic life stages are where predation is strongest due to greater resource predictability and limited escape opportunity. These vectors' anthropic forms usually use ephemeral water bodies and man-made containers as larval habitats; predators that occur in these are mobile, opportunistic and generalist. No literature indicates that any predator depends on larvae of either species. As adults, foraging theory predicts these mosquitoes are of low profitability to predators. Energy expended hunting and consuming will mostly outweigh their energetic benefit. Moreover, as adult biomass is mobile and largely disaggregated, any predator is likely to be a generalist and opportunist. This work, which summarizes much of the literature currently available on the predators of *Ae. aegypti* and *Ae. albopictus*, indicates it is highly unlikely that any predator species depends on them. Species-specific vector control to reduce nuisance and disease is thus likely to be of negligible or limited impact on nontarget predators. © 2022 The Authors. Pest Management Science published by John Wiley & Sons Ltd on behalf of Society of Chemical Industry.

Zika virus infection and pregnancy outcomes in the United States, 2017-2019.

Youssefzadeh, A., Mandelbaum, R., Donovan, K., Klar, M., Ouzounian, J., Matsuo, K.

18-03-2022

Int J Gynaecol Obstet

<https://doi.org/10.1002/ijgo.14173>

Arm Blanch Test-A Simple Sign for Dengue Diagnosis.

Adhisivam, B., Chandrasekaran, V.

08-03-2022

Indian J Pediatr

<https://doi.org/10.1007/s12098-022-04140-0>

Essential oil of *Piper purusianum* C.DC (Piperaceae) and its main sesquiterpenes: biodefensives against malaria and dengue vectors, without lethal effect on non-target aquatic fauna.

de Oliveira, A., Simões, R., Lima, C., da Silva, F., Nunomura, S., Roque, R., Tadei, W., Nunomura, R.
18-02-2022

Environ Sci Pollut Res Int

<https://doi.org/10.1007/s11356-022-19196-w>

The mosquito vectors of the genera *Aedes* and *Anopheles* present resistance to several commercial insecticides, which are also toxic to non-predator targets. On the other hand, essential oils are a promising source of insecticides. Thus, in this work, the essential oil from the leaves of *Piper purusum* was characterized by gas chromatography-based approaches and evaluated as biodefensive against malaria and dengue vectors. The main compounds of *P. purusum* essential oil were β -caryophyllene (57.05%), α -humulene (14.50%), and germacrene D (8.20%). The essential oil inhibited egg hatching (7.6 ± 1.5 to $95.6 \pm 4.5\%$), caused larval death (LC_{50} from 49.84 to 51.60 ppm), and inhibited the action of acetylcholinesterase (IC_{50} of 2.29 $\mu\text{g/mL}$), which can be related to the mechanisms of action. On the other hand, the biological activities of β -caryophyllene, α -humulene, and germacrene D were higher than that of essential oil. In addition, these sesquiterpenes and essential oil did not show a lethal effect on *Toxorhynchites splendens*, *Anisops bouvieri*, *Gambusia affinis*, and *Diplonychus indicus* (LC_{50} from 2098.80 to 7707.13 ppm), although *D. indicus* is more sensitive (SI/PSF from 48.56 to 252.02 ppm) to essential oil, representing a natural alternative against these relevant vectors.

Investigating Zika-Microcephaly's 'Crash'.

Bock, R.

11-02-2022

Am J Med

<https://pubmed.ncbi.nlm.nih.gov/35151616>

Differences in Placental Histology Between Zika Virus-infected Teenagers and Older Women.

Santos, G., Pinto, C., Prudente, R., Witkin, S., Arandes, A., Rodrigues, L., Zatz, M., Massad, E., Passos, S., Zika Consortium
04-08-2021

Int J Gynecol Pathol

<https://doi.org/10.1097/PGP.0000000000000807>

In pregnant women, Zika virus (ZIKV) is associated with a congenital syndrome, most frequently involving damage to embryo brain formation and the development of microcephaly. The mechanism(s) by which ZIKV enters the maternal-fetal interface and is transmitted to the fetus remains incompletely determined. We sought to evaluate histologic changes in the placenta of ZIKV-infected pregnant women and to determine if this varied by maternal age. Placental samples were obtained from 66 women, 33 of whom were positive for ZIKV. Histologic evaluations were performed on 4 areas of the placenta: fetal surface, maternal surface, umbilical cord, and membranes. Samples were analyzed by the tissue microarray technique and tested for CD4, CD8, CD20, CD68, FOXP3, and cyclooxygenase-2 expression. Data

were evaluated using Fisher exact test. ZIKV infection was more frequent in women less than 18yr of age (9/11, 81.8%) than in women above 18yr old (24/55, 43.6%) ($P=0.0440$). ZIKV detection was associated with neutrophilic chorioamnionitis ($P=0.0332$) and with septal ($P=0.0244$) and villous ($P=0.0534$) calcification. Hofbauer cell hyperplasia ($P=0.0260$) and cyclooxygenase-2 expression ($P=0.0346$) were more prevalent in ZIKV-positive women aged 18yr and below than in the older ZIKV-positive women. ZIKV infection during pregnancy occurs more frequently in adolescents and induces higher rates of damage at the maternal-fetal interface than in older women.

Our issue or their issue? Media coverage and framing of the Zika virus epidemic.

Jamieson, T., Rivera, J.

03-05-2022

Disasters

<https://doi.org/10.1111/disa.12497>

How does the news media respond to health emergencies abroad? Between 2015 and 2018, Zika virus spread rapidly throughout Latin America before arriving in the continental United States. Despite the risks to adults and newborns, it is unclear how media coverage developed and framed the threat for its audience. In this paper, we argue that while the frequency of coverage was responsive to infections, its content failed to promote proactive health behaviour. To assess these claims, we analyse each of 442 articles dealing with Zika virus published by The New York Times from 2015-18. We find that the amount of coverage reflected infections but did not change once the disease emerged in the US. Furthermore, content analysis using Linguistic Inquiry and Word Count software reveals that coverage emphasised differences between communities (those affected and those at home) and that present and past time orientations dominated coverage as opposed to future time orientations.

Computational-aided design: minimal peptide sequence to block dengue virus transmission into cells.

Arumugam, A., Agharbaoui, F., Khazali, A., Yusof, R., Abd Rahman, N., Ahmad Fuaad, A.

31-12-2020

J Biomol Struct Dyn

<https://doi.org/10.1080/07391102.2020.1866074>

Dengue virus (DV) infection is one of the main public health concerns, affecting approximately 390 million people worldwide, as reported by the World Health Organization. Yet, there is no antiviral treatment for DV infection. Therefore, the development of potent and nontoxic anti-DV, as a complement for the existing treatment strategies, is urgently needed. Herein, we investigate a series of small peptides inhibitors of DV antiviral activity targeting the entry process as the promising strategy to block DV infection. The peptides were designed based on our previously reported peptide

sequence, DN58opt (TWWCFYFCRRHHPFWFFYRHN), to identify minimal effective inhibitory sequence through molecular docking and dynamics studies. The *in silico* designed peptides were synthesized using conventional Fmoc solid-phase peptide synthesis chemistry, purified by RP-HPLC and characterized using LCMS. Later, they were screened for their antiviral activity. One of the peptides, **AC 001**, was able to reduce about 40% of DV plaque formation. This observation correlates well with the molecular mechanics-Poisson-Boltzmann surface area (MM-PBSA) analysis - **AC 001** showed the most favorable binding affinity through 60ns simulations. Pairwise residue decomposition analysis has revealed four key residues that contributed to the binding of these peptides into the DV2 E protein pocket. This work identifies the minimal peptide sequence required to inhibit DV replication and explains the behavior observed on an atomic level using computational study. Communicated by Ramaswamy H. Sarma.

Targeting a conserved pocket (n-octyl- β -D-glucoside) on the dengue virus envelope protein by small bioactive molecule inhibitors.

Naresh, P., Selvaraj, A., Shyam Sundar, P., Murugesan, S., Sathianarayanan, S., Namboori P K, K., Jubie, S.
21-12-2020

J Biomol Struct Dyn

<https://doi.org/10.1080/07391102.2020.1862707>

Dengue virus enters the cell by receptor-mediated endocytosis followed by a viral envelope (DENVE) protein-mediated membrane fusion. A small detergent molecule n-octyl- β -D-glucoside (β OG) occupies the hydrophobic pocket which is located in the hinge region plays a major role in the rearrangement. It has been reported that mutations occurred in this binding pocket lead to the alterations of pH threshold for fusion. In addition to this event, the protonation of histidine residues present in the hydrophobic pocket would also impart the conformational change of the E protein evidence this pocket as a promising target. The present study identified novel cinnamic acid analogs as significant blockers of the hydrophobic pocket through molecular modeling studies against DENVE. A library of seventy-two analogs of cinnamic acid was undertaken for the discovery process of DENV inhibitors. A Molecular docking study was used to analyze the binding mechanism between these compounds and DENV followed by ADMET prediction. Binding energies were predicted by the MMGBSA study. The Molecular dynamic simulation was utilized to confirm the stability of potential compound binding. The compounds CA and SCA derivatives have been tested against HSV-1 & 2 viruses. From the computational results, the compounds CA1, CA2, SCA 60, SCA 57, SCA 37, SCA 58, and SCA 14 exhibited favorable interaction energy. The compounds have *in-vitro* antiviral activity; the results clearly indicate that the compounds showed the activity against both the viruses (HSV-1 & HSV-2). Our study provides valuable information on the discovery of small molecules DENVE inhibitors. Communicated by Ramaswamy H. Sarma.

A program to automate the discovery of drugs for West Nile and Dengue virus-programmatic screening of over a billion compounds on PubChem, generation of drug leads and automated *in silico* modelling.

Geoffrey, B., Sanker, A., Madaj, R., Tresanco, M., Upadhyay, M., Gracia, J.

04-12-2020

J Biomol Struct Dyn

<https://doi.org/10.1080/07391102.2020.1856185>

Our work is composed of a python program for programmatic data mining of PubChem to collect data to implement a machine learning-based AutoQSAR algorithm to generate drug leads for the flaviviruses-Dengue and West Nile. The drug leads generated by the program are fed as programmatic inputs to AutoDock Vina package for automated *in silico* modelling of interaction between the compounds generated as drug leads by the program and the chosen Dengue and West Nile drug target methyltransferase, whose inhibition leads to the control of viral replication. The machine learning-based AutoQSAR algorithm involves feature selection, QSAR modelling, validation and prediction. The drug leads generated, each time the program is run, are reflective of the constantly growing PubChem database which is an important dynamic feature of the program which facilitates fast and dynamic drug lead generation against the West Nile and Dengue viruses. The program prints out the top drug leads after screening PubChem library which is over a billion compounds. The interaction of top drug lead compounds generated by the program and drug targets of West Nile and Dengue virus was modelled in an automated way through the tool. The results are stored in the working folder of the user. Thus, our program ushers in a new age of automatic ease in the virtual drug screening and drug identification through programmatic data mining of chemical data libraries and drug lead generation through machine learning-based AutoQSAR algorithm and an automated *in silico* modelling run through the program to study the interaction between the drug lead compounds and the drug target protein of West Nile and Dengue virus. The program is hosted, maintained and supported at the GitHub repository link given below. Communicated by Ramaswamy H. Sarma.

Structural determinants of TRPV4 inhibition and identification of new antagonists with antiviral activity.

Doñate-Macian, P., Duarte, Y., Rubio-Moscardo, F., Pérez-Vilaró, G., Canan, J., Díez, J., González-Nilo, F., Valverde, M.
15-10-2020

Br J Pharmacol

<https://doi.org/10.1111/bph.15267>

Background and Purpose: The transient receptor potential vanilloid 4 (TRPV4) cation channel participates in multiple physiological processes and is also at the core of different diseases, making this channel an interesting pharmacological target with therapeutic potential. However, little is known

about the structural elements governing its inhibition. **Experimental Approach:** We have now combined in silico drug discovery and molecular dynamics simulation based on *Xenopus tropicalis* xTRPV4 structure with functional studies measuring cell Ca^{2+} influx mediated by human TRPV4 channel to characterize the binding site of known TRPV4 inhibitors and to identify novel small molecule channel modulators. **Key Results:** We have found that the inhibitor HC067047 binds to a pocket conformed by residues from S2-S3 linker (xTRPV4-D542), S4 (xTRPV4-M583 and Y587 and S5 (xTRPV4-D609 and F613). This pocket was also used for structure-based virtual screening in the search of novel channel modulators. Forty potential hits were selected based on the lower docking scores (from ~250,000 compounds) and their effect upon TRPV4 functionally tested. Three were further analysed for stability using molecular dynamics simulation and functionally tested on TRPV4 channels carrying mutations in the binding pocket. Compound NSC151066, shown to require residue xTRPV4-M583 for its inhibitory effect, presented an IC_{50} of 145 nM and demonstrated to be an effective antiviral against Zika virus with a potency similar to HC067047. **Conclusion and Implications:** Together, we propose structural insights into the inhibition of TRPV4 and how this information can be used for the design of novel channel modulators.

RAGE

Safety and immunogenicity of a serum-free purified Vero rabies vaccine in healthy adults: A randomised phase II pre-exposure prophylaxis study.

Pichon, S., Moureau, A., Petit, C., Chu, L., Essink, B., Muse, D., Saleh, J., Guinet-Morlot, F., Minutello, A.
28-06-2022

Vaccine

<https://pubmed.ncbi.nlm.nih.gov/35778281>

A serum-free, highly purified Vero cell rabies vaccine (PVRV-NG) is under development. We previously demonstrated that pre-exposure prophylaxis (PrEP) with PVRV-NG had a satisfactory safety profile and was immunogenically non-inferior to the licensed purified Vero cell rabies vaccine in adults. Here, we evaluated the safety and immunogenic non-inferiority of PrEP with PVRV-NG compared to the licensed human diploid cell vaccine (HDCV) in healthy adults (NCT01784874). Participants received three vaccinations (days 0, 7, and 28) as PrEP with or without a booster injection after 12 months. Rabies virus neutralising antibodies (RVNA) were evaluated on days 0, 28 (subgroup only), and 42, and Months 6, 12, and 12 + 14 days (booster group only). Non-inferiority (first primary objective) was based on the proportion of participants with RVNA titres ≥ 0.5 IU/mL (World Health Organization criteria for seroconversion) on day 42, expected to be $\geq 99\%$ (second primary objective). Safety was evaluated after each dose and monitored throughout the study. At day

42, PVRV-NG was non-inferior to HDCV and the first primary objective was met; seroconversion was observed for 98.3% of PVRV-NG recipients and 99.1% of HDCV recipients. As $< 99\%$ of participants in the PVRV-NG group had RVNA titres ≥ 0.5 IU/mL, the second primary objective was not met. Booster vaccination produced a strong increase in RVNA titres for all groups, primed with PVRV-NG or HDCV. RVNA geometric mean titres tended to be higher for HDCV than PVRV-NG primary vaccine recipients. In a complementary evaluation using alternative criteria for seroconversion (complete virus neutralization at 1:5 serum dilution), 99.6% and 100% of participants in the PVRV-NG and HDCV groups, respectively, achieved seroconversion across the vaccine groups. No major safety concerns were observed during the study. PVRV-NG was well tolerated, with a similar safety profile to HDCV in terms of incidence, duration, and severity of adverse events after primary and booster vaccinations. ClinicalTrials.gov number: NCT01784874.

Accessibility to rabies centers and human rabies post-exposure prophylaxis rates in Cambodia: A Bayesian spatio-temporal analysis to identify optimal locations for future centers.

Baron, J., Chevalier, V., Ly, S., Duong, V., Dussart, P., Fontenille, D., Peng, Y., Martínez-López, B.

30-06-2022

PLoS Negl Trop Dis

<https://doi.org/10.1371/journal.pntd.0010494>

Rabies is endemic in Cambodia. For exposed humans, post-exposure prophylaxis (PEP) is very effective in preventing this otherwise fatal disease. The Institut Pasteur du Cambodge (IPC) in Phnom Penh was the primary distributor of PEP in Cambodia until 2018. Since then, and to increase distribution of PEP, two new centers have been opened by IPC in the provinces of Battambang and Kampong Cham. Data on bitten patients, who sometimes bring the head of the biting animal for rabies analyses, have been recorded by IPC since 2000. However, human cases are not routinely recorded in Cambodia, making it difficult to establish a human burden of disease and generate a risk map of dog bites to inform the selection of future PEP center locations in high-risk areas. Our aim was to assess the impact of accessibility to rabies centers on the yearly rate of PEP patients in the population and generate a risk map to identify the locations where new centers would be the most beneficial to the Cambodian population. To accomplish this, we used spatio-temporal Bayesian regression models with the number of PEP patients as the outcome. The primary exposure variable considered was travel time to the nearest IPC center. Secondary exposure variables consisted of travel time to a provincial capital and urban proportion of the population. Between 2000 and 2016, a total of 293,955 PEP patient records were identified. Our results showed a significant negative association between travel time to IPC and the rate of PEP patients: an increase in one hour travel time from the living location to IPC PEP centers leads to a reduction in PEP rate of 70% to 80%. Five provinces were identified as the most efficient locations for

future centers to maximize PEP accessibility: Banteay Meanchey, Siem Reap, Takeo, Kampot and Svay Rieng. Adding a PEP center in every provincial capital would increase the proportion of Cambodians living within 60 minutes of a PEP center from 26.6% to 64.9%, and living within 120 minutes from 52.8% to 93.3%, which could save hundreds of lives annually.

Spatial and temporal activity patterns of owned, free-roaming dogs in coastal eastern Australia.

Sparkes, J., Körtner, G., Ballard, G., Fleming, P.

04-04-2022

Prev Vet Med

<https://pubmed.ncbi.nlm.nih.gov/35461143>

Dogs are ubiquitous and strongly associated with human communities, but many roam freely, away from the owners' property and control. Free-roaming owned dogs can pose risks through disease transmission to and from other dogs, attacking domestic animals, fauna or humans, and involvement in road accidents. However, little research has focused on understanding their movement ecology, thereby hindering the development of effective management plans. We modified store-bought GPS collars and used them to track a sample of 43 free-roaming owned dogs from peri-urban sites in north-east New South Wales and south-east Queensland, Australia. Our aim was to quantify the activity ranges of owned dogs and the distances they travelled, whether free-roaming or accompanying people, and to identify some associated factors. The total activity ranges of our sample of dogs were variable (0.80-1776.20 ha), and the mean daily activity range of collared dogs was relatively large (7.23 ± 11.99 ha), with mean daily accumulated distances travelled ranging from 0.25 to 4.81 km (mean = 1.95 ± 1.10 km). The dogs exhibited two temporal activity peaks, one between 0700 and 1000 and a second between 1600 and 1900 hrs. Most human-mediated dog movements were short in duration, ranging from 45 min to 6 h, with dogs moving an average of 48.60 ± 64.00 km, but up to 329.00 km from their home. The large activity ranges and relatively long movements in this sample of free-roaming owned dogs suggests they have potential to contribute to the spread of exotic and endemic zoonotic and canid diseases in the peri-urban coastal regions of eastern Australia. The baseline information collected here is crucial to our understanding of disease transmission among peri-urban dogs, and modelling spread within and between communities. Additionally, it provides valuable information for authorities seeking to improve management of free-roaming owned dogs.

Compatibility between a rabies vaccine and two canine combined vaccines against canine distemper, adenovirus, parvovirus, parainfluenza virus disease and leptospirosis, with or without canine coronavirus.

Thibault, J., Bouvet, J., Cupillard, L., Cariou, C., Oberli, F.

02-04-2022

Comp Immunol Microbiol Infect Dis

<https://pubmed.ncbi.nlm.nih.gov/35429805>

In many countries, vaccination programs still require dogs to be vaccinated against rabies in addition to Canine distemper virus (CDV), adenovirus (CAV), parvovirus (CPV), parainfluenza virus (CPIV), Leptospira (L) or Canine coronavirus (CCV= Cv). Few vaccines containing all these antigens are commercially available and, unless compatibility between the vaccines was demonstrated, concurrent administration of a DAPPI-L(Cv) vaccine and a vaccine against rabies should not be recommended. This may be of concern for practitioners who wish to vaccinate dogs with all components on the same day. This study aimed at evaluating immunological compatibility between a monovalent rabies vaccine (Rabisin™) and two large combination vaccines against CDV, CAV, CPV, CPIV with 2 leptospira components +Cv (Recombitek® C6/Cv) or with 4 Leptospira components (Recombitek® C8), when injected concomitantly at two separate injection sites. Fourteen days after administration of the rabies vaccine, with or without concomitant administration of combo vaccines, all dogs had seroconverted against rabies and maintained protective titers over the duration of the study. In addition, 100% of the puppies vaccinated with one or the other combo vaccines seroconverted against CDV, CAV, CPV, CPIV (CCV) and Leptospira, whatever the vaccination group. Lack of immunological interference between Rabisin™ and all components of the Recombitek® C6/Cv or Recombitek® C8 Combo vaccines was demonstrated by non-inferiority analysis, except for CDV in the Recombitek®C8+ Rabisin™ group. Based on these results, a concomitant administration of Rabisin™ with Recombitek® C6/Cv or Recombitek® C8 can be recommended in daily practice, which can be essential for facilitating vaccination compliance.

Lentiviral Expression of Rabies Virus Glycoprotein in the Rat Hippocampus Strengthens Synaptic Plasticity.

Ghassemi, S., Asgari, T., Mirzapour-Delavar, H., Aliakbari, S.,

Pourbadie, H., Prehaud, C., Lafon, M., Gholami, A.,

Azadmanesh, K., Naderi, N., Sayyah, M.

19-01-2021

Cell Mol Neurobiol

<https://doi.org/10.1007/s10571-020-01032-9>

Rabies virus (RABV) is a neurotropic virus exclusively infecting neurons in the central nervous system. RABV encodes five proteins. Among them, the viral glycoprotein (RVG) plays a key role in viral entry into neurons and rabies pathogenesis. It was shown that the nature of the C-terminus of the RABV G protein, which possesses a PDZ-binding motif (PBM), modulates the virulence of the RABV strain. The neuronal protein partners recruited by this PBM may alter host cell function. This study was conducted to investigate the effect of RVG on synaptic function in the hippocampal dentate gyrus (DG) of rat. Two μ l (10^8 T.U./ml) of the lentiviral vector containing RVG gene was injected into the DG of rat hippocampus. After 2 weeks, the rat's brain was cross-

sectioned and RVG-expressing cells were detected by fluorescent microscopy. Hippocampal synaptic activity of the infected rats was then examined by recording the local field potentials from DG after stimulation of the perforant pathway. Short-term synaptic plasticity was also assessed by double pulse stimulation. Expression of RVG in DG increased long-term potentiation population spikes (LTP-PS), whereas no facilitation of LTP-PS was found in neurons expressing δ RVG (deleted PBM). Furthermore, RVG and δ RVG strengthened paired-pulse facilitation. Heterosynaptic long-term depression (LTD) in the DG was significantly blocked in RVG-expressing group compared to the control group. This blockade was dependent to PBM motif as rats expressing δ RVG in the DG-expressed LTD comparable to the RVG group. Our data demonstrate that RVG expression facilitates both short- and long-term synaptic plasticity in the DG indicating that it may involve both pre- and postsynaptic mechanisms to alter synaptic function. Further studies are needed to elucidate the underlying mechanisms.

TRACHOME

Mass drug administration of antibacterials: weighing the evidence regarding benefits and risks.

Revue de littérature

Rolfe, R., Shaikh, H., Tillekeratne, L.
30-06-2022

Infect Dis Poverty

<https://doi.org/10.1186/s40249-022-00998-6>

Background: Mass drug administration (MDA) is a strategy to improve health at the population level through widespread delivery of medicine in a community. We surveyed the literature to summarize the benefits and potential risks associated with MDA of antibacterials, focusing predominantly on azithromycin as it has the greatest evidence base. **Main body:** High-quality evidence from randomized controlled trials (RCTs) indicate that MDA-azithromycin is effective in reducing the prevalence of infection due to yaws and trachoma. In addition, RCTs suggest that MDA-azithromycin reduces under-five mortality in certain low-resource settings that have high childhood mortality rates at baseline. This reduction in mortality appears to be sustained over time with twice-yearly MDA-azithromycin, with the greatest effect observed in children <1 year of age. In addition, observational data suggest that infections such as skin and soft tissue infections, rheumatic heart disease, acute respiratory illness, diarrheal illness, and malaria may all be treated by azithromycin and thus incidentally impacted by MDA-azithromycin. However, the mechanism by which MDA-azithromycin reduces childhood mortality remains unclear. Verbal autopsies performed in MDA-azithromycin childhood mortality studies have produced conflicting data and are underpowered to answer this question. In addition to benefits, there are several

important risks associated with MDA-azithromycin. Direct adverse effects potentially resulting from MDA-azithromycin include gastrointestinal side effects, idiopathic hypertrophic pyloric stenosis, cardiovascular side effects, and increase in chronic diseases such as asthma and obesity. Antibacterial resistance is also a risk associated with MDA-azithromycin and has been reported for both gram-positive and enteric organisms. Further, there is the risk for cross-resistance with other antibacterial agents, especially clindamycin. **Conclusions:** Evidence shows that MDA-azithromycin programs may be beneficial for reducing trachoma, yaws, and mortality in children <5 years of age in certain under-resourced settings. However, there are significant potential risks that need to be considered when deciding how, when, and where to implement these programs. Robust systems to monitor benefits as well as adverse effects and antibacterial resistance are warranted in communities where MDA-azithromycin programs are implemented.

Evaluation of the efficacy of insecticide-treated scarves to protect children from the trachoma vector *Musca sorbens* (Diptera: Muscidae): A phase II randomised controlled trial in Oromia, Ethiopia.

Robinson, A., Gomes, L., Abdurahman, O., Alemayehu, W., Shuka, G., Melese, E., Guye, M., Legesse, D., Elias, E., Temam, K., Koro, K., Adugna, D., Seife, F., Aga, M., Sarah, V., Lambert, S., Walker, S., Habtamu, E., Solomon, A., Last, A., Macleod, D., Burton, M., Logan, J.
08-06-2022

EClinicalMedicine

<https://doi.org/10.1016/j.eclinm.2022.101487>

Background: The eye-seeking fly *Musca sorbens* can act as a vector for ocular *Chlamydia trachomatis*, causing trachoma, yet there has been very little research on control measures. We investigated whether insect repellent products, specifically insecticide-treated clothing, could provide personal protection to the user from eye-seeking flies. **Methods:** We first conducted a series of phase I laboratory studies to inform our choice of field intervention. We then conducted a phase II randomised controlled trial testing the efficacy of permethrin-treated scarves (PTS) in reducing fly-face contact in Oromia, Ethiopia. Children aged 4-10 years in full health and with no known adverse reactions to permethrin or other insecticides were allocated to either arm using restricted randomisation. Intervention arm children wore Insect Shield® versatile wraps (as PTS) for 28 days. The primary outcomes, fly-eye, -nose and -mouth contact, were assessed on the first day (0/30/60/180 minutes), on day 7 and on day 28. All participants present per timepoint were included in analyses. This trial was registered with ClinicalTrials.gov (NCT03813069). **Findings:** Participants were recruited to the field trial between 29/10/2019 and 01/11/2019, 58 were randomised to test or control arm. More fly (-eye, -nose and -mouth) contacts were observed in the PTS arm at baseline. After adjusting for baseline contact rates, across all timepoints there was a 35% decrease in fly-eye contacts in the PTS relative to control arm (rate ratio [RR] 0.65, 95% CI 0.52-0.83). Similar cross-timepoint reductions

were seen for fly-nose and fly-mouth contacts (RR 0.69, 95% CI 0.51-0.92 and RR 0.79, 95% CI 0.62-1.01, respectively). All children were included on day 0. Two in the control arm were absent on day 7, one left the study and four were excluded from analysis at day 28. No adverse events occurred in the trial. **Interpretation:** *Musca sorbens* flies are sufficiently repelled by PTS to reduce fly-eye contacts for the wearer, thus possibly reducing the risk of trachoma transmission. Permethrin-treated scarves may therefore be an alternative to insecticide space spraying for protection from these flies. **Funding:** Wellcome Trust.

ULCÈRE DE BURULI

PIAN

Mass drug administration of antibacterials: weighing the evidence regarding benefits and risks.

Revue de littérature

Rolfe, R., Shaikh, H., Tillekeratne, L.
30-06-2022

Infect Dis Poverty

<https://doi.org/10.1186/s40249-022-00998-6>

Background: Mass drug administration (MDA) is a strategy to improve health at the population level through widespread delivery of medicine in a community. We surveyed the literature to summarize the benefits and potential risks associated with MDA of antibacterials, focusing predominantly on azithromycin as it has the greatest evidence base. **Main body:** High-quality evidence from randomized controlled trials (RCTs) indicate that MDA-azithromycin is effective in reducing the prevalence of infection due to yaws and trachoma. In addition, RCTs suggest that MDA-azithromycin reduces under-five mortality in certain low-resource settings that have high childhood mortality rates at baseline. This reduction in mortality appears to be sustained over time with twice-yearly MDA-azithromycin, with the greatest effect observed in children <1 year of age. In addition, observational data suggest that infections such as skin and soft tissue infections, rheumatic heart disease, acute respiratory illness, diarrheal illness, and malaria may all be treated by azithromycin and thus incidentally impacted by MDA-azithromycin. However, the mechanism by which MDA-azithromycin reduces childhood mortality remains unclear. Verbal autopsies performed in MDA-azithromycin childhood mortality studies have produced conflicting data and are underpowered to answer this question. In addition to benefits, there are several important risks associated with MDA-azithromycin. Direct adverse effects potentially resulting from MDA-azithromycin include gastrointestinal side effects, idiopathic hypertrophic

pyloric stenosis, cardiovascular side effects, and increase in chronic diseases such as asthma and obesity. Antibacterial resistance is also a risk associated with MDA-azithromycin and has been reported for both gram-positive and enteric organisms. Further, there is the risk for cross-resistance with other antibacterial agents, especially clindamycin. **Conclusions:** Evidence shows that MDA-azithromycin programs may be beneficial for reducing trachoma, yaws, and mortality in children <5 years of age in certain under-resourced settings. However, there are significant potential risks that need to be considered when deciding how, when, and where to implement these programs. Robust systems to monitor benefits as well as adverse effects and antibacterial resistance are warranted in communities where MDA-azithromycin programs are implemented.

LEPRE

Hansen's disease and COVID-19 co-infection in Brazil.

Repsold, T., Collin, S., Bouth, R., Cerqueira, S., Brezinski, M., Peixoto, R., Fonseca, A., Peixoto, M., Rabelo Mendes, S., Gomes, C., Salgado, C., Daps, P.

01-07-2022

Int J Dermatol

<https://doi.org/10.1111/ijd.16319>

Background: The implications of COVID-19 co-infection in patients under treatment for Hansen's disease (HD, leprosy) remain uncertain. We aimed to describe clinical characteristics, treatments, and outcomes in patients with HD and COVID-19 in Brazil. **Methods:** Cross-sectional study recruiting adult HD patients with PCR-confirmed COVID-19 from five HD treatment centers in Brazil between March 1, 2020, and March 31, 2021. At the time of this study, no patient had received COVID-19 vaccine. **Results:** Of 1377 patients under treatment for HD, 70 (5.1%) were diagnosed with COVID-19. Of these, 41 (58.6%) had PCR-confirmed COVID-19, comprising 19 men and 22 women, aged 24-67 (median 45) years. HD was multibacillary in 39/41 patients. Eight patients ceased WHO Multi-Drug Therapy for HD, three for lack of drugs, two because of COVID-19, and three for other reasons. Of the 33 who continued treatment, 26 were on the standard regimen and seven on an alternative regimen. Seventeen patients were receiving oral prednisone, including nine patients with type 1 reaction, four with type 2 reaction, three with neuritis, and one with rheumatologic disease. Twelve patients were hospitalized for COVID-19, and six patients died, of whom three had hypertension and one also had type 2 diabetes and obesity. **Conclusions:** COVID-19 and Hansen's disease co-infection did not appear to change the clinical picture of either disease in this cross-sectional study. The wider impact of the pandemic on persons affected by HD requires follow-up and monitoring.

Nasal septal perforation in advanced lepromatous leprosy: A report of two cases with endoscopic findings.

Sambangi, J., Prabhakaran, N., Annam, C., Gopinath, H., Bakshi, S., Aggarwal, N.

01-07-2022

Trop Doct

<https://doi.org/10.1177/00494755221111698>

Sensitivity of different DNA extraction methods and PCR to detect resistance in patients with leprosy stratified by the bacilloscopic index.

Sevilha-Santos, L., Aquino, D., Neto, G., Costa, F., de Sousa, C., Morelo, E., Moreira Dos Santos Júnior, A., Gomes, C.

27-06-2022

Braz J Infect Dis

<https://pubmed.ncbi.nlm.nih.gov/35772498>

Introduction: Antimicrobial resistance in leprosy is an emerging problem, and the quantitative impact of low bacilloscopic indexes (BIs) on the sensitivity of molecular tests is unknown. We aimed to evaluate the sensitivity of gene sequencing for the detection of mutations related to antimicrobial resistance in *Mycobacterium leprae* in patients with low BIs using an analytical model. **Methods:** Patients with leprosy were included and divided into two groups depending on their BIs ($\geq 2+$ and $< 2+$). The sensitivities of the two DNA extraction methods were compared after amplifying and sequencing the repetitive element (RLEP), *folP1*, *rpoB* and *gyrA* in *M. leprae*. **Results:** We included 56 patients with leprosy: 35 had BIs less than 2+ (22 had negative slit-skin smear [SSS] results) and 21 patients had BIs greater than or equal to 2+. The sensitivity of the amplification of the RLEP target and the gene sequencing of *folP1*, *rpoB* and *gyrA* was 50 to 70% lower in patients with a BI less than 2+ and was significantly reduced in patients with lower BIs for all targets ($p < 0.001$). One patient had a mutation in the *folP1* gene, and 14 patients had mutations in the *gyrA* gene, but no mutations related to antimicrobial resistance were found. **Conclusions:** We can conclude that the sensitivity of molecular tests is directly related to the BI, but these tests can still detect up to 20% of the targets in patients with BIs $< 2+$. New strategies to improve the sensitivity for detecting antimicrobial resistance in leprosy patients and reasonable clinical criteria for follow-up and the introduction of alternative treatments must be developed.

Reactions in leprosy patients triggered by COVID-19 vaccination - A cross-sectional study from a tertiary care centre in India.

Bhandari, A., Shilpa, ., Gupta, S., Dogra, S., Narang, T.

30-06-2022

J Eur Acad Dermatol Venereol

<https://doi.org/10.1111/jdv.18390>

Virchowian leprosy madarosis: Histological evidence of a permanent non-cicatricial alopecia.

Brito, F., Donati, A., Kakizaki, P., Valente, N., Michalany, N., Machado, C., Hirata, S.

30-06-2022

J Eur Acad Dermatol Venereol

<https://doi.org/10.1111/jdv.18393>

Spectrum of skin diseases in Maroon villages of the Maroni area, French Guiana.

Valentin, J., Niemetzky, F., Gaillet, M., Michaud, C., Carbanar, A., Demar, M., Couppie, P., Blaizot, R.

29-06-2022

Int J Dermatol

<https://doi.org/10.1111/ijd.16324>

Background: Due to their genetic characteristics and their high exposure to infectious diseases, Maroons are likely to suffer from a specific spectrum of skin diseases. However, skin disorders have never been explored in this population. We aimed to describe all skin diseases in Maroon villages of the Maroni region in French Guiana. **Methods:** This retrospective study concerned all patients who consulted in the remote health centers of Apatou, Grand-Santi, Papaichton, and Maripasoula between October 5, 2017, and June 30, 2020. We included all patients registered with a skin disorder (International Classification of Diseases) in the medical database. We excluded patients whose diagnosis was invalidated after cross-checking by a dermatologist. **Results:** A total of 4741 patients presented at least one skin disease, for 6058 different disorders. Nonsexually transmitted infections represented 71.6% of all diagnoses, followed by inflammatory diseases (9.8%) and bites/envenomations (4.6%). The three most frequent conditions were scabies, abscesses, and impetigo. Besides scabies, neglected tropical diseases (NTDs) were still prevalent as we reported 13 cases of leprosy and 63 cutaneous leishmaniasis. Atopic dermatitis (AD) represented only 2.5% of our diagnoses. **Conclusions:** With the exception of AD, which was less frequent among Maroons, these results are similar to those previously reported in Amerindians. Therefore, a common exposure to rainforest pathogens seems to induce a common spectrum of skin diseases dominated by infections. The high prevalence of NTDs requires specific public health actions.

A spectrum of leprosy reactions triggered by Covid-19 vaccination: a series of four cases.

Saraswat, N., Tripathy, D., Kumar, S., Awasthi, P., Gopal, M.

29-06-2022

J Eur Acad Dermatol Venereol

<https://doi.org/10.1111/jdv.18339>

Chromoblastomycosis-Leprosy Co-Infection in Central West Brazil. Presentation of Three Cases and Literature Review.

Guevara, A., Vicente, V., de Souza Lima, B., Nery, A., Hagen, F., Hahn, R.

28-06-2022

Mycopathologia

<https://doi.org/10.1007/s11046-022-00646-5>

Chromoblastomycosis and leprosy are chronic diseases with high prevalence in tropical and subtropical regions. Brazil is one of the countries with the highest incidence and prevalence for both diseases, however, reports of co-infections are scarce. The aim of this study was to describe three cases of chromoblastomycosis-leprosy co-infection in patients from Mato Grosso state, Brazil. A review of chromoblastomycosis-leprosy co-infection was performed of English, Portuguese and Spanish publications in LILACS, SciELO, PubMed and Web of Science databases using the descriptors (chromoblastomycosis OR cromoblastomycose OR cromoblastomycosis) AND (leprosy OR hanseníase OR lepra), without time period delimitation. Nineteen cases were included, 16 cases were published in 11 articles, plus the three cases reported in the current study. Most reported coinfection cases came from Brazil. Majority of the patients were male with a mean age of 52.2 years. Farmer was the main occupational activity reported. In 12 patients, the clinical signs and symptoms of leprosy started first. No contacts with patients affected by leprosy, armadillos or history of injuries at the anatomical site of chromoblastomycosis lesions were reported. Five leprosy patients who received steroid treatment for leprosy reactions or neuropathies, were diagnosed with chromoblastomycosis during immunosuppressive therapy. Four cases (21.1%) were reported among the elderly patients. Co-infections in patients with chromoblastomycosis or leprosy are uncommon, but the possibility should always be considered, especially if the patient is undergoing immunosuppressive treatment or is elder.

Leprosy in the state of Amazonas: is there actually a decrease in its incidence and prevalence?

Silva, D., Palheta Júnior, J., Pedrosa, V., Talhari, C.

04-06-2022

An Bras Dermatol

<https://pubmed.ncbi.nlm.nih.gov/35672159>

Construction and Analysis of the Complete Genome Sequence of Leprosy Agent *Mycobacterium lepromatosis*.

Silva, F., Santos-Garcia, D., Zheng, X., Zhang, L., Han, X.

25-04-2022

Microbiol Spectr

<https://doi.org/10.1128/spectrum.01692-21>

Leprosy is caused by *Mycobacterium leprae* and *Mycobacterium lepromatosis*. We report construction and analyses of the complete genome sequence of *M. lepromatosis* FJ924. The genome contained 3,271,694 nucleotides to encode 1,789 functional genes and 1,564

pseudogenes. It shared 1,420 genes and 885 pseudogenes (71.4%) with *M. leprae* but differed in 1,281 genes and pseudogenes (28.6%). In phylogeny, the leprosy bacilli started from a most recent common ancestor (MRCA) that diverged ~30 million years ago (Mya) from environmental organism *Mycobacterium haemophilum*. The MRCA then underwent reductive evolution with pseudogenization, gene loss, and chromosomal rearrangements. Analysis of the shared pseudogenes estimated the pseudogenization event ~14 Mya, shortly before species bifurcation. Afterwards, genomic changes occurred to lesser extent in each species. Like *M. leprae*, four major types of highly repetitive sequences were detected in *M. lepromatosis*, contributing to chromosomal rearrangements within and after MRCA. Variations in genes and copy numbers were noted, such as three copies of the gene encoding bifunctional diguanylate cyclase/phosphodiesterase in *M. lepromatosis*, but single copy in *M. leprae*; 6 genes encoding the TetR family transcriptional regulators in *M. lepromatosis*, but 11 such genes in *M. leprae*; presence of *hemW* gene in *M. lepromatosis*, but absence in *M. leprae*; and others. These variations likely aid unique pathogenesis, such as diffuse lepromatous leprosy associated with *M. lepromatosis*, while the shared genomic features should explain the common pathogenesis of dermatitis and neuritis in leprosy. Together, these findings and the genomic data of *M. lepromatosis* may facilitate future research and care for leprosy. **IMPORTANCE** Leprosy is a dreaded infection that still affects millions of people worldwide. *Mycobacterium lepromatosis* is a recently recognized cause in addition to the well-known *Mycobacterium leprae*. *M. lepromatosis* is likely specific for diffuse lepromatous leprosy, a severe form of the infection and endemic in Mexico. This study constructed and annotated the complete genome sequence of *M. lepromatosis* FJ924 and performed comparative genomic analyses with related mycobacteria. The results afford new and refined insights into the genome size, gene repertoire, pseudogenes, phylogenomic relationship, genome organization and plasticity, process and timing of reductive evolution, and genetic and proteomic basis for pathogenesis. The availability of the complete *M. lepromatosis* genome may prove to be useful for future research and care for the infection.

Erythema nodosum leprosum post-COVID-19 vaccination: endemic while pandemic.

Fachler, T., Olshtain-Pops, K., Horev, L.

08-03-2022

J Eur Acad Dermatol Venereol

<https://doi.org/10.1111/jdv.18035>

Pediatric leprosy: no child's play.

Mehta, H., Narang, T., Dogra, S., Kumar, B.

21-02-2022

Int J Dermatol

<https://doi.org/10.1111/ijd.16152>

Childhood leprosy: a Pandora's box. A case report of tuberculoid leprosy downgrading to borderline tuberculoid leprosy in a 5-year-old child.

Bose, S.

15-11-2021

Int J Dermatol

<https://doi.org/10.1111/ijd.15982>

Use of mobile technology in preventing leprosy impairments.

Paul, S., Kumar, D.

07-08-2020

Disabil Rehabil Assist Technol

<https://doi.org/10.1080/17483107.2020.1804631>

Aim: Rapid development in telecommunication sector across the globe has revolutionised communication networks even in rural areas. At a tertiary leprosy referral hospital in Tamil Nadu, India, leprosy treatment was started for a male patient presenting with clinical signs and symptoms suggestive of leprosy. Since the patient was from a remote area, but needed close and continuous monitoring, he was provided with a mobile phone and a 12h toll free number. **Methods:** The patient was able to provide detailed regular information of his health status to the health worker, through the toll free number from the mobile phone given to him. The patient defaulted during his treatment. Within a few days of his defaulting, a follow up call was made and the patient revealed that he did not have enough financial resources to visit the hospital and continue his treatment. **Results:** The patient was visited by a health worker and was reassured. Arrangements were made by the hospital to reimburse his travel costs. **Conclusion:** Utilising the advancements in technology would help in solving some of the key unanswered issues existing in leprosy. The use of technology helps facilitate and complement the work of health workers in reaching out to patients living in remote areas.

IMPLICATIONS FOR REHABILITATION:

- The use of M (mobile) - health in treatment compliance and adherence
- The use of M-health in the prevention and management of impairments in leprosy
- Effective monitoring and follow up of patients with impairments through mobile.

TRYPANOSOMES (TRYPANOSOMIASE ET MALADIE DE CHAGAS)

The entrance route: oral, mucous, cutaneous, or systemic has a marked influence on the outcome of *Trypanosoma cruzi* experimental infection.

Gonçalves, K., Mazzeti, A., da Silva do Nascimento, A., de Castro

Lacerda, J., de Paiva, N., Mathias, F., Reis, A., Caldas, S., Bahia, M.

29-06-2022

Acta Trop

<https://pubmed.ncbi.nlm.nih.gov/35779591>

In recent decades, the oral infection of *Trypanosoma cruzi* has gathered increased attention due to frequent outbreaks that can lead to more severe clinical signs than those usually found in the areas of vector transmission. This study addresses the main routes of infection using metacyclic trypomastigotes (MT) and blood trypomastigotes (BT). Herein, BALB/c mice were infected with the Colombian (Tcl) strain via intraperitoneal (IP), oral, intragastric (IG), ocular (OC) and cutaneous (CT) routes with 10^6 culture-derived MT or BT. Parasitemia was intermittent and low in animals inoculated with MT, in contrast, high parasitemia levels were found in BT-mice. A tropism for the muscles was observed in oral or IG infection with BT. Differently, the parasite was widely distributed in the tissues of mice infected with MT. However, the intensity of the inflammation infiltrating the tissues was higher in oral or IG infection with BT. Animals inoculated with BT via the IG route had similar serum levels of IFN- γ and smaller IL-10 compared to those infected with MT via the IG route. TNF- α levels were higher in the serum from BT-animals, which could explain the higher intensity of heart inflammation in these animals. Our results suggest that the infective form and the route of infection differentially modulated the outcome of *Trypanosoma cruzi* mice infection.

Persistence of *Trypanosoma cruzi* vector-borne transmission among school-age children in the Bolivian Chaco documented by 24-month longitudinal serosurveillance.

Spinicci, M., Macchioni, F., Gamboa, H., Poma, V., Villagrán, A., Strohmeyer, M., Roselli, M., Vargas, R., Bartoloni, A., Gabrielli, S.

02-07-2022

Trans R Soc Trop Med Hyg

<https://pubmed.ncbi.nlm.nih.gov/35779279>

Background: Chagas disease represents a major public health concern in several Latin American countries, including Bolivia. **Methods:** We present a longitudinal serosurvey for *Trypanosoma cruzi* antibodies among a cohort of 120 school-age children from rural communities in the Bolivian Chaco at three time points between 2017 and 2019. Serum samples extracted from dry blood spots collected on filter paper were tested for *T. cruzi* antibodies by enzyme-linked immunosorbent assay and rapid diagnostic test. **Results:** *T. cruzi* antibodies were detected in 7/120 (5.8%), 8/120 (6.7%) and 11/120 (9.2%) samples in 2017, 2018 and 2019, respectively. An average incidence of 1.76 per 100 person-years was observed. **Conclusions:** Our findings support the persistence of vector-borne *T. cruzi* transmission in this area, highlighting the need for strengthening multidisciplinary efforts against Chagas disease.

Synthesis of Oligosaccharides Containing the S-Galp(α 1 \rightarrow 3)Galp Unit, Glycomimetic of the Epitope Recognized by Lytic Antibodies.

Morrone-Pozzuto, P., Uhrig, M., Agusti, R.

01-07-2022

J Org Chem

<https://doi.org/10.1021/acs.joc.2c01059>

Two important activities take place in the surface of *Trypanosoma cruzi*, the agent of Chagas disease: the *trans*-sialidase (TcTS) catalyzes the transfer of sialic acid from the host glycoconjugates to the mucin-like glycoproteins from the parasite and the presence of lytic antibodies recognize the epitope α -Galp(1 \rightarrow 3)- β -Galp(1 \rightarrow 4)- α -GlcNAcp. This antigenic structure is known to be present in the parasite mucins; however, in order to be substrates of *trans*-sialidase, some of the galactose residues should be in the β -Galp configuration. To study the interaction between both activities, it is important to count the synthetic structures as well as the structural-related glycomimetics. With this purpose, we addressed the synthesis of a trisaccharide and two isomeric tetrasaccharides containing the 1-S- α -Galp(1 \rightarrow 3)- β -Galp motif, the thio analog of the epitope recognized by lytic antibodies. Starting with a common lactose precursor, the sulfur function was incorporated by double inversion of the configuration of the galactose residue that was further glycosylated using different activated donors. Both tetrasaccharides were good acceptors of sialic acid in the reaction catalyzed by TcTS, as determined by high-performance anion exchange chromatography.

Long-term Survival Following Heart Transplantation for Chagas Versus Non-Chagas Cardiomyopathy: A Single-center Experience in Northeastern Brazil Over 2 Decades.

Vieira, J., Sobral, M., Macedo, F., Florêncio, R., Almeida, G., Vasconcelos, G., Fernandes, J., Marinho, L., Trompieri, D., Pasala, T., Mejia, J., Souza-Neto, J.

24-06-2022

Transplant Direct

<https://doi.org/10.1097/TXD.0000000000001349>

Background: Data on post-heart transplant (HT) survival of patients with Chagas cardiomyopathy (CC) are scarce. We sought to evaluate post-HT survival in patients with CC as compared with other causes of heart failure across different eras of HT. **Methods:** We conducted a retrospective, cohort study of 376 adult HT recipients between October 1997 and November 2019. Participants were classified according to the etiology of heart failure as CC (N=66), nonischemic cardiomyopathy (N=214), and ischemic cardiomyopathy (N=96), and according to the era of HT as early (1997-2009), recent (2010-2014), and current era (2015-2019). **Results:** After a mean follow-up of 5.0 y (0-20.5 y), post-HT survival rates at 1, 5, and 10 y were comparable between groups. One-year survival improved from 70% in the early eras to 80% in the current era (hazard ratio [HR], 0.63; 95% confidence interval [CI], 0.41-0.97; $P=0.034$). After adjustment for sex, age, and mechanical circulatory support, time-related improvement in

survival was observed only in patients without CC (HR, 0.54; 95% CI, 0.32-0.91; $P=0.019$) but not in those with CC (HR, 0.99; 95% CI, 0.36-2.73; $P=0.98$). Causes of death were similar between patients with CC and the other etiological subgroups.

Conclusions: Posttransplant survival is comparable between patients with CC, nonischemic cardiomyopathy, and ischemic cardiomyopathy. Although survival has improved significantly over years for most HT recipients, it has remained unchanged for those with Chagas disease. These trends underscore the importance of scientific research, policy discussions and a collaborative registry of heart transplantation in Chagas cardiomyopathy.

Infection susceptibility and vector competence of *Rhodnius robustus* Larrousse, 1927 and *R. pictipes* Stal, 1872 (Hemiptera, Reduviidae, Triatominae) for strains of *Trypanosoma cruzi* (Chagas, 1909) (Kinetoplastida, Trypanosomatidae) I, II and IV.

de Abreu, A., Lucas da Silva, H., Sarto, M., Iunklaus, G., Trovo, J., de Souza Fernandes, N., Teston, A., Toledo, M.

30-06-2022

Parasit Vectors

<https://doi.org/10.1186/s13071-022-05350-3>

Background: *Rhodnius robustus* and *Rhodnius pictipes* are vectors of *Trypanosoma cruzi*, the etiologic agent of Chagas disease (CD), that are found in the Brazilian Amazon region. Susceptibility to infection and vector competence depend on the parasite-vector relationship. Our objective was to evaluate the interaction between *T. cruzi* and these two triatomine vectors in pure and mixed experimental infections of *T. cruzi* strains from the same or different geographic regions.

Methods: Fifth-instar nymphs of *R. robustus* and *R. pictipes* were fed on mice infected with four *T. cruzi* strains, namely genotypes TcIAM, TcIMG, TcIIPR, and TcIVAM, respectively, from the Brazilian states of Amazonas, Minas Gerais and Paraná. Over a period of 120 days, excreta were examined every 20 days to assess vector competence, and intestinal contents (IC) were examined every 30 days to determine susceptibility to infection. **Results:** The highest positive rate in the fresh examination (%+FE, 30.0%), the highest number of parasitic forms (PF, $n = 1969$) and the highest metacyclogenesis rate (%MC, 53.8%) in the excreta were recorded for *R. robustus*/TcIVAM. Examination of the IC of *R. pictipes* revealed a higher number of PF in infections with TcIAM (22,680 PF) and TcIIPR (19,845 PF) alone or in association (17,145 PF), as well as a %+FE of 75.0% with TcII, in comparison with the other genotypes. The highest %MC (100%) was recorded for the mixed infections of TcIAM with TcIIPR or TcIVAM in the IC of *R. pictipes*. **Conclusions:** Overall, both species were found to be susceptible to the *T. cruzi* strains studied. *Rhodnius robustus* showed vector competence for genotypes TcIVAM and TcIAM+TcIVAM and *R. pictipes* for TcIAM+TcIVAM and TcIAM+TcIIPR; there was elimination of infective forms as early as at 20 days. Our results suggest that both the genetics of the parasite and its geographic origin influence the susceptibility to infection and vector competence, alone or in association.

Crystal Structure of Trypanosoma cruzi Heme Peroxidase and Characterisation of its Substrate Specificity and Compound I Intermediate.

Freeman, S., Skafar, V., Kwon, H., Fielding, A., Moody, P., Martínez, A., Issoglio, F., Inchausti, L., Smircich, P., Zeida, A., Piacenza, L., Radi, R., Raven, E.

27-06-2022

J Biol Chem

<https://pubmed.ncbi.nlm.nih.gov/35772495>

The protozoan parasite *Trypanosoma cruzi* is the causative agent of American trypanosomiasis, otherwise known as Chagas disease. To survive in the host, the *T. cruzi* parasite needs antioxidant defence systems. One of these is a hybrid heme peroxidase, the *T. cruzi* ascorbate peroxidase-cytochrome c peroxidase enzyme (TcAPx-CcP). TcAPx-CcP has high sequence identity to members of the class I peroxidase family, notably ascorbate peroxidase (APX) and cytochrome c peroxidase (CcP), as well as a mitochondrial peroxidase from *Leishmania major* (LmP). The aim of this work was to solve the structure and examine the reactivity of the TcAPx-CcP enzyme. Low temperature electron paramagnetic resonance (EPR) spectra support the formation of an exchange-coupled [Fe(IV)=O Trp₂₃₃*] Compound I radical species, analogous to that used in CcP and LmP. We demonstrate that TcAPx-CcP is similar in overall structure to APX and CcP, but there are differences in the substrate binding regions. Furthermore, the electron transfer pathway from cytochrome c to the heme in CcP and LmP is preserved in the TcAPx-CcP structure. Integration of steady state kinetic experiments, molecular dynamic simulations, and bioinformatic analyses indicates that TcAPx-CcP preferentially oxidizes cytochrome c, but is still competent for oxidation of ascorbate. The results reveal that TcAPx-CcP is a credible cytochrome c peroxidase which can also bind and use ascorbate in host cells, where concentrations are in the millimolar range. Thus, kinetically and functionally TcAPx-CcP can be considered a hybrid peroxidase.

Scaling up of tsetse control to eliminate Gambian sleeping sickness in northern Uganda.

Hope, A., Mugenyi, A., Esterhuizen, J., Tirados, I., Cunningham, L., Garrod, G., Lehane, M., Longbottom, J., Mangwiro, T., Opiyo, M., Stanton, M., Torr, S., Vale, G., Waiswa, C., Selby, R.

29-06-2022

PLoS Negl Trop Dis

<https://doi.org/10.1371/journal.pntd.0010222>

Background: Tsetse flies (*Glossina*) transmit *Trypanosoma brucei gambiense* which causes Gambian human African trypanosomiasis (gHAT) in Central and West Africa. Several countries use Tiny Targets, comprising insecticide-treated panels of material which attract and kill tsetse, as part of their national programmes to eliminate gHAT. We studied how the scale and arrangement of target deployment affected the efficacy of control. **Methodology and principal findings:** Between 2012 and 2016, Tiny Targets were deployed biannually along the larger rivers of Arua, Maracha, Koboko

and Yumbe districts in North West Uganda with the aim of reducing the abundance of tsetse to interrupt transmission. The extent of these deployments increased from ~250 km² in 2012 to ~1600 km² in 2015. The impact of Tiny Targets on tsetse population was assessed by analysing catches of tsetse from a network of monitoring traps; sub-samples of captured tsetse were dissected to estimate their age and infection status. In addition, the condition of 780 targets (~195/district) was assessed for up to six months after deployment. In each district, mean daily catches of tsetse (*G. fuscipes fuscipes*) from monitoring traps declined significantly by >80% following the deployment of targets. The reduction was apparent for several kilometres on adjacent lengths of the same river but not in other rivers a kilometre or so away. Expansion of the operational area did not always produce higher levels of suppression or detectable change in the age structure or infection rates of the population, perhaps due to the failure to treat the smaller streams and/or invasion from adjacent untreated areas. The median effective life of a Tiny Target was 61 (41.8-80.2, 95% CI) days. **Conclusions:** Scaling-up of tsetse control reduced the population of tsetse by >80% across the intervention area. Even better control might be achievable by tackling invasion of flies from infested areas within and outside the current intervention area. This might involve deploying more targets, especially along smaller rivers, and extending the effective life of Tiny Targets.

Transcriptomic modulation in response to an intoxication with deltamethrin in a population of Triatoma infestans with low resistance to pyrethroids.

Traverso, L., Latorre Estivalis, J., da Rocha Fernandes, G., Fronza, G., Lobbia, P., Mougabure Cueto, G., Ons, S.

29-06-2022

PLoS Negl Trop Dis

<https://doi.org/10.1371/journal.pntd.0010060>

Background: *Triatoma infestans* is the main vector of Chagas disease in the Southern Cone. The resistance to pyrethroid insecticides developed by populations of this species impairs the effectiveness of vector control campaigns in wide regions of Argentina. The study of the global transcriptomic response to pyrethroid insecticides is important to deepen the knowledge about detoxification in triatomines. **Methodology and findings:** We used RNA-Seq to explore the early transcriptomic response after intoxication with deltamethrin in a population of *T. infestans* which presents low resistance to pyrethroids. We were able to assemble a complete transcriptome of this vector and found evidence of differentially expressed genes belonging to diverse families such as chemosensory and odorant-binding proteins, ABC transporters and heat-shock proteins. Moreover, genes related to transcription and translation, energetic metabolism and cuticle rearrangements were also modulated. Finally, we characterized the repertoire of previously uncharacterized detoxification-related gene families in *T. infestans* and *Rhodnius prolixus*. **Conclusions and significance:** Our work contributes to the understanding of the detoxification

response in vectors of Chagas disease. Given the absence of an annotated genome from *T. infestans*, the analysis presented here constitutes a resource for molecular and physiological studies in this species. The results increase the knowledge on detoxification processes in vectors of Chagas disease, and provide relevant information to explore undescribed potential insecticide resistance mechanisms in populations of these insects.

Chagas disease affects the human placental barrier's turnover dynamics during pregnancy.

Mezzano, L., Morán, J., Moreira-Espinoza, M., Triquell, M., Mezzano, J., Díaz-Luján, C., Fretes, R.

27-06-2022

Mem Inst Oswaldo Cruz

<https://pubmed.ncbi.nlm.nih.gov/35766782>

Background: *Trypanosoma cruzi* crosses the placental barrier and produces the congenital transmission of Chagas disease (CD). Structural alterations of the chorionic villi by this parasite have been described in vitro, but little is known about trophoblast turnover in placentas from women with CD. **Objective:** To analyze the proliferation and fusion processes in placentas from women with CD. **Methods:** Archived human term placenta paraffin-embedded blocks were used, from women with CD (CDP), and no pathology (NP). Immunohistochemistry tests were performed for Ki67 to calculate the proliferation index (PI) of cytotrophoblast (CTB) and Syncytin-1, a fusion marker of syncytiotrophoblast (STB). Hematoxylin/Eosin stained sections were employed to analyze STB percentages, STB detachment areas and syncytial knots quantity. Non parametric Student's t-tests were performed ($p < 0.05$). **Results:** Syncytial knots and STB detachment significantly increased in placental villi from the CDP group. STB percentage was significantly lower in the CDP group as well as the PI and Syncytin-1 expression significantly decreased in these placentas, compared with control (NP). **Conclusion:** Dynamic of trophoblast turnover is altered in placentas from women with CD. These changes may lead into a gap in the placental barrier possibly allowing the parasite entry into the chorionic villi.

Heart rate variability as a biomarker in patients with Chronic Chagas Cardiomyopathy with or without concomitant digestive involvement and its relationship with the Rassi score.

Silva, L., Moreira, H., de Oliveira, M., Cintra, L., Salgado, H., Fazan, R., Tinós, R., Rassi, A., Schmidt, A., Marin-Neto, J.

28-06-2022

Biomed Eng Online

<https://doi.org/10.1186/s12938-022-01014-6>

Background: Dysautonomia plays an ancillary role in the pathogenesis of Chronic Chagas Cardiomyopathy (CCC), but is the key factor causing digestive organic involvement. We investigated the ability of heart rate variability (HRV) for death risk stratification in CCC and compared alterations of HRV in

patients with isolated CCC and in those with the mixed form (CCC+digestive involvement). Thirty-one patients with CCC were classified into three risk groups (low, intermediate and high) according to their Rassi score. A single-lead ECG was recorded for a period of 10-20 min, RR series were generated and 31 HRV indices were calculated. The HRV was compared among the three risk groups and regarding the associated digestive involvement. Four machine learning models were created to predict the risk class of patients. **Results:** Phase entropy is decreased and the percentage of inflection points is increased in patients from the high-, compared to the low-risk group. Fourteen patients had the mixed form, showing decreased triangular interpolation of the RR histogram and absolute power at the low-frequency band. The best predictive risk model was obtained by the support vector machine algorithm (overall F1-score of 0.61). **Conclusions:** The mixed form of Chagas' disease showed a decrease in the slow HRV components. The worst prognosis in CCC is associated with increased heart rate fragmentation. The combination of HRV indices enhanced the accuracy of risk stratification. In patients with the mixed form of Chagas disease, a higher degree of sympathetic autonomic denervation may be associated with parasympathetic impairment.

Updated Estimates and Mapping for Prevalence of Chagas Disease among Adults, United States.

Revue de littérature

Irish, A., Whitman, J., Clark, E., Marcus, R., Bern, C.

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Emerg Infect Dis

<https://doi.org/10.3201/eid2807.212221>

We combined American Community Survey data with age-specific *Trypanosoma cruzi* prevalence derived from US surveys and World Health Organization reports to yield estimates of Chagas disease in the United States, which we mapped at the local level. In addition, we used blood donor data to estimate the relative prevalence of autochthonous *T. cruzi* infection. Our estimates indicate that 288,000 infected persons, including 57,000 Chagas cardiomyopathy patients and 43,000 infected reproductive-age women, currently live in the United States; 22-108 congenital infections occur annually. We estimated $\approx 10,000$ prevalent cases of locally acquired *T. cruzi* infection. Mapping shows marked geographic heterogeneity of *T. cruzi* prevalence and illness. Reliable demographic and geographic data are key to guiding prevention and management of Chagas disease. Population-based surveys in high prevalence areas could improve the evidence base for future estimates. Knowledge of the demographics and geographic distribution of affected persons may aid practitioners in recognizing Chagas disease.

Contextual influence on poor self-rated health in patients with Chagas disease: multilevel study.

Ferreira, A., Sabino, E., Silva, L., Oliveira, C., Cardoso, C., Ribeiro, A., Damasceno, R., Leite, S., Vieira, T., Nunes, M., Haikal, D.

26-02-2022

Cien Saude Colet

<https://pubmed.ncbi.nlm.nih.gov/35730850>

Chagas disease (CD) is recognized by the World Health Organization as one of the thirteen most neglected tropical diseases in the world. Self-perceived health is considered a better predictor of mortality than objective measures of health status, and the context in which one lives influences this predictor. This study aimed to evaluate the prevalence and individual and contextual factors associated with poor self-rated health among CD patients from an endemic region in Brazil. It is a multilevel cross-sectional study. The individual data come from a cross-section of a cohort study named SaMi-Trop. Contextual data was collected from publicly accessible institutional information systems and platforms. The dependent variable was self-perceived health. The analysis was performed using multilevel binary logistic regression. The study included 1,513 patients with CD, where 335 (22.1%) had Poor self-rated health. This study revealed the influence of the organization/offer of the Brazilian public health service and of individual characteristics on the self-perceived health of patients with CD.

"Natural infections" with *Trypanosoma cruzi* via the skin of mice: size of mouthparts of vectors and numbers of invading parasites.

Waldeck, B., Schaub, G.

04-05-2022

Parasitol Res

<https://doi.org/10.1007/s00436-022-07516-5>

Investigating parameters influencing natural infections with *Trypanosoma cruzi* via the skin, the diameters of mouthparts of different stages of triatomines vectors were measured to determine the size of the channel accessible for *T. cruzi* during cutaneous infection. The mean diameters of the skin-penetrating mandibles of first to fifth instar nymphs of the vector *Triatoma infestans* increased from 18 to 65 µm. The mean diameter in fourth instar nymphs of *Dipetalogaster maxima* was 86 µm. Different numbers of isolated vector-derived metacyclic trypomastigotes (10-10,000) were injected intradermally into mice. Prepatent periods, parasitemia and mortality rates were compared with those of mice obtaining 10,000 metacyclic trypomastigotes that are usually present in the first drop of faeces onto the feeding wounds of fifth and fourth instar nymphs of *T. infestans* and *D. maxima*, respectively. After injection of 50-10,000 *T. cruzi*, in all 42 mice the infection developed. An injection of 10 parasites induced an infection in 8 out of 15 mice. With increasing doses of parasites, prepatent periods tended to decrease. The level of parasitemia was higher after injection of the lowest dose. Except for one mouse all infected mice died. After placement of 10,000 metacyclic trypomastigotes onto the feeding wound of fifth or fourth instar nymphs of *T. infestans* and *D. maxima*, respectively, the infection rates of the groups, prepatent periods and the levels of parasitemia of *T. cruzi* in mice indicated that about 10-1,000 metacyclic trypomastigotes entered the skin via this route. For the first

time, the present data emphasise the risk of an infection by infectious excreta of triatomines deposited near the feeding wound and the low number of invading parasites.

Anti-*Trypanosoma cruzi* activity of alkaloids isolated from *Habranthus brachyandrus* (Amaryllidaceae) from Argentina.

Martinez-Peinado, N., Ortiz, J., Cortes-Serra, N., Pinazo, M., Gascon, J., Tapia, A., Roitman, G., Bastida, J., Feresin, G., Alonso-Padilla, J.

19-04-2022

Phytomedicine

<https://pubmed.ncbi.nlm.nih.gov/35489322>

Background: Chagas disease, caused by the parasite *Trypanosoma cruzi*, affects over six million people worldwide, mainly in Latin American countries. Currently available drugs have variable efficacy in the chronic phase and significant side effects, so there is an urgent need for safer chemotherapeutic treatments. Natural products provide privileged structures that could serve as templates for the synthesis of new drugs. Among them, Amaryllidaceae plants have proved to be a potential natural source of therapeutic agents due to their rich diversity in alkaloids. **Purpose:** To identify alkaloids with anti-*T. cruzi* activity from *Habranthus brachyandrus* (Baker) Sealy (Amaryllidaceae, subfamily Amaryllidoideae) collected in Argentina. **Methods:** An *H. brachyandrus* alkaloid extract was tested against *T. cruzi*, and its cytotoxicity profile was evaluated against two mammalian cell lines to ascertain its selectivity against the parasite and potential liver toxicity. It was also assessed by a stage-specific anti-amastigote assay and analysed by GC/MS to determine its alkaloid profile. The isolated alkaloids were also tested using the aforementioned assays. **Results:** The extract showed high and specific activity against *T. cruzi*. The alkaloids lycoramine, galanthindole, 8-O-demethylmaritidine, 8-O-demethylhomolycorine, nerinine, trisphaeridine, deoxytazettine, and tazettamide were identified by means of GC-MS. In addition, hippeastidine (also named alicine), tazettine, ismine, and 3-epimacronine were isolated. The alkaloid ismine was specifically active against the parasite and had low toxicity against HepG2 cells, but did not show anti-amastigote activity. **Conclusion:** The extract had specific anti-*T. cruzi* activity and the isolated alkaloid ismine was partially responsible of it. These results encourage further exploration of *H. brachyandrus* alkaloids in search of novel starting points for Chagas disease drug development.

Polymorphisms of the TLR4 gene: Risk factor for chronicity and severity in oral vectorial Chagas disease.

Sánchez, G., Salazar-Alcalá, E., Hernández, F., Deglesne, P., Bello, Z., de Noya, B., Noya, O., Fernández-Mestre, M.

10-03-2022

Exp Parasitol

<https://pubmed.ncbi.nlm.nih.gov/35278458>

Chagas disease is one of the parasitic infections with the greatest socio-economic impact in Latin America. In

Venezuela, epidemiological data has shown different sources of infection, such as the vectorial route by oral transmission. Given the importance of the TLR4 gene in the innate immune response triggered by infection with *Trypanosoma cruzi*, this work analyses the role of TLR4 polymorphisms and its possible effect on cytokine expression. Genomic DNA was extracted from the peripheral blood of patients from the main outbreak of oral Chagas disease in Venezuela (n = 90), as well as from a group of healthy individuals (n = 183). Subsequently, peripheral blood was also extracted from individuals with different TLR4 haplotypes and then stimulated with LPS to determine the cytokine concentration by ELISA. The internalization of TLR4 was evaluated by flow cytometry. In comparison to healthy individuals, the analysis showed a significantly increased frequency of the Asp/Gly genotype in symptomatic patients. Also, observed a correlation of the 299/399 haplotype with a significant decrease in cytokine concentration and disease severity. Finally, the parasites' trypomastigotes cause the internalization or negative regulation of TLR4. The variants of TLR4 associated with low production of cytokines may be a risk factor for chronicity and severity (cardiac involvement) in oral vectorial Chagas disease.

Upregulation of sialyltransferases ST3Gal1 and ST6Gal1 promotes stabilization of erythrocyte mass and recovery of anemia in *Trypanosoma brucei* brucei-infected pigs.

Atata, J., Enam, S., Ogbuagu, N., Balogun, E., Adamu, S., Esievo, K.

08-02-2022

Res Vet Sci

<https://pubmed.ncbi.nlm.nih.gov/35180660>

The role of Sialyltransferases (STs) specifically subfamilies ST3Gal1 and ST6Gal1 tissue expression was investigated in the liver and kidney of *Trypanosoma brucei* brucei-infected and uninfected control pigs. The study was aimed to provide emerging target for treatment. Pigs were experimentally infected with 2×10^6 T. b. brucei (Federe strain); parasitemia was monitored by microscopy and tissue expression levels of ST3Gal1 and ST6Gal1 in the liver and kidney were assessed using quantitative real-time polymerase chain reaction (qRT-PCR). Parasitemia were undulating and anemia occurred significantly ($P < 0.01$) on day 13 in the infected pigs with an attempt to recover toward the termination of the study on day 21. The gene expressions for hepatic and renal ST3Gal1 and ST6Gal1 were significantly ($P < 0.0001$) upregulated 5-42 folds in the infected pig compared to the non-infected control group. It was concluded from the findings in this study that increased tissue expression of ST3Gal1 and ST6Gal1 in T. b. brucei-infected pigs may play a pivotal role in the resialylation of desialylated red blood cells, thereby promoting recovery of the red blood cells and stabilization of erythrocyte mass in trypanosome-infected pigs. It is recommended that the expression of serum ST3Gal1 and ST6Gal1 be investigated further, in trypano-susceptible against trypano-tolerant breeds of animals to determine the role of these genes in trypano-tolerance.

First appropriate implantable defibrillator shocks in patients with Chagasic heart disease

García-Chamorro, L., Zaidel, E., Gheco, L., Oliva, M., de-la-Vega, A., Orosco, A., Armentano, J., Sosa-Liprandi, Á.

01-07-2022

Arch Cardiol Mex

<https://doi.org/10.24875/ACM.21000218>

Objectives: To assess if patients with Chagasic heart disease (CHD) received effective automatic implantable defibrillator (AID) shocks earlier than patients with ischemic heart disease (IHD). **Methods:** Retrospective cohort of patients with CHD and IHD who received an implantable cardioverter defibrillator (ICD) between 2009 and 2018, in a tertiary hospital. We evaluated the time between the implant of ICD and the first effective shock in patients with CHD and compared it with the IHD control population. **Results:** We included a total of 64 patients, 20 with CHD and 44 with IHD. CHD patients presented earlier an effective shock than patients with IHD during the first year (hazard ratio [HR]: 8.4; 95% confidence interval [95%CI]: 2.09-34.02; $p = 0.0027$), and at three years (HR: 4.61; 95%CI: 1.51-14.07; $p = 0.0072$). 100% of CHD patients who received the ICD as secondary prevention of sudden cardiac death presented an effective shock during the first 26 months of follow-up. **Conclusions:** Patients with CHD received effective ICD shocks earlier than the IHD patients. All patients with CHD and ICD as secondary prevention had an appropriate ICD shock at short term, representing the highest risk population, and supporting the indication of the device in a setting where randomized clinical trials are lacking.

LEISHMANIOSE

The Possible Role of Selected Vitamins and Minerals in the Therapeutic Outcomes of Leishmaniasis.

Revue de littérature

Kumar, V., Kt, M., Sharma, A., Bisht, P., Dhingra, S., Ravichandiran, V., Ramesh, M., Murti, K.

02-07-2022

Biol Trace Elem Res

<https://doi.org/10.1007/s12011-022-03311-6>

Leishmaniasis is a protozoal disease declared as an endemic in areas suffering from severe malnutrition and poverty. The factors associated with poverty like low income, ecological factors, and malnutrition cause disruption in immunity and host defense increasing risk of infection. Altered resistance to infection and host susceptibility are associated with low micronutrient levels in undernourished patients. Malnutrition has been recognized as a poor predictive marker for leishmaniasis, in particular the deficiency of trace elements like zinc, iron, and vitamin A, B, C, D which has a prominent function in the regulation of innate and adaptive immunity, cell proliferation, human physiology, etc. Malnourishment can

exacerbate host sensitivity and pathophysiologic intensity to infection in variety of ways, whereas infection can enhance underlying poor nutrition or enhance host vulnerability and sandfly's urge to attack specific hosts. The intensity of leishmaniasis can be influenced by body mass and micronutrient availability in the blood. Vitamin D, C, zinc, and iron are proved effective in inhibiting the growth of leishmaniasis in both amastigote or promastigote forms, either directly or by acting as precursor for a pathway which inhibits the parasite growth. This article elucidates a new perception to the crucial role of micronutrients and their probable role in the therapeutic outcomes of leishmaniasis. Since there is requirement of novel drugs to fight drug resistance and relapse of leishmaniasis, this article may pave way to understand the importance of micronutrients and their role in therapeutic outcomes of leishmaniasis.

Association between interleukin 10 (IL-10) polymorphisms and leishmaniasis progression: a systematic review and meta-analysis.

da Silva, R., Vasconcelos, F., Tavares, D., Dos Santos, P.

01-07-2022

Sci Rep

<https://doi.org/10.1038/s41598-022-15377-2>

Interleukin 10 (IL-10) is associated with the progression of leishmaniasis because it inhibits the leishmanicidal action of macrophages and the production of mediators such as IFN- γ and nitric oxide. Studies have shown that specific polymorphisms are associated with the regulatory role of IL-10 and the development of more relevant clinical forms of leishmaniasis. We performed a systematic review and meta-analysis to determine whether single nucleotide polymorphisms (SNPs) of IL-10 influence the progression of leishmaniasis. The selected articles were read in full and only those consistent with the eligibility criteria were included in our study. Seven studies were eligible according to the inclusion criteria and were included in the present systematic review, but only five were subjected to statistical analysis. The pooled odds ratios showed no significant association between the rs1800871 SNP and the progression of leishmaniasis in all genotype models, including the dominant, recessive, homozygote, heterozygote, and allelic models. Regarding the association between rs1800896 SNP and the progression of leishmaniasis, the pooled odds ratios showed no association under all genotype models. Hence, IL-10 SNPs did not show significant association and were not considered a risk factor for the progression of leishmaniasis.

[Cutaneous leishmaniasis after renal transplantation: Report of 7 cases and review of the literature].

Yaich, S., Abid, H., Toumi, S., Fendri, B., Chaker, H., Agrebi, I., Dammak, N., Masmoudi, M., Masmoudi, A., Turki, H., Kammoun, K., Hmida, M.

28-06-2022

Nephrol Ther

<https://pubmed.ncbi.nlm.nih.gov/35778263>

Leishmaniasis is a zoonosis acquired from the bite of a sandfly that introduces the amastigote forms of leishmania into the bloodstream. It is a frequent infection in the countries of the Mediterranean basin and in Tunisia, where it is rife in an endemo-epidemic mode. However, it is rare after kidney transplantation. It constitutes a challenge due to the diagnostic difficulty, the variability and the polymorphism of the clinical picture in immunocompromised patients. We report seven observations of cutaneous leishmaniasis after kidney transplantation through which we try to identify diagnostic and therapeutic difficulties.

Hemophagocytic lymphohistiocytosis secondary to AIDS-related histoplasmosis and visceral leishmaniasis.

Tomaino, M., Barletta, J., Andreani, M., Sisto, A., Abusamra, L., Guelfand, L., Rolón, M.

01-07-2022

Int J STD AIDS

<https://doi.org/10.1177/09564624221110986>

Hemophagocytic Lymphohistiocytosis (HLH) is a rare, highly aggressive syndrome involving dysregulated immune response. Most cases are secondary to underlying diseases including infections, autoimmune disorders and malignancies. The burden of disease of histoplasmosis and leishmaniasis associated with advanced HIV is still significant in low-and-middle income countries (LMIC). We present a case of histoplasmosis and leishmaniasis associated HLH in a man with an AIDS diagnosis.

Imported cases of cutaneous leishmaniasis in Cuba, 2017: role of human movement.

Monzote, L., González, D., Blanco, O., Fraga, J., Capó, V., Herrera, A., Montalvo, A.

01-07-2022

Trop Dis Travel Med Vaccines

<https://doi.org/10.1186/s40794-022-00171-9>

Background: Leishmaniasis is a vector-borne disease caused by several species from genus *Leishmania*. An increase in the number of cases related to human movement has been informed in the last years. Due to the increase of suspicious leishmaniasis cases arriving in Cuba during 2017, a general analysis is presented herein. **Methods:** Clinical samples were collected from 5 patients suspicious of leishmaniasis, received from January to December 2017 at the Institute of Tropical Medicine Pedro Kourí, Cuba. Skin lesion samples were analyzed using different diagnostic assays: direct smear, histological examination, and molecular analysis for species identification. Epidemiological and demographic data were requested from each case and analyzed. Treatment and follow up of patient was also performed. **Results:** Five cases were confirmed as *Leishmania* infection according to microscopic observation and molecular methods results. PCR-18S, PCR-N/RFLP and PCR-F/RFLP identified the following species: *L.*

panamensis (2 cases), *L. braziliensis* (1 case), *L. panamensis/L. guyanensis* (1 case), *L. mexicana* complex (1 case). In treated patients, drugs were well tolerated, cure were documented and no relapse have been currently reported (3 years later). **Conclusions:** Clinical characteristics, demographic data, and epidemiological features of infection for each case evidence the potential risk related with travel to endemic areas of leishmaniasis.

Successful Isolation of Leishmania RNA Virus (LRV) from *Leishmania major* in a Cutaneous Leishmaniasis Focus in Central Iran: An Update on Cases.

Moin-Vaziri, V., Zare, F., Seyyed Tabaei, S., Saberi, R., Hajjaran, H.

30-06-2022

Acta Parasitol

<https://doi.org/10.1007/s11686-022-00575-9>

Purpose: Cutaneous leishmaniasis (CL) is a major vector-borne disease that affects people globally, including Iran. Different factors are associated with leishmaniasis pathogenicity; recently, a link of the possible relationship between *Leishmania* RNA Virus (LRV) and disease severity was proposed, especially in the New World leishmaniasis (NWL). This study was aimed to investigate the presence of LRV2 in *Leishmania* isolates in Aran o Bidgol, Isfahan province. **Methods:** Samples were collected from 110 CL-suspected patients referred to the health center. In this study, we aimed to investigate CL cases (parasitologically and clinically), identify *Leishmania* species (by ITS1-PCR-RFLP), and finally detection of LRV2 (by RdRp-semi-nested PCR). **Results:** Parasitological methods showed 60 positive cases, based on the *HaeIII* enzyme restriction profile, 59 cases were caused by *L. major* and 1 case by *L. tropica*. Our project is the first study on LRV2 isolation in Aran o Bidgol city and the LRV was successfully detected from a single *L. major* isolated in a women's hand lesion. Using BLAST, 94.8-100% similarity was observed in the RdRp sequence of current LRV isolate with those available in GenBank from Iran or overseas. **Conclusion:** *L. major* was the main cause of CL in Aran o Bidgol, although *L. tropica* is also present in a much lower proportion in the area. This is the first report on the presence of LRV2 in Aran o Bidgol and the fifth in Iran.

Spectrum of skin diseases in Maroon villages of the Maroni area, French Guiana.

Valentin, J., Niemetzky, F., Gaillet, M., Michaud, C., Carbutar, A., Demar, M., Couppie, P., Blaizot, R.

29-06-2022

Int J Dermatol

<https://doi.org/10.1111/ijd.16324>

Background: Due to their genetic characteristics and their high exposure to infectious diseases, Maroons are likely to suffer from a specific spectrum of skin diseases. However, skin disorders have never been explored in this population. We

aimed to describe all skin diseases in Maroon villages of the Maroni region in French Guiana. **Methods:** This retrospective study concerned all patients who consulted in the remote health centers of Apatou, Grand-Santi, Papaichton, and Maripasoula between October 5, 2017, and June 30, 2020. We included all patients registered with a skin disorder (International Classification of Diseases) in the medical database. We excluded patients whose diagnosis was invalidated after cross-checking by a dermatologist. **Results:** A total of 4741 patients presented at least one skin disease, for 6058 different disorders. Nonsexually transmitted infections represented 71.6% of all diagnoses, followed by inflammatory diseases (9.8%) and bites/envenomations (4.6%). The three most frequent conditions were scabies, abscesses, and impetigo. Besides scabies, neglected tropical diseases (NTDs) were still prevalent as we reported 13 cases of leprosy and 63 cutaneous leishmaniasis. Atopic dermatitis (AD) represented only 2.5% of our diagnoses. **Conclusions:** With the exception of AD, which was less frequent among Maroons, these results are similar to those previously reported in Amerindians. Therefore, a common exposure to rainforest pathogens seems to induce a common spectrum of skin diseases dominated by infections. The high prevalence of NTDs requires specific public health actions.

High-throughput microfluidic real-time PCR for the simultaneous detection of selected vector-borne pathogens in dogs in Bosnia and Herzegovina.

Colella, V., Huggins, L., Hodžić, A., Galon, C., Traub, R., Alić, A., Iatta, R., Halos, L., Otranto, D., Vayssier-Taussat, M., Moutailler, S.

29-06-2022

Transbound Emerg Dis

<https://doi.org/10.1111/tbed.14645>

A scarcity of information on the occurrence of zoonotic vector-borne pathogens (VBPs), alongside a lack of human and animal health authorities' awareness of pre-existing data, augment the risk of VBP infection for local people and limit our ability to establish control programs. This holds especially true in low-middle income countries such as Bosnia and Herzegovina (BiH). This dearth of information on zoonotic VBPs is bolstered by the inability of previously used diagnostic tests, including conventional molecular diagnostic methods, to detect the full spectrum of relevant pathogens. Considering this, we set out to apply a microfluidic qPCR assay capable of detecting 43 bacterial and protozoan pathogens from blood to accrue critical baseline data for VBPs occurrence in BiH. A total of 408 dogs were tested of which half were infected with at least one VBP of zoonotic or veterinary importance. *Leishmania infantum* was found in 18% of dogs, reaching a prevalence as high as 38% in urbanized areas of Sarajevo. These data highlight substantially higher levels of *L. infantum* prevalence when compared to that previously reported using conventional methods using the same samples. Additionally, this high-throughput microfluidic qPCR assay was able to detect pathogens rarely or never reported in canines in BiH, including *Anaplasma phagocytophilum* (3%), *Anaplasma platys*

(0.2%), haemotropic Mycoplasma (1%), and Hepatozoon canis (26%). Our report of the endemicity of important zoonotic pathogens and those of clinical significance to dogs emphasizes the need for urgent implementation of surveillance and control for VBPs in BiH, targeting both animal and human infections within the country. This article is protected by copyright. All rights reserved.

Zika, Nipah and Kala-azar: Emerging lethal infectious diseases amid COVID-19 as an escalating public health threat in South India.

Uday, U., Tadi, L., Islam, Z., Mohanan, P., Ghazanfar, S., Babar, M., Ismail, S.

15-06-2022

Ann Med Surg (Lond)

<https://doi.org/10.1016/j.amsu.2022.103972>

As of 6 June 2022, a sum 25,782 of active cases and 524,701 deaths due to Coronavirus disease-19 (COVID-19) have been recorded in India. Stewing in the flares of the pandemic, Kerala is entwined in the wrath of multiple emerging infectious diseases. India, a home to 1.3 billion people, recently faced a devastating second wave of COVID-19 during May of 2021, with a ruckus of chronic shortage of medicine, oxygen supplies, ventilators, besides, being challenged by secondary infections and chronic health ailments. The state of Kerala, alone contributes to 50% COVID-19 caseload, besides, recent simultaneous outbreaks of Zika Virus Disease (ZVD), Nipah Virus Disease (NiVD) and Kala-azar (black fever) on July 8, September 5 and 8, 2021 respectively. Syndemicity and a high case fatality rates of these highly contagious diseases coupled with post infection sequelae, overwhelm the already fragile healthcare system. Thus, these lethal infectious diseases along with an anticipated third wave of COVID-19 pose a serious public health threat in and around South India. With this narrative review, we aim to discuss the challenges that the emergence of intersecting outbreaks of Zika, Nipah, Kala-azar presents with, in the nation, amidst the global pandemic of COVID-19 and provide recommendations so as to help alleviate the situation. The syndemicity of COVID-19 with other infectious diseases, calls for adequate surveillance and monitoring of diseases' outbreaks. To avoid the worst situations like pandemic, the health ministry, public and private health stakeholders in India should strengthen the public healthcare delivery system and providence of quick medical facilities to control the rate of mortality and morbidity during outbreaks.

First report of imported canine visceral leishmaniasis cases in Panama, Central America: Public health implications.

Terrero, I., Pineda, V., Vásquez, V., Miranda, A., Saldaña, A., Calzada, J., González, K.

03-06-2022

Vet Parasitol Reg Stud Reports

<https://pubmed.ncbi.nlm.nih.gov/35725108>

According to the last leishmaniasis report from the Pan American Health Organization (2021) so far Panama is considered free of visceral leishmaniasis (VL). Although the presence of potential vectors and reservoirs involved in the VL transmission cycle have been described in some rural regions of the country, no cases have been reported in humans and domestic or wild animals. Dogs play an important role in the urban transmission of VL; therefore, it is important to detect possible cases of canine visceral leishmaniasis (CVL) in the country. In this sense, this study reports for the first time the Leishmania (Leishmania) infantum infection in imported dogs in Panama. Eleven dogs with clinical suspicion of CVL were evaluated by parasitological (bone marrow aspirate smear), serological (indirect immunofluorescence and/or reference immunochromatographic rapid test) and molecular tests (conventional PCR). The dogs included in this study were analyzed during the period from 2013 to 2020. All dogs presented clinical manifestations compatible with CVL. The samples were initially evaluated by smears and/or rapid serological tests by private practice veterinarians, and later confirmed by serological and/or molecular tests at the national reference laboratory for Leishmania diagnosis. The diagnosis was confirmed in 5/11 dogs by serological, parasitological and/or conventional PCR targeting kDNA minicircle and Hsp70 gene. Leishmania (L.) infantum species was identified in 3/5 dogs by PCR-RFLP and by sequencing Hsp70-PCR products. This study evidenced the need to increase awareness of private practitioners as well as public health veterinarians on visceral leishmaniasis (VL), and to consider this parasitosis in the differential diagnosis of dogs with clinical and epidemiological characteristics compatible with the disease.

Vector-borne pathogens in dogs from areas where leishmaniosis is endemic.

Ramos, R., Giannelli, A., Ubirajara-Filho, C., Ramos, C., Betbder, D., Bezerra-Santos, M., Dantas-Torres, F., Alves, L., Otranto, D.

09-06-2022

Vet Parasitol Reg Stud Reports

<https://pubmed.ncbi.nlm.nih.gov/35725105>

Many vector-borne pathogens (VBPs), including Ehrlichia canis and Dirofilaria immitis, may infect simultaneously dogs in areas where Leishmania infantum is endemic, especially in the tropics, where highly abundant arthropod vectors thrive. The aim of this study was to compare the frequency of simultaneous VBPs infection in Leishmania-positive and Leishmania-negative dogs. Animals enrolled in this study were divided in two groups (G1 and G2), G1 being comprised of L. infantum-infected dogs (n = 58) and the G2 of L. infantum-negative dogs (n = 58). Blood samples were screened using a qualitative ELISA test (SNAP® 4Dx® Plus, IDEXX Laboratory, Westbrook, Maine, USA) for detection of antibodies against Anaplasma spp., Borrelia burgdorferi sensu lato, Ehrlichia spp. and antigens of Dirofilaria immitis. Overall, 89.7% (52/58) of dogs from G1 were positive for at least one VBP, whereas 50.0% (29/58) of dogs from G2 dogs were positive as well. The

highest positivity was to *E. canis* (67.2%; 78/116), followed by *D. immitis* (12.9%; 15/116), and *A. platys* (6.0%; 7/116). None of the animals scored positive for *B. burgdorferi* s.l.. There was a statistically significant difference for the simultaneous positivity to *E. canis* plus *D. immitis* between groups. Furthermore, 43.1% (25/58) of dogs from G1 were infested by ectoparasites (ticks, fleas, or both), compared to 20.6% (12/58) of dogs from G2. In conclusion, *Leishmania*-infected dogs were more co-infected with other VBPs than *Leishmania*-negative animals. Therefore, it is pivotal to increase the awareness of veterinarian and dog owners about the importance of testing *Leishmania*-infected dogs for other VBPs, as this may directly affect treatment decisions and management.

Bats as hosts of *Leishmania (Leishmania) infantum* in Minas Gerais, an endemic area for visceral leishmaniasis.

de Araújo, G., de Mello, É., de Oliveira, V., Dos Santos, T., Nunes, R., de Andrade, H., Furtado, L., Rabelo, É.

18-05-2022

Vet Parasitol Reg Stud Reports

<https://pubmed.ncbi.nlm.nih.gov/35725103>

Bats are parasitized by a wide spectrum of ecto and endoparasites, but their role as a reservoir for some zoonoses is not fully understood. The objective of this work was to evaluate the presence of *Leishmania* DNA in the blood of bats from 30 municipalities in the state of Minas Gerais, Brazil. We analyzed samples of 120 bats, covering 29 species. The blood samples were used for DNA extraction and submitted to conventional PCR analysis with primers directed to the *Leishmania* ITS-1 region of the rRNA. In total, 1.67% (2/120 samples) were positive for *Leishmania* spp., detected in animals from the metropolitan region of Belo Horizonte, the state capital. Sequencing of the positive samples revealed that both bats were infected with *Leishmania (Leishmania) infantum*. Considering the adaptability of some bats species to synanthropic environments, the results of the present work can contribute to a better comprehension of the leishmaniasis cycle and epidemiology.

Distribution and epidemiological features of cutaneous leishmaniasis in Asir province, Saudi Arabia, from 2011 to 2020.

Alraey, Y.

11-06-2022

J Infect Public Health

<https://pubmed.ncbi.nlm.nih.gov/35724436>

Background: Cutaneous leishmaniasis (CL) places a major burden on the health authorities in Saudi Arabia. Information about the geographical reach and seasonality of CL in Asir province remains limited. Therefore, this study aimed to investigate the epidemiological features of CL in southwest Saudi Arabia. **Methods:** Retrospective data from CL patients was collected from the regional vector control unit in Asir

province over 9 years. Information analysis was performed using R statistic language (version 4.0.5) and the spatial distribution of cases was mapped using QGIS (version 3.20.0).

Results: A total of 1565 CL cases were recorded from 2011 to 2020. Saudi male citizens were at the highest risk of CL infection. However, children under the age of 13 years were most at risk of contracting CL. CL lesions were primarily located on the face and most cases were reported in the winter and autumn seasons. Spatially, the governorates of Abha, Sarat-Abidah and Khamis-Mushait had the highest CL infection prevalence. Moreover, a geographical expansion of CL from Abha to Khamis-Mushait governorate was noted during past ten years. **Conclusions:** This is the first large scale study to investigate the seasonality, spatial distribution and demographics of CL in Asir province. It describes how the geographical change of CL incidence differs in Asir province and reveals those people most at of CL infections. This study highlights the importance of incorporating improved living conditions, school education and public awareness in the development of CL control policies.

In vitro activity and cell death mechanism induced by acrylonitrile derivatives against *Leishmania amazonensis*.

Bethencourt-Estrella, C., Delgado-Hernández, S., López-Arencibia, A., San Nicolás-Hernández, D., Tejedor, D., García-Tellado, F., Lorenzo-Morales, J., Piñero, J.

15-05-2022

Bioorg Chem

<https://pubmed.ncbi.nlm.nih.gov/35597192>

Leishmaniasis produces approximately-one million of new cases annually, making it one of the most important tropical diseases. As current treatments are not fully effective and are toxic, it is necessary to develop new therapies that are more effective and less toxic, and cause a controlled cell death, with which we can avoid the immunological problems caused by necrosis. In this work 32 acrylonitriles were studied in vitro against *Leishmania amazonensis*. Three compounds Q20 (12.41), Q29 (11.2) and Q31 (11.56) had better selectivity than the reference compound, miltefosine (11.14) against promastigotes of these parasites, for this reason they were selected to determine their mechanism of action to know the cell death type of they produce. The results of the mechanisms of action show that these three acrylonitriles tested produce chromatin condensation, decreased mitochondrial membrane potential, altered plasma permeability and production of reactive oxygen species. All these characteristic events seem to indicate programmed cell death. Therefore, this study demonstrates the activity of acrylonitriles derivatives as possible leishmanicidal agents.

Interferon inducible guanylate binding protein 1 restricts the growth of *Leishmania donovani* by modulating the level of cytokines/chemokines and MAP kinases.

Kumar, R., Kushawaha, P.

09-05-2022

Microb Pathog<https://pubmed.ncbi.nlm.nih.gov/35537595>

Visceral Leishmaniasis (VL) is a zoonotic chronic endemic infectious disease caused by *Leishmania donovani* infection and a well-studied model for intracellular parasitism. Guanylate binding proteins (GBPs) are induced by interferons (IFNs), and play a crucial role in cell autonomous immunity and the regulation of inflammation. Guanylate-binding protein 1 (GBP1) has been shown vital for the host immune response against various pathogens. However, the role of GBP1 during VL is undefined. In the present study, we have investigated the role of GBP1 in *Leishmania donovani* infection using in vitro model. For that, knock down of the *Gbp1* gene was carried out in both PMA differentiated human monocyte cell line THP-1 and mouse macrophages RAW264.7 cell line using siRNA based RNA interference. Infection of these cell lines revealed a high parasite load in knock down cells at 24 and 48h post infection as compared to control cells. A significant increase was observed in the level of different cytokines (IL-4, IL-10, IL-12b, IFN- γ , TNF- α) and chemokines (CXCL9, CXCL 10, and CXCL 11) in GBP1 knock down cell lines after post-infection. In GBP1 knock down cells the expression level of IFN effector molecules (iNOS and PKR) was found to be elevated in THP1 cells and remained almost unchanged in RAW264.7 cells after *Leishmania donovani* infection as compared to the control cells. Moreover, interestingly, the level of MAPK activated ERK1/2, and p38 MAPK were considerably induced by the parasite in knock down cells as compared to control after 24 h post-infection. This study, first time reported the involvement of GBP1 in *Leishmania donovani* infection by modulating the level of important cytokines, chemokines, IFN effector molecules, and MAP kinases.

Primary cutaneous lymphoma and risk for severe COVID-19: a prospective study of 48 cases in Morocco.

Kerrouch, H., Khalidi, M., Frikh, R., Hjira, N., Boui, M.

07-03-2022

J Eur Acad Dermatol Venereol<https://doi.org/10.1111/jdv.18057>

Retinoic acid restores the levels of cellular cholesterol in *Leishmania donovani* infected macrophages by increasing *npc1* and *npc2* expressions.

Prakash, S., Saini, S., Kumari, S., Singh, B., Kureel, A., Rai, A.

07-03-2022

Biochimie<https://pubmed.ncbi.nlm.nih.gov/35272007>

Visceral leishmaniasis (VL) is a fatal form among all forms of leishmaniasis and is caused by visceralization of the *Leishmania donovani* (Ld) parasite to the critical organs. Mild to severe malnutrition is common in VL patients and the deficiency of retinoic acid (RA), an important micronutrient,

results in a compromised state of immune response in macrophages (m ϕ) leading to the increased parasite load. In the continuation of our earlier work, we observed loss of cellular cholesterol in infected m ϕ in the absence of RA i.e., upon inhibition of RALDH pathway. Moreover, the *Leishmania* utilizes host cholesterol for the establishment of infection and causes a decrease in the expressions of Niemann-Pick C2 (*npc2*) and Niemann-Pick C1 (*npc1*) genes involved in the uptake of extracellular cholesterol. This results in reduced levels of cellular cholesterol in infected m ϕ . Intrigued by this, as the first sign of our hypothesis, we investigated the presence of RA Response Element (RARE) sequences in the upstream of *npc1* and *npc2* genes. To functionally confirm this, we measured their expressions and the levels of cellular cholesterol in Ld infected m ϕ in the absence (i.e., using an inhibitor of RALDH pathway) and presence of RA. We found restoration of the levels of cellular cholesterol in infected m ϕ under the supplementation of RA resulting in the decreased parasite load. Hence, the supplementation of RA with the standard therapy and/or preventive use of RA could be potentially an advancement in the treatment and cure of VL patients.

Intralesional injections of meglumine antimoniate to treat complex facial leishmania infantum acquired in Spain: a case report.

Mostmans, Y., Van Gysel, J., Vanden Nest, H., Mervillie, K., Richert, B., Clevenbergh, P.

25-02-2022

J Eur Acad Dermatol Venereol<https://doi.org/10.1111/jdv.18019>

The alteration of the suitability patterns of *Leishmania infantum* due to climate change in Iran.

Trájer, A.

08-03-2021

Int J Environ Health Res<https://doi.org/10.1080/09603123.2021.1897535>

Leishmaniasis is the most important parasitic infection in Iran. The aim of this study was to model the changing suitability patterns of *Leishmania infantum*, the causative agent of visceral leishmaniasis for the 21st century in the country. Temperature, precipitation, and aridity-nature distribution limiting bioclimatic variables were involved in the ecological modelling. The altitudinal trends were considered by using 100 m bars. In Iran, the topographical patterns strongly impact the changing patterns of the suitability of *L. infantum* due to climate change. In general, climate change will decrease the parasite's suitability in the areas at low altitudes and increase in the middle and higher elevation regions. Increasing values are mainly predicted in the West, the decreasing suitability values in the East part of Iran. The altitudinal shifts and the reduced spatial distribution of *L. infantum* in the arid regions of East and Central Iran were modelled.

CYSTICERCOSIS

Evaluating the effect of curcumin on the metacestode of *Taenia crassiceps*.

Martínez-González, J., Ríos-Morales, S., Guevara-Flores, A., Ramos-Godínez, M., López-Saavedra, A., Rendón, J., Del Arenal Mena, I.

28-06-2022

Exp Parasitol

<https://pubmed.ncbi.nlm.nih.gov/35777452>

Curcumin, a curcuminoid present in the rhizome of the plant *Curcuma longa* has multiple pharmacological effects including anticarcinogenic and anti-inflammatory properties. This work evaluates the anthelmintic effect of the curcumin molecule (98% pure) on *Taenia crassiceps* cysticerci viability in vitro. Cysticerci incubated in the presence of increasing concentrations of curcumin showed a dose-dependent mortality correlated with a significant increase in the production of reactive oxygen species and a partial inhibition of thioredoxin-glutathione reductase, the only disulfide reductase present in these parasites. At 500 μ M curcumin, a 100% of cysticerci lethality was obtained after 2 h of treatment. These results suggest the curcumin-induced oxidative stress could be in the origin of the anthelmintic effect of curcumin. Mice with cysticerci were injected intraperitoneally with 20, 40, or 60 mM curcumin daily for 30 days. A decrease in the burden of cysticerci (46%) was observed with a 60 mM dose of curcumin, supporting this compound as a potential anthelmintic drug.

Knowledge, attitude, and practices of the community and meat industry workers towards *Taenia saginata* taeniosis and bovine cysticercosis in and around Jimma and Ambo towns of Ethiopia.

Jorga, E., Van Damme, I., Mideksa, B., Gabriël, S.

19-04-2022

Prev Vet Med

<https://pubmed.ncbi.nlm.nih.gov/35500336>

Taenia saginata taeniosis and bovine cysticercosis are prevalent in Ethiopia, however, data on the knowledge/attitude, and practice (KAP) of the community and meat industry workers in this regard is scarce. The present study aimed to investigate the KAP of the community and meat industry workers about *T. saginata* taeniosis/cysticercosis in Jimma and Ambo towns of Ethiopia. A cross-sectional KAP survey was performed on 293 community members selected using multistage random sampling and 97 meat industry workers from the two study towns. A questionnaire was constructed to collect sociodemographic variables, knowledge/attitudes about taeniosis/cysticercosis, raw meat consumption, latrine usage, and taeniosis treatment practices. Mixed effect (generalized) linear models were used to assess the association of self-reported taeniosis as well as the KAP scores with the demographic variables. The predicted proportion of self-

reported taeniosis was 54% and 75% for Jimma and 44% and 70% for Ambo community and meat industry workers, respectively. The odds of self-reported taeniosis was higher for men (OR_{adj} , 1.68, 95%CI, 0.97-2.93), and elementary/illiterate (OR_{adj} , 1.46, 95%CI, 0.75-2.86) and high school education level (OR_{adj} , 2.65, 95%CI, 1.45-4.93) compared to their counterparts. Most of the community members and the vast majority of the meat industry workers were knowledgeable about taeniosis but less conscious about cysticercosis. The knowledge/attitude score of the community was positively associated with the Jimma community (β_{adj} = 1.20, 95%CI 0.60-1.80), age (β_{adj} =0.03 points higher per year, 95%CI 0.00- 0.04), and men (β_{adj} = 1.20, 95%CI 0.64-1.76), while it was lower in elementary education/illiterate (β_{adj} = -1.60, 95%CI -2.31 to -0.95) and secondary/high school (β_{adj} = -0.83, 95%CI -1.46 to -0.23). The good practice scores of the community within both towns were negatively associated with increasing age (β_{adj} =-0.01 per year, 95%CI, -0.02 to 0.00), elementary/illiterate (β_{adj} = -0.60, 95%CI -1.01 to -0.19) and secondary/high school education (β_{adj} = -0.09, 95%CI -0.45 to -0.28), and urban community (β_{adj} = -0.47 95%CI, -0.82 to -0.12), while protestant/other (β_{adj} = 0.76, 95%CI 0.36 1.16) religion had higher scores compared to Orthodox religion. In conclusion, the predicted self-reported taeniosis proportion was moderately high, and the knowledge/attitude was substantial whereas, the practice was inferior. The association between the knowledge/attitude score and practice score was very weak. Therefore, public education to improve hygienic practices, risky culinary habits, taeniosis treatment, and backyard slaughtering were suggested.

Neurocysticercosis control for primary epilepsy prevention: a systematic review.

Wang, Z., Garcia, R., Huff, H., Niquen-Jimenez, M., Marcos, L., Lam, S.

20-12-2021

Pathog Glob Health

<https://doi.org/10.1080/20477724.2021.2015869>

Neurocysticercosis (NCC) is a leading cause of preventable epilepsy in lower- and upper- middle-income countries (LMICs/UMICs). NCC is a human-to-human transmitted disease caused by ingestion of *Taenia solium* eggs from a *Taenia* carrier. *T. solium* infection control is the key to reduce NCC incidence. This systematic review aims to identify *T. solium* control programs that can provide frameworks for endemic areas to prevent NCC-related epilepsy. A systematic search was conducted in PubMed/Medline, Embase, Web of Science, and Cochrane Library databases in March 2021. After title and abstract review, full texts were screened for qualitative analysis. Additional articles were identified via citation search. Of 1322 total results, 34 unique studies were included. Six major intervention types were identified: national policy (8.8%), community sanitation improvement (8.8%), health education (8.8%), mass drug administration (29.4%), pig vaccination and treatment (32.4%), and combined human and pig treatment (11.8%). Overall, 28 (82.4%) studies reported decreased cysticercosis prevalence following the

intervention. Only health education and combined human and pig treatment were effective in all selected studies. NCC causes preventable epilepsy in LMICs/UMICs and its incidence can be reduced through *T. solium* control. Most interventions that disrupt the *T. solium* transmission cycle are effective. Long-term sustained results require comprehensive programs, ongoing surveillance, and collaborative effort among multisectoral agencies.

DRACUNCULOSE

ECHINOCOCCOSE

Differentiation of hepatic alveolar echinococcosis with a hemangioma-like pattern compared to typical liver hemangioma using contrast-enhanced ultrasound: a pilot study.

Philipp, J., Schmidberger, J., Schlingeloff, P., Kratzer, W.
01-07-2022

Infection

<https://doi.org/10.1007/s15010-022-01866-z>

Purpose: Echinococcus multilocularis infects humans as a false intermediate host, primarily with intrahepatic manifestation. Incorrect diagnostic interpretation of these liver tumors, especially the hemangioma-like pattern, can lead to progressive disease. The aim of the study was to investigate the differentiation of typical hemangioma and a hemangioma-like pattern of *E. multilocularis* using contrast-enhanced ultrasound (CEUS). **Methods:** This prospective clinical pilot study comprised patients with hemangioma (n=14) and patients with alveolar echinococcosis (AE) and hemangioma-like pattern (n=7). Inclusion criteria were the detection of a liver lesion according to a hemangioma-like pattern on *E. multilocularis* Ulm classification-ultrasound (EMUC-US) and "confirmed" or "probable" AE according to WHO case definition. The comparison group had hepatic hemangioma with typical B-scan sonographic morphology. All participants underwent conventional and contrast-enhanced ultrasonography. **Results:** The patient group comprised five men (71.4%) and two women (28.6%) with a mean average age of 64.1±11.2 years. The patient group with hemangioma comprised nine female subjects (64.3%) and five male subjects (35.7%) with a mean average age of 56.1±12.0 years. Early arterial bulbous ring enhancement (p<0.0001) and iris diaphragm phenomenon could only be visualized in the patients with hemangioma (p<0.0001). Furthermore, the patients with hemangioma exhibited hyperenhancement in the late phase (p=0.0003). In contrast, the patients exhibited typical early arterial rim enhancement (p<0.0001) and, in the portal venous and late phase, complete or incomplete non-

enhancement (black hole sign; p=0.0004). **Conclusion:** The behavior of hemangioma-like AE lesions and typical liver hemangiomas is significantly different on CEUS. AE should be considered as a possible differential diagnosis, especially in high-endemic areas.

Wind-borne dispersion of Echinococcus multilocularis eggs - a flight model.

Siegert, S., Neumann, S.

28-06-2022

J Helminthol

<https://doi.org/10.1017/S0022149X22000360>

The alveolar hydatid disease, also known as alveolar echinococcosis, of humans is certainly one of the most dangerous zoonoses worldwide. The disease is caused by *Echinococcus multilocularis* - the fox tapeworm. Red foxes (*Vulpes vulpes*) are currently counted as the most important carriers (reservoirs) of *E. multilocularis* in the Northern Hemisphere. The possible routes of infection of *E. multilocularis* to humans are complex and still require research. Until now, it has been unknown whether *E. multilocularis* eggs can be moved by wind at all. This analysis shows, based on calculations, that *E. multilocularis* eggs can be transported by wind. Using a mathematical model, flight distances depending on wind speed and take-off heights are calculated for dense and less dense (coniferous) forest areas. The results - differentiated for seasons and as overall average - are based on mean values of wind speeds which were measured over a ten-year period in an experimental forest stand in the Solling (Germany). Due to their rate of descent, wind-related spreading of *E. multilocularis* eggs is possible. The average flight distance covered by *E. multilocularis* eggs in forest areas, depending on their starting altitude and wind speed, is between approximately 1.3 m and approximately 17 m. From the mathematical point of view, the wind factor can definitely be seen as one of the multiple vectors associated with environmental contamination by *E. multilocularis* eggs. Consequently, the possible wind-borne spread of *E. multilocularis* eggs poses an infection risk to humans that should be considered and requires further research.

Meta-analysis on the prevalence of bovine hydatid disease in China from 2000 to 2021.

Fan, S., Dong, H., Ma, H., Wang, B., Iqbal, M., Zou, M., Qi, M., Cao, Z.

20-05-2022

Microb Pathog

<https://pubmed.ncbi.nlm.nih.gov/35605738>

Cystic Echinococcosis (hydatidosis) is caused by the larval stage of Echinococcus spp. It is an animal-borne zoonotic parasitic disease with local epidemic and natural foci, which is very common in northwest China. In recent years, a considerable attention has been paid to the epidemic investigation of hydatid disease in humans and sheep, but there are few large-scale epidemic investigation and data

analysis of bovine hydatid disease. We systematically reviewed and analyzed the prevalence of bovine hydatid disease (2000-2021) in China for the first time. Several databases including CNKI, Wanfang, VIP Chinese periodical database, Baidu Library, PubMed and ScienceDirect were used to search 57 articles and 72 sets of valid data about bovine hydatid disease in China from 2000 to 2021. We used the random effect model in META package of R software, and PAS for rate conversion. The subgroup analysis and univariate meta regression analysis were used to reveal the factors leading to the heterogeneity of the study. The total prevalence rate of bovine hydatid disease in China from 2000 to 2021 is estimated to be 17.27% (10898/63113). According to the analysis of sampling years, the lowest positive rate since 2016 is 7.54% (1503/19929). The highest prevalence rate of bovine hydatid disease is 53.93% (4340/8048). The infection rate of bovine liver accounted for the highest proportion of the total infections, 45.2% (2040/4507). We also assessed the effects of different geographical and climatic factors on the prevalence of bovine hydatid disease. The results showed that the prevalence rate of hydatid disease was higher in cold and humid areas. Although the infection rate of bovine hydatid disease has declined in recent years, it is still necessary to carry out long-term surveillance and control of hydatid disease, cut off the infection route and reduce the risk of infection in high-risk areas.

Hydatid cysts of the liver with concomitant massive peritoneal hydatidosis: a case report.

Trajkovski, G., Antovic, S., Kostovski, O., Trajkovska, V., Nikolovski, A.

06-05-2022

Radiol Case Rep

<https://doi.org/10.1016/j.radcr.2022.04.008>

The worldwide distribution of *Echinococcus granulosus* and its capability to persist in the human organism by causing serious medical and economical damage makes this parasite popular in terms of diagnosis and treatment implementation. Besides the liver as the primary target organ for this parasite, cases of secondary peritoneal hydatidosis are reported. Although rarely, they present with unusual abdominal symptoms with a bizarre presentation on abdominal ultrasound and Computerized Tomography scans. We present a case of a 44 years old male patient with concomitant presence of liver hydatid cysts and massive peritoneal hydatidosis treated with a combination of surgery and postoperative medications. The treatment of peritoneal hydatidosis consists of surgical removal of all the present cysts. In addition, anti-parasitic drugs are recommended to prevent a recurrence. The concomitant presence of liver hydatid cysts and peritoneal echinococcosis can appear as a result of abdominal trauma or iatrogenic spillage during abdominal surgery.

The 'bridge effect' by intermediate hosts may explain differential distributions of *Echinococcus* species.

Revue de littérature

Massolo, A., Simoncini, A., Romig, T.

01-05-2022

Trends Parasitol

<https://pubmed.ncbi.nlm.nih.gov/35508436>

Zoonotic cestodes of the genus *Echinococcus* show marked differences in their distribution patterns which have not been satisfactorily explained. *Echinococcus multilocularis* is limited to the Holarctic, whereas species in the *Echinococcus granulosus sensu lato* (s.l.) complex mostly have a worldwide distribution. We proposed and tested a 'bridge effect' hypothesis stating that the low virulence of species in the *E. granulosus* s.l. complex for their intermediate hosts and a longer lifespan of infected hosts explain the differential distributions, particularly in hot and dry regions. This does not exclude the contribution of other factors such as human-mediated dispersal and intermediate host distribution. In the light of globalization and climate change, understanding what drives the distribution of zoonotic parasites is critical for preventing outbreaks of disease caused by these pathogens.

Prevalence and risk factors associated with gastrointestinal parasites of pet dogs in North-Central Algeria.

Ziam, H., Kelanemer, R., Belala, R., Medrouh, B., Khater, H., Djerbal, M., Kernif, T.

20-04-2022

Comp Immunol Microbiol Infect Dis

<https://pubmed.ncbi.nlm.nih.gov/35490504>

The prevalence and risk factors associated with gastrointestinal parasites in dogs were conducted in Blida, North-Central Algeria. The study was carried out over 131 clinically healthy dogs, from March to June 2019, by coprological methods. Of the 131 collected dogs, 61.07% (n = 80) were found infected by gastrointestinal parasites. Sixty-four dogs were carriers of a single infection with the following parasites *Ancylostoma* spp (15.27%), *Uncinaria* spp (14.50%) *Toxocara canis* (4.58%), *Trichuris vulpis* (3.82%), *Toxascaris leonina* (2.29%), *Taenia/Echinococcus* spp. (2.29%), *Mesocestoides* spp (0.76%), *Cystoisospora* spp. (3.05%) and *Neospora caninum*-like (2.29%). Sixteen dogs harbored mixed infection. Male (OR = 1.18) German shepherds' dogs were more infected (OR = 1.08) by helminthic parasites (OR = 13.64). The frequency of single infections (OR = 6.86) increased with the animal's age (OR = 1.73-3.46). Identifying hookworms, *T. canis*, and *T. vulpis* suggests a continuing risk of contamination of pet dogs as a source of human infection with the zoonotic parasites in Blida.

Comparison and evaluation of analytic and diagnostic performances of four commercial kits for the detection of antibodies against *Echinococcus granulosus* and *multilocularis* in human sera.

Peruzzo, A., Mastrandrea, S., Fancellu, A., Bonelli, P.,

Muehlethaler, K., Masala, G., Santucci, C.

15-04-2022

Comp Immunol Microbiol Infect Dis<https://pubmed.ncbi.nlm.nih.gov/35472655>

Cystic echinococcosis (CE) is a disease caused by *Echinococcus granulosus sensu lato* (s.l.), an ubiquitous worldwide zoonotic agent affecting humans and animals. Diagnosis of CE in humans is usually performed by image techniques along with immunoassays. The aim of our study was to evaluate and compare four commercial diagnostic kits, based on the detection of IgG antibodies against *E. granulosus* and *E. multilocularis*. The study was performed on a total of 259 sera: the positive (n = 74) and the negative (n = 185) group. The following analytic and diagnostic performances of the four kits were evaluated: operator skills, specificity, sensitivity, repeatability, reproducibility, accuracy, positive and negative predictive values. Based on the parameters evaluated, all four tests demonstrated excellent quality and proved to be reliable diagnostic tools to support the clinical evaluation of human patients suspected of having CE. The four commercial assays, in our hands, presented altogether, a range of performances from good to excellent, being immunoblotting (IB) the most reliable, used as gold standard, followed by the immunochromatographic test (ICT) and finally the two enzyme linked immunosorbent assay (ELISAs).

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

Differences in microbiome of healthy Sprague Dawley rats with *Paragonimus proliferus* infection and potential pathogenic role of microbes in paragonimiasis.

Sun, L., Zhu, M., Zhang, L., Peng, M., Li, C., Wang, L., Wang, W., Ma, Z., Li, S., Zeng, W., Yin, M., Wang, W., Chunyu, W.

29-06-2022

Acta Trop<https://pubmed.ncbi.nlm.nih.gov/35779592>

Paragonimiasis, which is caused by *Paragonimus*, is considered to be a neglected tropical disease by the World Health Organization. The pathogenicity of *Paragonimus* mainly manifests as mechanical damage and immunotoxicity caused by adult worms and larvae. However, microbiota associated with *Paragonimus* and potential disturbance of host microbiota after infection are unknown. *Paragonimus proliferus* is a rare species, and its successful infection rate in experimental rats is 100%. In the current study, we compared the microbial community in lung tissues, small intestine contents, and fecal samples from Sprague Dawley (SD) rats with and without *P. proliferus* infection. To determine the

impact of *P. proliferus* on the microbial community in rats, we identified the microbiota in adult worms of *P. proliferus* via high-throughput sequencing. Results showed dramatic differences in the composition of microbiota in lung tissues between infected and uninfected rats. *Paragonimus metacercariae* introduced both environmental and gut microbes into the lung tissues of rats. Many potentially pathogenic microbes were also found in the lung of infected rats. *Paragonimus* infection increased the chances of potentially pathogenic microbiota invading and colonizing the lungs. However, for the purpose of long-term parasitism, there might be a complex interrelationship between *Paragonimus* and microorganisms. Our study might shed lights on the understanding of the pathogenicity of *Paragonimus*.

An Unusual Cause of Gastric Variceal Bleeding.

Zhu, Y., Shi, H., He, S.

28-06-2022

Gastroenterology<https://pubmed.ncbi.nlm.nih.gov/35777478>

Gross and histologic description of trematodosis in fetal and neonatal beef calves in North Dakota and Minnesota.

Pecoraro, H., Stenger, B., Rice, L., Webb, B.

30-06-2022

J Vet Diagn Invest<https://doi.org/10.1177/10406387221109619>

Hepatic trematodes, such as *Fasciola hepatica* and *Fascioloides magna*, have variable distribution throughout the United States. *F. magna* is endemic in the upper midwestern United States, and *F. magna* infections are diagnosed frequently in weaned calves and adult beef cattle at the North Dakota State University Veterinary Diagnostic Laboratory (NDSU-VDL). Rarely, liver fluke infestation has also been observed in much younger calves, including aborted fetuses. We describe here, in 2 fetal and 7 neonatal beef calves submitted to the NDSU-VDL between 2011 and 2020, parasitic migration tracts in livers, consisting of regionally extensive, random, linear tracts of fibrosis admixed with black porphyrin pigment, along with foci of necrosis and hemorrhage, and mixed inflammatory cells, which were caused presumptively by *F. magna* infection. Samples were not available from our 9 cases for PCR assay and sequencing, but we did confirm *F. magna* within liver samples collected from regional cattle in 2020 and 2021. Fetal and neonatal trematodosis was often concurrent with other common causes of fetal abortion and neonatal calf loss in our cases; however, based on the prepatent period of *F. magna*, fetal and neonatal beef calf trematode infestations occurred in utero.

Status of Helminthic Infections in Residents around River Basins in the Republic of Korea for 10 Years (2011-2020).

Lee, M., Shin, H., Back, S., Lee, Y., Lee, H., Ju, J.

30-06-2022

Korean J Parasitol<https://doi.org/10.3347/kjp.2022.60.3.187>

The positive rate of *Clonorchis sinensis* is the highest among intestinal parasites in the Republic of Korea (Korea). More than 1.2 million people were at risk of *C. sinensis* infection in Korea in 2012. An intensive control program is being implemented for residents of the 5 major river basins to reduce helminthic infections, including *C. sinensis* infection. This study evaluated the continuous intensive control program for parasitic diseases including clonorchiasis in areas near the 5 major river basins in Korea over the past 10 years (2011-2020). A total of 335,020 fecal samples (one sample per resident) prepared by the modified sedimentation technique were microscopically examined. Those who expelled helminth eggs were treated with anthelmintics through local health centers and re-examined 3 months later. The overall positive rate of helminth egg was 7.1%. The annual positive rates were dramatically decreased from 14.4% (2011) to 5.9% (2020). The egg positive rate was highest in *C. sinensis* (5.3%), followed by heterophyid flukes (1.5%) and *Trichuris trichiura* (0.2%). The prevalence of *C. sinensis* was significantly higher in males (7.6%) than in females (3.7%), and the highest in the 50-59 years (7.0%) age group. Our results are beneficial to establish prevention and control policies against helminthiasis including clonorchiasis in endemic areas in this country.

FILARIOSE LYMPHATIQUE

Diethylcarbamazine citrate-fortified salt for lymphatic filariasis elimination in India.

Sabesan, S., Krishnamoorthy, K., Hoti, S., Subramanian, S., Srividya, A., Roy, N., Jain, T., Kumar, A., Rahi, M.

01-07-2022

Indian J Med Reshttps://doi.org/10.4103/ijmr.ijmr_171_22

Lymphatic filariasis (LF) is a vector-borne neglected tropical disease, causing permanent disability. The disease is debilitating and widespread, leading to tremendous productivity and economic loss. The Government of India (GOI) prioritized the elimination of LF through the annual mass drug administration (MDA) programme in 2004 and continued with a single dose of diethylcarbamazine citrate (DEC), 6 mg/kg of body weight, plus albendazole annually over a period of 5-6 years. The GOI had set the target to achieve LF elimination by 2015 and now by 2030. The progress so far has been suboptimal. Much remains to be done as about 84 per cent of the total 328 endemic districts are still under MDA. The major challenge in implementing MDA is poor compliance. It is necessary to have a feasible alternative strategy addressing the above challenge to achieve the desired goal of LF elimination. At this juncture, a well-researched approach, i.e. the use of DEC-fortified salt, also

advocated by the World Health Organization, as a unique form of MDA, is proposed. As per this strategy, a low dose of DEC (0.2% w/w) is added to the cooking salt at the manufacturing facility of iodized salt and consumed by the LF-endemic communities for about two years. Many examples of successful use of this strategy for LF elimination in small- and large-scale trials have been documented in India and several other endemic countries in the world. Implementing DEC-iodine-fortified salt is a safe, less expensive, more efficient and prompt approach for achieving the elimination of LF in India. Adverse effects are none or minor and self-limiting. The DEC-fortified salt strategy can easily piggyback on the existing nationwide deployment of iodized salt under the National Iodine Deficiency Disorders Control Programme (NIDDCP), which has achieved a great success in reducing iodine-deficiency disorders such as hypothyroidism. This existing robust programme can be leveraged to launch DEC-fortified salt for the community. If implemented appropriately, this strategy will ensure the complete cessation of LF transmission within two years from its introduction. If the said strategy is implemented in 2022, it is expected that India will be able to achieve the LF elimination by 2024, much before the global target of 2030.

Mass drug administration for lymphatic filariasis elimination amidst COVID-19 pandemic in Odisha, India: A step towards achieving SDG-3.

Sinha, A., Mohapatra, S., Mohanty, S., Pati, S., Sahoo, P.

30-06-2022

Trop Doct<https://doi.org/10.1177/00494755221098532>

Sustainable Development Goal-3 (SDG) aims to eliminate lymphatic filariasis by 2030 through >65% coverage and compliance of mass drug administration (MDA), the preventive chemotherapy strategy of delivering anthelmintic drugs. However, the ongoing COVID-19 pandemic has disrupted such programmes, yet MDA was administered during February 2021 in Odisha, India. We aimed to assess the coverage and compliance of the present round of MDA amidst the pandemic and explore factors for non-compliance in Cuttack district of Odisha, a filariasis endemic area. Community-based participants enrolled through multistage stratified sampling were administered a semi-structured questionnaire following COVID-19 protocols. The coverage of MDA was 93.2% whereas consumption was 73.7%. Participants reported that healthcare workers were motivated and satisfactorily explained the benefits of MDA but still fear of side-effects was the major cause of non-compliance. Nonetheless, this recent round of MDA was effective, despite challenges posed by the ongoing pandemic.

MYCETOME

Mini-mycetoma due to *Nocardia asteroides*: a short report from Mexico.

Chandler, D., Fuentes-Gonzalez, M., Bonifaz, A.

11-04-2022

Clin Exp Dermatol

<https://doi.org/10.1111/ced.15172>

An illustrative case of mini-mycetoma in a 54-year-old female agricultural worker from Mexico.

Spinal and cranio-cervical mycetoma: A difficult surgery, with poor prognosis.

Aggad, M., Bielle, F., Planty-Bonjour, A., Terrier, L., Cook, A., Amelot, A.

19-06-2021

Neurochirurgie

<https://pubmed.ncbi.nlm.nih.gov/34157340>

Background: Few central nervous systems (CNS) cases of actinomycetoma have been recorded in the literature, and most were reported in tropical and subtropical regions. The management of this invasive infection is difficult, especially when it affects the spine and the cranio-cervical regions. **Case:** We report an unusual case of a cranio-cervical junction actinomycetoma, in a patient presenting a cerebellar syndrome from brainstem compression. The CT scan showed a compressive solid osteolytic lesion in the cranio-cervical junction. The patient underwent cranio-cervical decompression and lesion resection. The diagnosis of actinomycetoma was confirmed on immune-histochemistry and molecular analysis. At 4 months' follow-up, the patient presented a fatal recurrence disseminating within the cerebellum and the spine. **Conclusion:** The surgical treatment of CNS actinomycetoma presented poor prognosis and a disseminating recurrence. We believe that clinicians and surgeons must be informed about these "new" infectious pathologies that are so difficult to treat, especially with the arrival of migrant patients from endemic countries in conflict.

ONCHOCERCOSE

Helminth antigens differentially modulate the activation of CD4⁺ and CD8⁺ T lymphocytes of convalescent COVID-19 patients in vitro.

Adjibimey, T., Meyer, J., Terkeš, V., Parcina, M., Hoerauf, A.

28-06-2022

BMC Med

<https://doi.org/10.1186/s12916-022-02441-x>

Background: The coronavirus disease 2019 (COVID-19) is a respiratory disease caused by SARS-CoV-2, a recently discovered strain of coronavirus. The virus has spread rapidly,

causing millions of death worldwide. Contrary to the predictions, prevalence and mortality due to COVID-19 have remained moderate on the African continent. Several factors, including age, genetics, vaccines, and co-infections, might impact the course of the pandemic in Africa. Helminths are highly endemic in Sub-Saharan Africa and are renowned for their ability to evade, skew, and suppress human immune responses through various immune-modulatory mechanisms. Such effects will likely impact SARS-CoV-2 transmission and disease progression. **Methods:** Here, we analyzed in vitro the impact of antigen extracts from three major helminth parasites, including *Onchocerca volvulus*, *Brugia malayi*, and *Ascaris lumbricoides*, on the immune reactivity to SARS-CoV-2 peptides in COVID-19 patients. Activation of CD4⁺ and CD8⁺ T cells was investigated using flow cytometry to monitor the expression of CD137 (4-1BB) and CD69. Cytokine expression, including IL-6, IL-10, IFN- γ , and TNF α , was measured by Luminex in cell culture supernatants. **Results:** We observed that helminth antigens significantly reduced the frequency of SARS-CoV-2-reactive CD4⁺ T helper cells. In contrast, the expression of SARS-CoV-2-reactive CD8⁺ T cells was not affected and even significantly increased when PBMCs from COVID-19 patients living in Benin, an endemic helminth country, were used. In addition, stimulation with helminth antigens was associated with increased IL-10 and a reduction of IFN γ and TNF α . **Conclusions:** Our data offer a plausible explanation for the moderate incidence of COVID-19 in Africa and support the hypothesis that helper T cell-mediated immune responses to SARS-CoV-2 are mitigated in the presence of helminth antigens, while virus-specific cytotoxic T cell responses are maintained.

SCHISTOSOMIASE

Protective role of *Balanites aegyptiaca* fruit aqueous extract in mice infected with *Schistosoma mansoni*.

Elmalawany, A., Osman, G., Elashwal, M., Mohamed, A.

29-06-2022

Exp Parasitol

<https://pubmed.ncbi.nlm.nih.gov/35779646>

the target of this research was to investigate the effect of *Balanites aegyptiaca* fruit aqueous extract (200 mg/kg BW), alone or in combination with Praziquantel PZQ (300 mg/kg BW) on some biochemical, parasitological, liver histopathology and immunohistochemical parameters in mice infected with *Schistosoma mansoni*. Results showed that treatment of *S. mansoni*-infected mice with *B. aegyptiaca* alone or in combination with PZQ significantly reduced the activities of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) as compared to that of the *S. mansoni*-infected mice group. Treatment of *S. mansoni*-infected mice with *B. aegyptiaca* or PZQ and their combination

led to a significant reduction in the activity of malondialdehyde (MDA) as compared with the infected control group. While a significant elevation was observed in the activities of antioxidant enzymes glutathione (GSH), catalase (CAT), superoxide dismutase (SOD) and nitric oxide (NO) compared with the infected. Results revealed that the diameter and number of egg granuloma were significantly condensed after treatment of *S. mansoni*-infected mice with *B. aegyptiaca*, PZQ or their combination in hepatic and intestinal tissue. The histopathological alterations observed in the liver of *S. mansoni*-infected mice were remarkably recovered after *B. aegyptiaca* treatments. The reduction in angiogenesis was mostly observed in the group receiving the combination of *B. aegyptiaca* and PZQ. The alterations in vascular endothelial growth factor (VEGF) expression were significantly less in the liver sinusoids. Overall, *B. aegyptiaca* significantly inhibited the liver and intestinal damage accompanied by schistosomiasis. It demonstrated potent antioxidant and immunoprotective activities. This study advises that *B. aegyptiaca* can be considered promising for the development of a complementary and/or alternative against schistosomiasis.

The WHO new guideline to control and eliminate human schistosomiasis: implications for the verification of transmission interruption and surveillance of *Schistosoma japonicum* in China.

Xu, J., Li, S., Guo, J., Zhou, X., Djirmay, A.

01-07-2022

Infect Dis Poverty

<https://doi.org/10.1186/s40249-022-01003-w>

Different panel of toll-like receptors expression during chronic *Schistosoma mansoni* infection in experimental animals.

Saad, A., Ashour, D., Osman, E.

28-06-2022

Exp Parasitol

<https://pubmed.ncbi.nlm.nih.gov/35777451>

Background: Many studies have reported the immunomodulatory effect of helminths to avoid the lethal immunopathology. During schistosomiasis, the immune response is orchestrated by toll-like receptors (TLRs). Modulating TLRs can alter the function of antigen presentation cells with the shift of the host's Th1 response to a dominant regulatory Th2 response. The objective of our study was to clarify which TLRs are related to the immune response of chronic *Schistosoma* infection. **Methods:** The study animals were divided into two groups; group I: uninfected mice; control group and group II: *Schistosoma mansoni* infected mice. mRNA expression of TLR2, 3, 4, 7, and 9 in different organs (liver, large intestine, and spleen) were assessed on day 90 post-infection. **Results:** TLR gene expression has changed depending on the tissue studied as the mRNA level of TLR2, TLR7, and TLR9 were significantly upregulated in all examined organs while TLR3 expression

showed only significant upregulation in the liver of infected mice. On the other hand, TLR4 expression was significantly upregulated in the liver while significantly downregulated in the large intestine. **Conclusion:** This study provides a better understanding of TLRs profile in different organs against *S. mansoni* parasites during the chronic phase of infection.

Mapping of schistosomiasis and soil-transmitted helminthiases across 15 provinces of Angola.

Mendes, E., Okhai, H., Cristóvão, R., Almeida, M., Katondi, N., Thompson, R., Mupoyi, S., Mwinzi, P., Ndayishimiye, O., Djerandouba, F., Chimbili, M., Ramirez, J., Van Goor, E., Lopes, S.

30-06-2022

PLoS Negl Trop Dis

<https://doi.org/10.1371/journal.pntd.0010458>

Introduction: Schistosomiasis (SCH) and soil transmitted helminthiases (STH) have been historically recognized as a major public health problem in Angola. However, lack of reliable, country wide prevalence data on these diseases has been a major hurdle to plan and implement programme actions to target these diseases. This study aimed to characterize SCH and STH prevalence and distribution in Angola. **Methods:** A country wide mapping was conducted in October 2018 (1 province) and from July to December 2019 (14 provinces) in school aged (SAC) children in 15 (of 18) provinces in Angola, using WHO protocols and procedures. A total of 640 schools and an average of 50 students per school (N = 31,938 children) were sampled. Stool and urine samples were collected and processed using the Kato-Katz method and Urine Filtration. Prevalence estimates for SCH and STH infections were calculated for each province and district with 95% confidence intervals. Factors associated with SCH and STH infection, respectively, were explored using multivariable logistic regression accounting for clustering by school. **Results:** Of the 131 districts surveyed, 112 (85.5%) are endemic for STH, 30 (22.9%) have a prevalence above 50%, 24 (18.3%) are at moderate risk (prevalence 20%-50%), and 58 (44.3%) are at low risk (<20% prevalence); similarly, 118 (90.1%) of surveyed districts are endemic for any SCH, 2 (1.5%) are at high risk (>50% prevalence), 59 (45.0%) are at moderate risk (10%-50% prevalence), and 57 (43.5%) are at low risk (<10% prevalence). There were higher STH infection rates in the northern provinces of Malanje and Lunda Norte, and higher SCH infection rates in the southern provinces of Benguela and Huila. **Conclusions:** This mapping exercise provides essential information to Ministry of Health in Angola to accurately plan and implement SCH and STH control activities in the upcoming years. Data also provides a useful baseline contribution for Angola to track its progress towards the 2030 NTD roadmap targets set by WHO.

Application of kNN and SVM to predict the prognosis of advanced schistosomiasis.

Zhou, X., Wang, H., Xu, C., Peng, L., Xu, F., Lian, L., Deng, G., Ji, S., Hu, M., Zhu, H., Xu, Y., Li, G.

29-06-2022

Parasitol Res<https://doi.org/10.1007/s00436-022-07583-8>

Predictive models for prognosis of small sample advanced schistosomiasis patients have not been well studied. We aimed to construct prognostic predictive models of small sample advanced schistosomiasis patients using two machine learning algorithms, k nearest neighbour (kNN) and support vector machine (SVM) utilising routinely available data under the government medical assistance programme. The predictive models were derived from 229 patients from Xiantao and externally validated by 77 patients of Jiayu, two county-level cities in Hubei province, China. Candidate predictors were selected according to expert opinions and literature reports, including clinical features, sociodemographic characteristics, and medical examinations results. An area under the receiver operating characteristic curve (AUC), sensitivity, and specificity were used to evaluate the models' predictive performances. The AUC values were 0.879 for the kNN model and 0.890 for the SVM model in the training set, 0.852 for the kNN model, and 0.785 for the SVM model in the external validation set. The kNN and SVM models can be used to improve the health services provided by healthcare planners, clinicians, and policymakers.

Schistosome dipeptide of love.

Le Govic, Y., Boissier, J., Papon, N.

14-05-2022

Trends Parasitol<https://pubmed.ncbi.nlm.nih.gov/35581129>

The female schistosome's dependence on the male to reach sexual maturity has puzzled scientists for decades. Using various molecular techniques, Chen et al. dissect the synthesis pathway of the β -alanyl-tryptamine dipeptide (BATT), emitted by the male into its environment, which induces sexual maturation and egg-laying in the female.

A genomic can of worms for schistosome host-specificity.

Nikolakis, Z., Carlton, E., Pollock, D., Castoe, T.

01-05-2022

Trends Parasitol<https://pubmed.ncbi.nlm.nih.gov/35504822>

Understanding the genetic underpinnings of schistosome host preferences is critical. Luo et al. recently identified genes associated with intermediate and definitive host-switching based on a new chromosome-level genome for *Schistosoma japonicum*, population genetic comparisons, and follow-up experiments. This represents a guide to fully map-selected schistosome genes using population genetics.

Shared sugars - parasite glycan homology in HIV-1 vaccine design.

Deimel, L., Sattentau, Q.

29-04-2022

Trends Parasitol<https://pubmed.ncbi.nlm.nih.gov/35501266>

Immune tolerance to self-glycans is a host mechanism to avoid autoimmunity, which is exploited by HIV-1 coating its envelope glycoproteins with glycans to evade neutralising antibodies (nAbs). Huettnner et al. describe cross-reactivity between *Schistosoma mansoni* glycans and HIV-1 envelope glycoprotein glycans, suggesting a strategy for induction of HIV-1 nAbs by vaccination.

Schistosoma japonicum translationally controlled tumour protein, which is associated with the development of female worms, as a target for control of schistosomiasis.

Zhong, H., Ren, Y., Qin, F., Li, X., Hou, L., Gu, S., Jin, Y.

19-03-2022

Int J Parasitol<https://pubmed.ncbi.nlm.nih.gov/35318950>

Schistosomiasis is a globally important helminthic disease of both humans and animals, and is the second most common parasitic disease after malaria. Although praziquantel is extensively used for treatment of parasitic diseases, drug resistance has been reported. Therefore, new drugs and effective vaccines are needed for continuous control of schistosomiasis. Eggs produced by schistosomes are responsible for the occurrence and spread of schistosomiasis. Revealing the reproductive mechanism of schistosomes will help to control this disease. In this study, the proteomic profiles of single-sex infected female worms and bisexual infected mature female worms of *Schistosoma japonicum* at 18, 21, 23 and 25 days p.i. were identified with isobaric tags for relative quantitation-coupled liquid chromatography-tandem mass spectrometry. Differentially expressed proteins were subsequently used for bioinformatic analysis. Six highly expressed differentially expressed proteins in mature female worms were selected and long-term interference with small interfering RNA (siRNA) was conducted to determine biological functions. siRNA against *S. japonicum* translationally controlled tumour protein (SjTCTP) resulted in the most significant effect on the growth and development of MF worms. SjTCTP mRNA expression gradually increased over time with a high level of expression maintained at 25-42 days p.i., while levels were significantly higher in mature female worms than male and SF worms. The subsequent animal immune protection experiments showed that recombinant SjTCTP (rSjTCTP) reduced the number of adults by 44.7% ($P < 0.01$), average egg burden per gram of liver by 57.94% ($P < 0.01$), egg hatching rate by 47.57% ($P < 0.01$), and oviposition of individual females by 43.16%. rSjTCTP induced higher levels of serum IgG, IL-2, and IL-10 in mice. Collectively, these results show that SjTCTP is vital to reproduction of female worms and, thus, is a candidate antigen for immune protection.

Efforts to eliminate schistosomiasis in Hubei province, China: 2005-2018.

Zhu, H., Liu, J., Xiao, Y., Tu, Z., Shan, X., Li, B., Wu, J., Zhou, X., Sun, L., Xia, J., Liu, S., Huang, X.

19-03-2022

Acta Trop

<https://pubmed.ncbi.nlm.nih.gov/35318000>

Background: The Hubei province is one of the most schistosomiasis-epidemic-prone provinces in China. A series of strategies were adopted by the government to curb the rebound schistosomiasis endemic status that has prevailed since the early 2000s. This study aimed to elucidate the trends of schistosomiasis transmission and to appraise the effectiveness of the integrated control strategy in lake and marshland areas. **Methods:** Surveillance data of schistosomiasis in the Hubei province between 2005 and 2018 were analyzed, including conventional health control measures, integrated strategies, and measures that focused on the infection source. According to the local annual plan for schistosomiasis control in endemic counties, previous measures were human and snail control and surveillance. Residents aged 6-65 years were screened by an immunological detection method called indirect hemagglutination assay (IHA) after the transmission season each year. All residents who tested positive were then asked to provide a fecal sample for examination by the miracidium hatching technique (MHT) to detect the presence of schistosomes. Moreover, systematic snail surveys were conducted as a part of the combined environmental sampling method. The latter included integrated strategies and measures that focused on the infection source. Bovine stool samples were also collected and concurrently assessed using the MHT by the agriculture department, river-hardening slope protection was constructed by the water conservancy department, and forestation promotion was conducted by the forest department. The effectiveness of the integrated control strategy was assessed using two indicators of resident and livestock infection rates and three indicators of snail epidemics across all endemic areas. **Results:** From 2005 to 2018, a total of 28.46 million and 2.05 million residents were assessed by immunological (IHA) and etiological (MHT) detection techniques, respectively. Snail surveys and molluscicide application were performed in 2.26 hectares and 0.37 hectares, respectively. Moreover, 2.60 million bovines were assessed by etiological detection techniques (MHT). The river-hardening slope protection project was implemented in 503 places, and 46 thousand hectares in endemic areas underwent environmental modification. Forestation was implemented at an area of 0.15 million hectares. Between 2005 and 2018, the epidemic indicators, including resident and livestock infection rates and the infested areas and infection rate of snails, all presented downward trends. The resident infection rate decreased from 3.78% in 2005 to 0% in 2016, which persisted through 2018. The livestock infection rate decreased from 5.63% in 2005 to 0% in 2013, which also persisted through 2018. From 2005 to 2018, the snail-inhabited area was slightly reduced, but the area of infected snails decreased to 0 in 2012; this persisted through 2018. All counties met the goal for schistosomiasis

infection control, transmission control, and disruption of schistosomiasis activity in 2008, 2013, and 2018 separately. That means the goal has been achieved in each stage.

Conclusions: The decline of the schistosomiasis epidemic rate demonstrates that the Chinese government was successful in meeting its public health goal in Hubei province. In the next decade, precision interventions must be implemented in endemic counties with a relatively low epidemic status to achieve the goals of the Outline of the Healthy China 2030 Plan. A similar strategy can be applied in other countries to eliminate schistosomiasis globally.

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

The effect of compliance to Hand hygiene during COVID-19 on intestinal parasitic infection and intensity of soil transmitted helminthes, among patients attending general hospital, southern Ethiopia: Observational study.

Seid, M., Yohanes, T., Goshu, Y., Jemal, K., Siraj, M.

29-06-2022

PLoS One

<https://doi.org/10.1371/journal.pone.0270378>

Background: Intestinal parasitic infection (IPIs) is one of the major health problems in Sub-Saharan Africa where water, sanitation and hygiene practices are inadequate. Taking into account the national level implementation of intensive hand hygiene against COVID-19 pandemic and general protective effect this study assessed its effect on intestinal parasite.

Objective: This study aim to investigate the effect of compliance to hand hygiene practice on the prevalence of intestinal parasitic infection (IPIs) and intensity of Soil transmitted helminthes (STH) among patients attending tertiary care hospital in southern Ethiopia. **Methods:** Observational study was conducted from June to September 2021. Data on socio demographic, hand hygiene practice and intestinal parasite (prevalence and intensity of helminthic infection) was collected from randomly selected and consented patients. Compliance to hand hygiene practice was assessed using pre-tested questionnaire. Fresh stool sample from each participant was examined by direct wet mount, concentration and Ziehl-Neelson (ZN) staining technique to detect intestinal parasite. Intensity of STH measurements was done through direct egg-count per gram using Kato Katz methods. Data analysis was done using SPSS version 25. Odds ratio with 95% confidence interval was used to measure association and p-value <0.05 was considered as statistically significant. **Results:** The study population (N = 264) consisted of 139(52.65%) male and 125 (47.34%) female with the mean ages of 36 ±16.12(±SD). The proportion of good compliance to

hand hygiene during COVID-19 to was 43.93% (95%CI: 37% to 47) and prevalence of intestinal parasite was 26.14% (95%CI:21.2% to 31.75) comprising 23.48% intestinal protozoa and 6.43% of soil transmitted helminthic infection. *Gardia lamblia*, *Entamoeba histolytica/dispar*, *Ascaris lumbricoides* were the common parasite in the study area with prevalence of 15.53%, 6.44%, and 1.52% respectively. Prevalence of intestinal parasite among participants with good compliance to hand hygiene group and poor compliance to hand hygiene were (14.65% vs. 35.13%)(AOR: 0.48,95%CI:0.13 to 0.68) ($p = 0.002$) implying that good compliance to hand hygiene can reduce the risk of IPIs by 52%. Moreover significantly lower odds of intestinal protozoa among good compliance to hand hygiene group than the control (OR:0.38; (95%CI: 0.20 to 0.71); $P = 0.001$). However, no significant difference in the odds of intensity of STH infection in good compliance hand hygiene and poor compliance group. The result of this study also confirmed the association between intestinal parasitic infections and younger /adolescent age, education status, habit of eating raw vegetable and figure nail status. **Conclusion:** Good hand hygiene compliance during COVID-19 significantly associated with reduction of intestinal parasitic infection. This finding highlights the secondary protective effect of improved hand hygiene against IPIs and suggest it can be used in augmenting the existing parasitic control strategies in the study setting.

Assessment of the nail contamination with soil-transmitted helminths in schoolchildren in Jimma Town, Ethiopia.

Tadege, B., Mekonnen, Z., Dana, D., Tiruneh, A., Sharew, B., Dereje, E., Loha, E., Ayana, M., Levecke, B.

29-06-2022

PLoS One

<https://doi.org/10.1371/journal.pone.0268792>

Background: Large-scale deworming programs have been successful in reducing the burden of disease due to soil-transmitted helminth (STH; *Ascaris lumbricoides*, *Trichuris trichiura* and hookworm) infections, but re-infection in absence of other measures is unavoidable. We assessed the role of nail contamination as a source of infection with the goal to evaluate the potential of nail clipping as a simple measure to further reduce STH-attributable morbidity. **Methods:** A cross-sectional study was conducted in Jimma Town (Ethiopia). Both stool samples and clipped nails were collected from 600 schoolchildren and microscopically screened for the presence of STHs. We also interviewed the children to gain insights into their hygiene practices. Subsequently, we explored any associations between infection, nail contamination and personal hygiene. **Results:** Any STH infections were observed in 24.3% of the children (*A. lumbricoides*: 18.5%; *T. trichiura*: 9.8%; hookworm: 0.5%). The intensity of the infections was mainly low, only in a few cases a moderate-to-heavy intensity infection was observed (*A. lumbricoides*: 4.3%; *T. trichiura*: 0.2%). Other helminth species observed were *Schistosoma mansoni* (5.0%), *Hymenolepis nana* (2.7%), *Taenia* spp. and *Enterobius vermicularis* (<1.0%).

The analysis of the nail material revealed the presence of *A. lumbricoides* (1.7%), *Taenia* spp. (1.0%), *T. trichiura* (0.5%), *E. vermicularis* (0.5%) and *H. nana* (0.2%). The odds of infection with any STH increased as the frequency of trimming decreased. The odds of nail contamination with any STH and *A. lumbricoides* were higher for younger children. **Conclusions:** The presence of helminth eggs under the nails of children highlights a poor personal hygiene. The association between any STH infection and frequency of nail trimming needs to be explored in an intervention study. The recent prevalence of any STH infections indicated that scaling down of the frequency of deworming is justified but that STH is still a public health problem.

Helminth antigens differentially modulate the activation of CD4⁺ and CD8⁺ T lymphocytes of convalescent COVID-19 patients in vitro.

Adjibimey, T., Meyer, J., Terkeš, V., Parcina, M., Hoerauf, A. 28-06-2022

BMC Med

<https://doi.org/10.1186/s12916-022-02441-x>

Background: The coronavirus disease 2019 (COVID-19) is a respiratory disease caused by SARS-CoV-2, a recently discovered strain of coronavirus. The virus has spread rapidly, causing millions of death worldwide. Contrary to the predictions, prevalence and mortality due to COVID-19 have remained moderate on the African continent. Several factors, including age, genetics, vaccines, and co-infections, might impact the course of the pandemic in Africa. Helminths are highly endemic in Sub-Saharan Africa and are renowned for their ability to evade, skew, and suppress human immune responses through various immune-modulatory mechanisms. Such effects will likely impact SARS-CoV-2 transmission and disease progression. **Methods:** Here, we analyzed in vitro the impact of antigen extracts from three major helminth parasites, including *Onchocerca volvulus*, *Brugia malayi*, and *Ascaris lumbricoides*, on the immune reactivity to SARS-CoV-2 peptides in COVID-19 patients. Activation of CD4⁺ and CD8⁺ T cells was investigated using flow cytometry to monitor the expression of CD137 (4-1BB) and CD69. Cytokine expression, including IL-6, IL-10, IFN- γ , and TNF α , was measured by Luminex in cell culture supernatants. **Results:** We observed that helminth antigens significantly reduced the frequency of SARS-CoV-2-reactive CD4⁺ T helper cells. In contrast, the expression of SARS-CoV-2-reactive CD8⁺ T cells was not affected and even significantly increased when PBMCs from COVID-19 patients living in Benin, an endemic helminth country, were used. In addition, stimulation with helminth antigens was associated with increased IL-10 and a reduction of IFN γ and TNF α . **Conclusions:** Our data offer a plausible explanation for the moderate incidence of COVID-19 in Africa and support the hypothesis that helper T cell-mediated immune responses to SARS-CoV-2 are mitigated in the presence of helminth antigens, while virus-specific cytotoxic T cell responses are maintained.

Plasmodium falciparum coinfection is associated with improved IgE and IgG3 response against hookworm antigens.

Sakyi, S., Wilson, M., Adu, B., Opoku, S., Brewoo, A., Larbi, A., Baafour, E., Tchum, S., Saahene, R., Aniagyei, W., Sewor, C., Courtin, D., Cappello, M., Gyan, B., Amoani, B.

14-06-2022

Health Sci Rep

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Background: *Plasmodium falciparum* and Hookworm infections are prevalent in West Africa and they cause iron deficiency anemia and protein malnutrition in Children. Immune response of these parasites interact and their interactions could have repercussions on vaccine development and efficacy. The current goal of hookworm eradication lies on vaccination. We evaluated the effect of *P. falciparum* coinfection and albendazole treatment on naturally acquired antibody profile against hookworm L3 stage larvae antigen. **Methods:** In a longitudinal study, 40 individuals infected with *Necator americanus* only, 63 participants infected with *N. americanus* and *P. falciparum*, and 36 nonendemic controls (NECs) were recruited. The study was done in the Kintampo North Metropolis of Ghana. Stool and blood samples were taken for laboratory analyses. Serum samples were obtained before hookworm treatment and 3 weeks after treatment. **Results:** The malaria-hookworm (*N. americanus* and *P. falciparum*) coinfecting subjects had significantly higher levels of IgE ($\beta=0.30$, 95% CI=[0.12, 0.48], $p=0.023$) and IgG3 ($\beta=0.15$, 95% CI=[0.02, 0.52], $p=0.004$) compared to those infected with hookworm only (*N. americanus*). The *N. americanus* groups had significantly higher levels of IgG3 ($\beta=0.39$, 95% CI=[0.14-0.62], $p=0.002$) compared to the control group. Similarly, *N. americanus* and *P. falciparum* coinfecting participants had significantly higher levels of IgE ($\beta=0.35$, 95% CI=[0.70-0.39], $p=0.002$) and IgG3 ($\beta=0.54$, 95% CI=[0.22-0.76], $p=0.002$). Moreover, albendazole treatment led to a significant reduction in IgE, IgA, IgM, and IgG3 antibodies against hookworm L3 stage larvae ($p<0.05$). **Conclusion:** *P. falciparum* is associated with improved IgE and IgG response against hookworm L3 stage larvae. Treatment with single dose of albendazole led to reduction in naturally acquired immune response against hookworm infection. Thus, *P. falciparum* infection may have a boosting effect on hookworm vaccine effectiveness.

immunocompromised children and adults. It is rarely reported in the neonatal age group. We present such a case.

Spectrum of skin diseases in Maroon villages of the Maroni area, French Guiana.

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Int J Dermatol

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Background: Due to their genetic characteristics and their high exposure to infectious diseases, Maroons are likely to suffer from a specific spectrum of skin diseases. However, skin disorders have never been explored in this population. We aimed to describe all skin diseases in Maroon villages of the Maroni region in French Guiana. **Methods:** This retrospective study concerned all patients who consulted in the remote health centers of Apatou, Grand-Santi, Papaichton, and Maripasoula between October 5, 2017, and June 30, 2020. We included all patients registered with a skin disorder (International Classification of Diseases) in the medical database. We excluded patients whose diagnosis was invalidated after cross-checking by a dermatologist. **Results:** A total of 4741 patients presented at least one skin disease, for 6058 different disorders. Nonsexually transmitted infections represented 71.6% of all diagnoses, followed by inflammatory diseases (9.8%) and bites/envenomations (4.6%). The three most frequent conditions were scabies, abscesses, and impetigo. Besides scabies, neglected tropical diseases (NTDs) were still prevalent as we reported 13 cases of leprosy and 63 cutaneous leishmaniasis. Atopic dermatitis (AD) represented only 2.5% of our diagnoses. **Conclusions:** With the exception of AD, which was less frequent among Maroons, these results are similar to those previously reported in Amerindians. Therefore, a common exposure to rainforest pathogens seems to induce a common spectrum of skin diseases dominated by infections. The high prevalence of NTDs requires specific public health actions.

Topical ivermectin: an off-label alternative to treat neonatal Scabies in the era of permethrin resistance.

Bassi, A., Piccolo, V., Argenziano, G., Mazzatenta, C.

17-03-2022

J Eur Acad Dermatol Venereol

<https://doi.org/10.1111/jdv.18026>

Epidemiology of dermatologic disease in Palau: a cross-sectional study in the national public and community health service.

Lee, W., Lee, C., Wu, C., Lin, C., Lo, T., Huang, C., Kahler, S., Thong, H.

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GALE

Neonatal Norwegian scabies.

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Trop Doct

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Norwegian scabies is a severe form of scabies usually seen in

Background: Dermatologic disease is a neglected public health challenge that disproportionately affects resource-poor settings. Globally, dermatologic disease contributes the fourth highest burden of nonfatal disability with the most acute impact in the Oceanic region, including the Republic of Palau. Efforts to address the dermatologic health inequality are hindered without the necessary epidemiologic evidence to guide health policy in the resource-poor setting of Palau.

Methods: We conducted a 4-year cross-sectional study of all Dermatology Service patients in the Belau National Hospital and outreach community health centers from 2015 to 2018. No other specialized dermatology service was available. Skin disease was classified by both diagnosis and Global Burden of Disease criteria and analyzed by age, gender, region, and surrounding Oceanic nations. **Results:** The study enrolled 494 patients comprising 179 males and 315 females between 2015 and 2018. The most prevalent diseases were eczema (48.8%), superficial fungal infection (24.5%), and pruritus (22.7%). The neglected tropical disease of scabies was detected in four patients. Males were significantly more likely to present with cellulitis, keratinocyte carcinoma, stasis dermatitis, wounds, marine-related dermatitis, viral skin disease, tinea faciei, verruca, and xerosis and females with melasma and hyperpigmentation. **Conclusion:** This study presents the first primary epidemiologic data describing the prevalence of dermatologic disease in the Palauan adult population. The significant burden of disease in Palau compared with other Oceanic nations validates ongoing dermatology services and informs public health implications for resource allocation and disease management to achieve health equality in the resource-poor nation.

of *Jatropha curcas* were obtained from the NCBI nonredundant protein sequence (nr) database. Molecular docking analyses performed with the peptide against a metalloendopeptidase belonging to *Crotalus adamanteus* snake venom suggested the cyclic peptide establishes favorable interactions with the catalytic site of the enzyme. Therefore, it could inhibit enzyme catalysis. This belief was corroborated by the formation of 6 hydrogen bonds with the linear form of the peptide. Tighter complexation of the cyclic form (41kcal/mol more energetic) revealed better spatial blocking. The linear form outperformed the cyclic form in complexing the required energy, recruiting more catalytic residues (6/2), and in establishing more hydrogen bonds (6/3). However, cyclic folding provided a more significant spatial block within the catalytic site. The set of results suggests that the cycle peptide, here called Jatromollistatin, which was previously described as jatrophidin and pohlianin A in two other species of *Jatropha*, is a promising candidate to inhibit venom proteases. This belief is corroborated by the topical use of the latex for initial treatment of snakebites.

MORSURES DE SERPENT

Insights on the inhibition properties of Jatromollistatin (a cyclic heptapeptide) against *Crotalus adamanteus* metalloendopeptidase using molecular docking analysis.

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07-03-2022

J Mol Recognit

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Jatropha mollissima is endemic to Brazil and is used for traditional medicinal purposes, including the treatment of snakebite. In this study, latex obtained from this plant was fractioned using reversed-phase chromatography, and the fractions were then screened for peptides. A 755g/mol peptide was obtained, and MS/MS analyses indicated it had a cyclic sequence (Pro-Leu-Gly-Val-Leu-Leu-Tyr). This peptide sequence was present in the *Jatropha* genome database, and an identity value of 90.71%, an E-value of 0.0, and a score of 883 with NO-associated protein 1/chloroplast/mitochondria