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Veille scientifique Maladies tropicales négligées

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DENGUE, CHIKUNGUNYA ET MALADIE A VIRUS ZIKA

Circulation of Dengue Virus Serotype 2 in Humans and Mosquitoes During an Outbreak in El Quseir City, Egypt.

El-Kady, A., Osman, H., Alemam, M., Marghani, D., Shanawaz, M., Wakid, M., Al-Megrin, W., Elshabrawy, H., Abdella, O., Allemailem, K., Almatroudi, A., El-Amir, M.

30-05-2022

Infect Drug Resist

<https://doi.org/10.2147/IDR.S360675>

In recent decades, the rate of infection with dengue virus (DENV) has risen significantly, now affecting nearly 400 million individuals annually. Dengue fever among humans is caused via specific mosquito vectors bites. Sporadic cases have been reported in Egypt. The goal of this study was to identify the serotype of the DENV outbreak in both human and mosquito vector along the coast of the Red Sea, Upper Egypt, in 2017. Identification of the serotype of the virus may help identify its source and assist in applying epidemiological and control measures. The current study was carried out in El Quseir City, Red Sea Governorate, Upper Egypt, on 144 patients complaining of symptoms indicative of dengue fever at the time of the 2017 Egypt outbreak. Human blood samples and the mosquito reservoirs were identified as having dengue virus infection serologically and molecularly. Overall, 97 (67.4%) patients were positive for dengue virus IgM antibodies. Molecular examination of the human samples and pools of mosquitoes revealed that DENV-2 virus was the serotype responsible for the outbreak. Only one pool of female mosquitoes containing *Aedes aegypti* was infected with dengue fever virus (DENV-2). This was the first serotyping of the DENV responsible for dengue virus outbreak in Egypt in 2017. Determining the serotype of dengue virus can help to avoid and monitor outbreaks. The serotype identified in this study was DENV-2, while DENV-1 was the serotype found in the previous outbreak in 2015 in the province of Assiut. This study thus raises concerns that a new dengue serotype could have been introduced into Egypt. It is necessary for a comprehensive risk assessment to be carried out in the country, including an entomological survey, to assess the presence and potential geographical expansion of mosquito vectors there.

Establishment of Wolbachia infection in *Aedes aegypti* from Pakistan via embryonic microinjection and semi-field evaluation of general fitness of resultant mosquito population.

Sarwar, M., Jahan, N., Ali, A., Yousaf, H., Munzoor, I.

06-06-2022

Parasit Vectors

<https://doi.org/10.1186/s13071-022-05317-4>

Background: Dengue is a mosquito-borne viral disease that is mainly spread by *Aedes aegypti*. It is prevalent on five

continents, predominantly in tropical and sub-tropical zones across the world. Wolbachia bacteria have been extensively used in vector control strategies worldwide. The focus of the current study was to obtain a natural population of *Ae. aegypti* harbouring Wolbachia and to determine the impact of this bacteria on the new host in a semi-field environment.

Methods: Wolbachia-infected *Aedes albopictus* was collected from the city of Lahore, Punjab, Pakistan, and Wolbachia were successfully introduced into laboratory-reared *Ae. aegypti* via embryonic microinjection. The stable vertical transmission of wAlbB in the host population was observed for eight generations, and the impact of Wolbachia on the general fitness of the host was evaluated in semi-field conditions.

Results: In the laboratory and semi-field experiments, wAlbB Wolbachia presented a strong cytoplasmic incompatibility (CI) effect, evidenced as zero egg hatching, in crosses between Wolbachia-infected males and wild (uninfected) females of *Ae. aegypti*. Wolbachia infection had no noticeable impact on the general fitness ($P > 0.05$), fecundity, body size (females and males) and mating competitiveness of the new host, *Ae. aegypti*. However, there was a significant decrease in female fertility (egg hatch) ($P < 0.001$). In addition, under starvation conditions, there was a remarkable decrease ($P < 0.0001$) in the life span of Wolbachia-infected females compared to uninfected females (4 vs. > 5 days, respectively). **Conclusions:** Wolbachia strain wAlbB has a great potential to control the dengue vector in *Ae. aegypti* populations by producing 100% CI with a limited burden on its host in natural field conditions. This strain can be used as a biological tool against vector-borne diseases.

New tools for Aedes control: mass trapping.

Revue de littérature

Barrera, R.

03-06-2022

Curr Opin Insect Sci

<https://pubmed.ncbi.nlm.nih.gov/35667560>

Aedes aegypti, the main vector of dengue, chikungunya, and Zika viruses uses artificial containers around homes to undergo immature development, making household-level detection and control extremely difficult in large urban areas. Mass trapping is an emerging methodology to control container-*Aedes* species such as *Aedes aegypti* and *Aedes albopictus* because effective traps for adult stages of these mosquitoes were developed recently. There are three main approaches to mass-trapping these mosquitoes: 1) Pull (attract/kill), 2) push (repel) - pull (attract/kill), and 3) pull (attract/contaminate/infect) - push (fly away). Effective mass-trapping depends on trap quality (capture efficiency, sturdiness, frequency of servicing), trap density and areal coverage, community involvement, and safety. Recent studies showed that *Ae. aegypti* populations can be sustainably controlled by mass trapping, although more area-wide studies showing effectiveness at preventing disease are needed for all trapping systems. Cost-effectiveness studies are needed for all emerging *Aedes* control approaches.

IL-1Ra and sVCAM-1 in Chikungunya virus infection.

Chirathaworn, C., Chansaenroj, J., Chaisuriyong, W., Lertmaharit, S., Poovorawan, Y.

03-06-2022

Acta Trop

<https://pubmed.ncbi.nlm.nih.gov/35667454>

Mediators involving in inflammation induction and regulation have been investigated as biomarkers for severe joint pain induced by chikungunya virus (CHIKV) infection. In this report, observational study was conducted to determine levels of an antagonist of interleukin-1 receptor (IL-1Ra) and soluble vascular cell adhesion molecule-1 (sVCAM-1) in CHIKV patients with different disease severity. CHIKV infection patients presented without (n = 199) and with joint pain (n = 262) were included. IL-1Ra and sVCAM-1 levels in patient sera were determined. Levels of sVCAM-1 were strongly and significantly higher in the group of patients with joint pain than in the group without joint pain ($p < 0.0001$). The levels of both IL-1Ra and sVCAM-1 were not significantly increased with age.

Treatment of chikungunya-associated joint pain: a systematic review of controlled clinical trials.

Rodrigo, C., Herath, T., Wickramarachchi, U., Fernando, D., Rajapakse, S.

06-06-2022

Trans R Soc Trop Med Hyg

<https://pubmed.ncbi.nlm.nih.gov/35666998>

Post-chikungunya joint pain (arthritis or arthralgia) is a clinical concern in endemic regions as it may cause a debilitating illness sometimes years after the acute infection. This systematic review analyses evidence from controlled clinical trials regarding the efficacy of pharmacological and non-pharmacological interventions to treat post-chikungunya joint pain. PubMed, EMBASE, Scopus, Cochrane library and Web of Science were searched for eligible studies without any language or time limits, excluding retrospective studies, and prospective observational studies without a control group. Eleven studies met the inclusion criteria. Seven assessed pharmacological interventions and four assessed non-pharmacological interventions (exercise, neuromodulation). The number of participants in each intervention arm varied from 10 to 75 and, given the heterogeneity of interventions, a meta-analysis was not possible. Available evidence does not show any added benefit of chloroquine, hydroxychloroquine, stand-alone methotrexate or ribavirin compared with anti-inflammatory drugs or placebo/no treatment. Non-steroidal anti-inflammatory drugs may reduce pain up to 24 wk of treatment but long-term residual impact after stopping treatment is unassessed. Currently, there is also no high certainty evidence to recommend non-pharmacological methods such as exercise and neuromodulation.

Self-association features of NS1 proteins from different flaviviruses.

Poveda-Cuevas, S., Etchebest, C., da Silva, F.

31-05-2022

Virus Res

<https://pubmed.ncbi.nlm.nih.gov/35662566>

Flaviviruses comprise a large group of arboviral species that are distributed in several countries of the tropics, neotropics, and some temperate zones. Since they can produce neurological pathologies or vascular damage, there has been intense research seeking better diagnosis and treatments for their infections in the last decades. The flavivirus NS1 protein is a relevant clinical target because it is involved in viral replication, immune evasion, and virulence. Being a key factor in endothelial and tissue-specific modulation, NS1 has been largely studied to understand the molecular mechanisms exploited by the virus to reprogram host cells. A central part of the viral maturation processes is the NS1 oligomerization because many stages rely on these protein-protein assemblies. In the present study, the self-associations of NS1 proteins from Zika, Dengue, and West Nile viruses are examined through constant-pH coarse-grained biophysical simulations. Free energies of interactions were estimated for different oligomeric states and pH conditions. Our results show that these proteins can form both dimers and tetramers under conditions near physiological pH even without the presence of lipids. Moreover, pH plays an important role mainly controlling the regimes where van der Waals interactions govern their association. Finally, despite the similarity at the sequence level, we found that each flavivirus has a well-characteristic protein-protein interaction profile. These specific features can provide new hints for the development of binders both for better diagnostic tools and the formulation of new therapeutic drugs.

Scanning electron microscopy for identification of local strain of *Aspergillus Parasiticus* and its larvicidal efficacy against *Aedes Aegypti* and non-target toxicity testing on fingerlings of *Hypophthalmichthys Molitrix*.

Abbar, A., Abbas, M., Mehmood, S., Ghani, N., Fatima, A., Shahzadi, R.

06-06-2022

Microsc Res Tech

<https://doi.org/10.1002/jemt.24176>

Scanning electron microscopy proved to be helpful in identification of *Aspergillus parasiticus*. *A. parasiticus* has a worldwide occurrence with high entomopathogenic efficacy against *Aedes aegypti*. However, assessment of pathogenic effects of entomopathogenic fungi on non-target organisms is required to evaluate its use as bio control agent. Aim of the present research is to study the parricidal activity of the local strain of *A. parasiticus* (MK371710) against *A. aegypti* and its toxicity assessment against aquatic model organism *Hypophthalmichthys molitrix*. *A. parasiticus* was isolated from the soil of Jallo Park, Lahore. The larvicidal effect of *A. parasiticus* was evaluated against fourth instar larvae of *A. aegypti*. Hundred percent of mortality of larvae was observed after exposure to 1×10^7 conidia/ml of fungal suspension after

72h post treatment. The LC₅₀ value of *A. parasiticus* in 24h post treatment and 48h post treatment was recorded as 1.0×10^7 conidia/ml and 2.99×10^5 conidia/ml, respectively. However, an in-depth understanding safety to non-target organisms is necessary, if we are to properly control the action of these entomopathogenic fungi under natural conditions. For the toxicity assessment fingerlings of *H. molitrix* were exposed to conidial suspensions of *A. parasiticus*. Eye pop (64%), fin hemorrhage (33%), and scale infection (30%) were the major morphological effects observed during the study. Results reveal that although *A. parasiticus* is highly pathogenic to dengue vector but also have significant effects on organisms other than insects and its application as biological control agent requires safety considerations.

Accuracy and efficacy of pre-dengue vaccination screening for previous dengue infection with a new dengue rapid diagnostic test: a retrospective analysis of phase 3 efficacy trials.

Savarino, S., Bonaparte, M., Wang, H., Dayan, G., Forrat, R., Zhu, M., Hodge, S., Ataman-Önal, Y., DiazGranados, C.
04-05-2022

Lancet Microbe

<https://pubmed.ncbi.nlm.nih.gov/35659904>

A dengue pre-vaccination test that is convenient, highly specific, and highly sensitive is still needed. The OnSite Dengue IgG rapid diagnostic test (RDT) is a new rapid diagnostic test specifically designed for pre-vaccination screening. We aimed to retrospectively assess the efficacy of a tetravalent dengue vaccine (CYD-TDV) in participants determined to be dengue seropositive by the OnSite IgG RDT and to evaluate assay performances. This was a complementary study using pre-vaccination samples from two CYD-TDV efficacy trials done in five countries in the Asia-Pacific region (NCT01373281) and five countries in Latin America (NCT01374516). Baseline dengue serostatus was determined by the OnSite IgG RDT on samples from the immunogenicity subsets of the two trials. In participants who were test positive, we calculated CYD-TDV vaccine efficacy against symptomatic virologically confirmed dengue (VCD) over 25 months, and against hospitalisation with VCD over 72 months of follow-up after the first vaccination. We used a reference algorithm to determine the reference dengue serostatus for each sample, and sensitivity and specificity of the OnSite IgG RDT were calculated. Analyses were done on the whole population (aged 2-16 years), and on those aged 6 years or older and those aged 9 years or older. Of 3983 participants in the immunogenicity subsets of the efficacy trials CYD14 and CYD15, 3962 had complete dengue reference test results enabling baseline serostatus classification and 3833 had sufficient serum samples remaining for evaluation with the OnSite IgG RDT. Of the samples tested, 2486 (64.9%) of 3833 were OnSite IgG RDT-positive. In participants aged 2-16 years who were OnSite IgG RDT-positive, vaccine efficacy was 84.1% (95% CI 71.6-91.1) against symptomatic VCD, and 69.2% (38.8-84.5) against hospitalisation with VCD, with similar findings in those aged 6 years or older and those aged

9 years or older. The OnSite IgG RDT showed very high sensitivity (91.1%, 89.9-92.1) and high specificity (92.8%, 91.2-94.2) in participants aged 2-16 years, with significantly higher specificity in those aged 9 years or older (96.6%, 94.9-97.8). The OnSite IgG RDT should provide a valuable tool for screening for previous dengue infection at the point of vaccination. In individuals who were OnSite IgG RDT-positive, the vaccine efficacy of CYD-TDV was high across all three age groups. Sanofi Pasteur.

Acute appendicitis during the recovery phase of dengue hemorrhagic fever: two case reports.

Thadchanamoorthy, V., Ganeshrajah, A., Dayasiri, K., Jayasekara, N.
05-06-2022

J Med Case Rep

<https://doi.org/10.1186/s13256-022-03443-2>

Dengue fever is one of the most common tropical diseases, with high prevalence in many tropical countries including Sri Lanka. Dengue infection can present from subclinical infection to dengue shock syndrome. Further, the disease also shows a variety of atypical presentations and has been reported to mimic a number of causes of acute abdomen. The authors report two children (a 6-year-old Tamil girl and an 8-year-old Muslim girl) who were diagnosed to have acute appendicitis during the early recovery phase of dengue hemorrhagic fever (DHF) and late recovery period of dengue hemorrhagic fever with platelet count of 92×10^3 /cumm and 102×10^3 /cumm, respectively. Both children were investigated with abdomen ultrasound as they developed severe abdominal pain and tenderness on palpation during the recovery phase, which was felt to be very unusual. Acute appendicitis was diagnosed in one child, while the other child had a ruptured appendicular abscess. Both children were treated with laparoscopic appendectomy and a 7-day course of intravenous antibiotics. Both children were reviewed in 1 month following treatment and had complete recovery. Although precise pathophysiology and associations of the surgical abdomen with dengue fever remain to be elucidated, there are known factors in dengue fever that can potentially lead to secondary bacterial infections and surgical abdomen. Awareness and increased suspicion by the clinician are paramount to detect such complications early, especially in children who demonstrate unusual clinical features during various stages of dengue infection.

Impact of a spatial repellent product on Anopheles and non-Anopheles mosquitoes in Sumba, Indonesia.

Permana, D., Zubaidah, S., Syahrani, L., Asih, P., Syafruddin, D., Rozi, I., Hidayati, A., Kosasih, S., Dewayanti, F., Rachmawati, N., Risandi, R., Bangs, M., Bøgh, C., Davidson, J., Hendershot, A., Burton, T., Grieco, J., Eugenio, E., Liu, F., Achee, N., Lobo, N.
03-06-2022

Malar J

<https://doi.org/10.1186/s12936-022-04185-8>

The East Nusa Tenggara province, Indonesia, contributed to 5% of malaria cases nationally in 2020, with other mosquito-borne diseases, such as dengue and filariasis also being endemic. Monitoring of spatial and temporal vector species compositions and bionomic traits is an efficient method for generating evidence towards intervention strategy optimization and meeting disease elimination goals. The impact of a spatial repellent (SR) on human biting mosquitoes was evaluated as part of a parent cluster-randomized, double-blinded, placebo-controlled trial, in Sumba, East Nusa Tenggara. A 10-month (June 2015-March 2016) baseline study was followed by a 24-month intervention period (April 2016 to April 2018)-where half the clusters were randomly assigned either a passive transfluthrin emanator or a placebo control. Human-landing mosquito catches documented a reduction in landing rates related to the SR. Overall, there was a 16.4% reduction (21% indoors, and 11.3% outdoors) in human biting rates (HBR) for *Anopheles*. For *Aedes*, there was a 44.3% HBR reduction indoors and a 35.6% reduction outdoors. This reduction was 38.3% indoors and 39.1% outdoors for *Armigeres*, and 36.0% indoors and 32.3% outdoors for *Culex* species. Intervention impacts on the HBRs were not significant and are attributed to large inter-household and inter cluster variation. *Anopheles flavirostris*, *Anopheles balabacensis* and *Anopheles maculatus* individually impacted the overall malaria infections hazard rate with statistical significance. Though there was SR-based protection against malaria for all *Anopheles* species (except *Anopheles sondaicus*), only five (*Anopheles aconitus*, *Anopheles kochi*, *Anopheles tessellatus*, *An. maculatus* and *An. sondaicus*) demonstrated statistical significance. The SR numerically reduced *Anopheles* parity rates indoors and outdoors when compared to the placebo. Evidence demonstrating that *Anopheles* vectors bite both indoors and outdoors indicates that currently implemented indoor-based vector control tools may not be sufficient to eliminate malaria. The documented impact of the SR intervention on *Aedes*, *Armigeres* and *Culex* species points to its importance in combatting other vector borne diseases. Studies to determine the impact of spatial repellents on other mosquito-borne diseases is recommended.

Armigeres subalbatus is a potential vector for Zika virus but not dengue virus.

Yang, W., Zhao, S., Xie, Y., Liu, T., Kong, L., Guo, Y., Xie, Z., Liu, P., Chen, X.

04-06-2022

Infect Dis Poverty

<https://doi.org/10.1186/s40249-022-00990-0>

Zika virus (ZIKV) and dengue virus (DENV) are closely related flaviviruses primarily transmitted by *Aedes* mosquitoes. *Armigeres subalbatus* is an emerging and widely distributed mosquito, and ZIKV has been detected and isolated from it. However, it is not clear whether *Ar. subalbatus* could be a vector for ZIKV and DENV or not. In this study, we investigated the infection and transmission of *Ar. subalbatus* to ZIKV and DENV. A line of *Ar. subalbatus* was isolated from Guangdong, China, and further identified by the mitochondrial cytochrome

oxidase subunit 1 (COI) gene. The adults of *Ar. subalbatus* were fed with blood meal containing ZIKV or DENV-2. At 4, 7, 10, 14, and 21 days post-inoculation (dpi), the infections of ZIKV or DENV-2 in the midguts, ovaries and salivary glands were detected and quantified by RT-PCR and RT-qPCR. To assess the transmissibility, suckling mice were exposed to bites of ZIKV-infected mosquitoes, and ZIKV was detected in brain tissue by RT-qPCR and plaque assays. Furthermore, the larvae of *Ar. subalbatus* were reared in artificial urine containing ZIKV or DENV-2. The infection rates and viral titers of larvae and adults were analyzed by RT-PCR and RT-qPCR, and the viral distribution in larval tissues was observed by immunohistochemistry. Chi-square test and one-way ANOVA analysis were used for assessing the infection rate and viral titer in varied tissues and different time points, respectively. Following oral inoculation, ZIKV but not DENV-2 could be detected in *Ar. subalbatus* midguts at 4 dpi, ovaries at 7 dpi and salivary glands at 10 dpi. The highest infection rate (IR) of ZIKV was 27.8% in midgut at 7 dpi, 9.7% in ovary and 5.6% in salivary gland at 21 dpi. Eight days after being bitten by ZIKV-positive mosquitoes, ZIKV was detected in three brain tissues out of four suckling mice exposed to bites. ZIKV could be detected in the larvae reared in artificial urine contained ZIKV at a high concentration of 10^5 pfu/ml and various tissues of adults with a low infection rate (0.70-1.35%). ZIKV could be observed in anal papillae and midgut of larvae at 4 dpi under laboratory conditions. ZIKV but not DENV-2 can infect *Ar. subalbatus* by blood meal and artificial urine, and the infected mosquitoes can transmit ZIKV to suckling mice by bite. From these findings, we can conclude that the *Ar. subalbatus* isolated from Guangdong province, China, is a potential vector for ZIKV and should therefore be considered in vector control programs to prevent and control of Zika virus disease.

A poisson-multinomial spatial model for simultaneous outbreaks with application to arboviral diseases.

Schmidt, A., Freitas, L., Cruz, O., Carvalho, M.

05-06-2022

Stat Methods Med Res

<https://doi.org/10.1177/09622802221102628>

Dengue, Zika, and chikungunya are arboviral diseases (AVD) transmitted mainly by *Aedes aegypti*. Rio de Janeiro city, Brazil, has been endemic for dengue for over 30 years, and experienced the first joint epidemic of the three diseases between 2015-2016. They present similar symptoms and only a small proportion of cases are laboratory-confirmed. These facts lead to potential misdiagnosis and, consequently, uncertainty in the registration of the cases. We have available the number of cases of each disease for the $n = 160$ neighborhoods of Rio de Janeiro. We propose a Poisson model for the total number of cases of *Aedes*-borne diseases and, conditioned on the total, we assume a multinomial model for the allocation of the number of cases of each of the diseases across the neighborhoods. This provides simultaneously the estimation of the associations of the relative risk of the total cases of AVD with environmental and socioeconomic

variables; and the estimation of the probability of presence of each disease as a function of available covariates. Our findings suggest that a one standard deviation increase in the social development index decreases the relative risk of the total cases of AVD by 28%. Neighborhoods with smaller proportion of green area had greater odds of having chikungunya in comparison to dengue and Zika. A one standard deviation increase in population density decreases the odds of a neighborhood having Zika instead of dengue by 18% but increases the odds of chikungunya in comparison to dengue by 18% and by 43% in comparison to Zika.

Transchromosomal bovine (TcB)-derived broadly neutralizing antibodies as potent biotherapeutics to counter important emerging viral pathogens with a special focus on SARS-CoV-2, MERS-CoV, Ebola, Zika, HIV-1 and Influenza A virus.

Revue de littérature

Saied, A., Nascimento, M., Rangel, A., Skowron, K., Grudlewska-Buda, K., Dhama, K., Shah, J., Abdeen, A., El-Mayet, F., Ahmed, H., Metwally, A.

02-06-2022

J Med Virol

<https://doi.org/10.1002/jmv.27907>

Historically, passive immunotherapy is an approved approach for protecting and treating humans against various diseases when other alternative therapeutic options are unavailable. Human polyclonal antibodies (hpAbs) can be made from convalescent human donor serum, although it is considered limited due to pandemics and the urgent requirement. Additionally, pAbs could be generated from animals, but they may cause severe immunoreactivity and, once "humanized," may have lower neutralization efficiency. Transchromosomal bovine (TcB) have been developed to address these concerns by creating robust neutralizing hpAbs, which are useful in preventing and/or curing human infections in response to hyperimmunization with vaccines holding adjuvants and/or immune stimulators over an extensive period. Unlike other animal-derived polyclonal antibodies, potent hpAbs could be promptly produced from TcB in large amounts to assist against an outbreak scenario. Some of these highly efficacious TcB-derived antibodies have already neutralized and blocked diseases in clinical studies. SARS-CoV-2 has numerous variants classified into variants of concern (VOCs), variants of interest (VOIs), and variants under monitoring (VUM). Although these variants possess different mutations, such as N501Y, E484K, K417N, K417T, L452R, T478K, and P681R, SAB-185 has shown broad neutralizing activity against VOCs, such as Alpha, Beta, Gamma, Delta, and Omicron variants, and VOIs, such as Epsilon, Iota, Kappa, and Lambda variants. This article highlights recent developments in the field of bovine-derived biotherapeutics, which are seen as a practical platform for developing safe and effective antivirals with broad activity, particularly considering emerging viral infections such as SARS-CoV-2, Ebola, MERS-CoV, Zika, HIV-1, and Influenza A virus. Antibodies in the bovine serum or colostrum, which have been proved to be more protective than their human

counterparts, are also reviewed. This article is protected by copyright. All rights reserved.

Addressing delayed case reporting in infectious disease forecast modeling.

Beesley, L., Osthus, D., Del Valle, S.

03-06-2022

PLoS Comput Biol

<https://doi.org/10.1371/journal.pcbi.1010115>

Infectious disease forecasting is of great interest to the public health community and policymakers, since forecasts can provide insight into disease dynamics in the near future and inform interventions. Due to delays in case reporting, however, forecasting models may often underestimate the current and future disease burden. In this paper, we propose a general framework for addressing reporting delay in disease forecasting efforts with the goal of improving forecasts. We propose strategies for leveraging either historical data on case reporting or external internet-based data to estimate the amount of reporting error. We then describe several approaches for adapting general forecasting pipelines to account for under- or over-reporting of cases. We apply these methods to address reporting delay in data on dengue fever cases in Puerto Rico from 1990 to 2009 and to reports of influenza-like illness (ILI) in the United States between 2010 and 2019. Through a simulation study, we compare method performance and evaluate robustness to assumption violations. Our results show that forecasting accuracy and prediction coverage almost always increase when correction methods are implemented to address reporting delay. Some of these methods required knowledge about the reporting error or high quality external data, which may not always be available. Provided alternatives include excluding recently-reported data and performing sensitivity analysis. This work provides intuition and guidance for handling delay in disease case reporting and may serve as a useful resource to inform practical infectious disease forecasting efforts.

Vomiting and Gastric Motility in Early Brain Damaged Children With Congenital Zika Syndrome.

de Paula, G., da Silva, G., E Silva, E., Lins, M., Martins, O., Oliveira, D., Ferreira, E., Antunes, M.

01-06-2022

J Pediatr Gastroenterol Nutr

<https://doi.org/10.1097/MPG.0000000000003504>

This study investigated the occurrence of vomiting and gastric dysmotility in dysphagic children with congenital Zika syndrome (CZS) and assessed possible associations of these findings with the severity of dysphagia and the presence of tube feeding. Forty-six children with CZS were assessed for dysphagia, and the occurrence of vomiting, dietary volume tolerance <15 mL/kg, and feeding time per meal >30 min were evaluated. Gastric antrum ultrasonography was used to detect the frequency of contractions and measure antral areas (at fasting and 15 min postprandial), from which the gastric

emptying rate (GER) was calculated. Antral ultrasonography findings were compared with those of ten healthy controls. Vomiting and gastric motility were compared between CZS patients according to the severity of dysphagia and the requirement for tube feeding. Overall, 76% (35/46) of children with CZS had moderate-to-severe dysphagia (MSD), among whom 60% (21/35) were tube fed (MSDTF). Vomiting occurred in 54% (25/46) of children, whereas dietary volume intolerance and prolonged feeding time were observed in 59% (27/46) and 37% (17/46), respectively, most frequently in MSDTF patients. On ultrasound, 61% (28/46) of children with CZS had no antral contractions, whereas 90% (9/10) of controls did. Compared to healthy controls, GER was eight-fold lower in children with CZS and 60-fold lower in MSDTF children. In dysphagic children with CZS, vomiting, volume intolerance, and prolonged feeding time were frequent and possibly associated with impaired antral contraction and delayed gastric emptying, especially in cases of severe dysphagia and tube feeding.

The Dengue Virus Nonstructural Protein 1 (NS1) Interacts with the Putative Epigenetic Regulator DIDO1 to Promote Flavivirus Replication in Mosquito Cells.

Caraballo, G., Rosales, R., Vietri, M., Castillo, J., Cruz, R., Ding, S., Greenberg, H., Ludert, J.
02-06-2022

J Virol

<https://doi.org/10.1128/jvi.00704-22>

Dengue virus (DENV) NS1 is a multifunctional protein essential for viral replication. To gain insights into NS1 functions in mosquito cells, the protein interactome of DENV NS1 in C6/36 cells was investigated using a proximity biotinylation system and mass spectrometry. A total of 817 mosquito targets were identified as protein-protein interacting with DENV NS1. Approximately 14% of them coincide with interactomes previously obtained in vertebrate cells, including the oligosaccharide transferase complex, the chaperonin containing TCP-1, vesicle localization, and ribosomal proteins. Notably, other protein pathways not previously reported in vertebrate cells, such as epigenetic regulation and RNA silencing, were also found in the NS1 interactome in mosquito cells. Due to the novel and strong interactions observed for NS1 and the epigenetic regulator DIDO1 (Death-Inducer Obliterator 1), the role of DIDO1 in viral replication was further explored. Interactions between NS1 and DIDO1 were corroborated in infected mosquito cells, by colocalization and proximity ligation assays. Silencing DIDO1 expression results in a significant reduction in DENV and ZIKV replication and progeny production. Comparison of transcription analysis of mock or DENV infected cells silenced for DIDO1 revealed variations in multiple gene expression pathways, including pathways associated with DENV infection such as RNA surveillance, IMD, and Toll. These results suggest that DIDO1 is a host factor involved in the negative modulation of the antiviral response necessary for flavivirus replication in mosquito cells. Our findings uncover novel mechanisms of NS1

to promote DENV and ZIKV replication, and add to the understanding of NS1 as a multifunctional protein.

IMPORTANCE Dengue is the most important mosquito-borne viral disease to humans. Dengue virus NS1 is a multifunctional protein essential for replication and modulation of innate immunity. To gain insights into NS1 functions, the protein interactome of dengue virus NS1 in *Aedes albopictus* cells was investigated using a proximity biotinylation system and mass spectrometry. Several protein pathways, not previously observed in vertebrate cells, such as transcription and epigenetic regulation, were found as part of the NS1 interactome in mosquito cells. Among those, DIDO1 was found to be a necessary host factor for dengue and Zika virus replication in mosquito cells. Transcription analysis of infected mosquito cells silenced for DIDO1 revealed alterations of the IMD and Toll pathways, part of the antiviral response in mosquitoes. The results suggest that DIDO1 is a host factor involved in modulation of the antiviral response and necessary for flavivirus replication.

Bisacodyl Limits Chikungunya Virus Replication *In Vitro* and Is Broadly Antiviral.

LoMascolo, N., Cruz-Pulido, Y., Mounce, B.
02-06-2022

Antimicrob Agents Chemother

<https://doi.org/10.1128/aac.00292-22>

Identifying novel antivirals requires significant time and resource investment, and the continuous threat of viruses to human health necessitates commitment to antiviral identification and development. Developing antivirals requires years of research and validation, and recent outbreaks have highlighted the need for preparedness in counteracting pandemics. One way to facilitate development is to repurpose molecules already used clinically. By screening such compounds, we can accelerate antiviral development. Here, we screened compounds from the National Institutes of Health's Developmental Therapeutic Program for activity against chikungunya virus, an alphavirus that is responsible for a significant outbreak in the Americas in 2013. Using this library, we identified several compounds with known antiviral activity, as well as several novel antivirals. Given its favorable *in vitro* activity and well-described *in vivo* activity, as well as its broad availability, we focused on bisacodyl, a laxative used for the treatment of constipation, for follow-up studies. We find that bisacodyl inhibits chikungunya virus infection in a variety of cell types, over a range of concentrations, and over several rounds of replication. We find that bisacodyl does not disrupt chikungunya virus particles or interfere with their ability to attach to cells, but, instead, bisacodyl inhibits virus replication. Finally, we find that bisacodyl is broadly antiviral against a variety of RNA viruses, including enteroviruses, flaviviruses, bunyaviruses, and alphaviruses; however, it exhibited no activity against the DNA virus vaccinia virus. Together, these data highlight the power of compound screening to identify novel antivirals and suggest that bisacodyl may hold promise as a broad-spectrum antiviral.

Modifying mosquitoes to suppress disease transmission: Is the long wait over?

Powell, J.
02-06-2022

Genetics

<https://pubmed.ncbi.nlm.nih.gov/35652239>

For more than 50 years it has been a dream of medical entomologists and public health workers to control diseases like malaria and dengue fever by modifying, through genetics and other methods, the arthropods that transmit them to humans. A brief synopsis of the history of these efforts as applied to mosquitoes is presented; none proved to be effective in reducing disease prevalence. Only in the last few years have novel approaches been developed or proposed that indicate the long wait may be over. Three recent developments are particularly promising: CRISPR-Cas9 driven genetic modification, shifting naturally occurring allele frequencies, and microbe-based modifications. The last is the furthest along in implementation. Dengue fever incidence has been reduced between 40% and 96% in 4 different regions of the world where Wolbachia-infected *Aedes aegypti* have been established in the field. It is not yet clear how sustainable such control programs will prove to be, but there is good reason for optimism. In light of this, the time is ripe for reinvigorated research on vectors, especially genetics. Vector-borne diseases primarily affect under-developed countries and thus have not received the attention they deserve from wealthier countries with well-developed and funded biomedical research establishments.

Association of systemic vitamin D on the course of dengue virus infection in adults: a single-centre dengue cohort study at a large institution in Singapore.

Sadarangani, S., Htun, H., Ling, W., Hawkins, R., Yeo, T., Rivino, L., MacAry, P., Leo, Y.

02-06-2022

Singapore Med J

<https://doi.org/10.11622/smedj.2022064>

Host immune responses may impact dengue severity in adults. Vitamin D has multiple immunomodulatory effects on innate and adaptive immunity. We evaluated the association between systemic 25-hydroxyvitamin D [25-(OH) D] and dengue disease severity in adults. We measured plasma for total 25-(OH) D levels with an electrochemiluminescence immunoassay using stored samples from participants with laboratory confirmed dengue who were prospectively enrolled in 2012-2016 at our institution. 80 participants (median age 43 years) were enrolled. Six participants had severe dengue based on the World Health Organisation (WHO) 1997 criteria (i.e. dengue haemorrhagic fever/dengue shock syndrome) and another six had severe dengue based on the WHO 2009 criteria. Median 25-(OH) D at acute phase of dengue was 6.175 µg/L (interquartile range 3.82-8.21; range 3.00-15.29) in all participants. 25-(OH) D showed inverse linear trend with severe dengue manifestations based on the WHO 2009

criteria (aRR 0.72; 95% confidence interval 0.57-0.91; $p < 0.01$) after adjustment for age, gender and ethnicity. Limited studies have evaluated the role of systemic 25-(OH) D on dengue severity. Our study found low systemic 25-(OH) D was associated with increased dengue disease severity, particularly for severe bleeding that was not explained by thrombocytopenia. Further studies investigating the underlying immune mechanisms and effects on the vascular endothelium are needed.

Modeling the impact of genetically modified male mosquitoes in the spatial population dynamics of *Aedes aegypti*.

da Silva, M., Lugão, P., Prezoto, F., Chapiro, G.

01-06-2022

Sci Rep

<https://doi.org/10.1038/s41598-022-12764-7>

The mosquito *Aedes aegypti* is the primary vector of diseases such as dengue, Zika, chikungunya, and yellow fever. Improving control techniques requires a better understanding of the mosquito's life cycle, including spatial population dynamics in endemic regions. One of the most promising techniques consists of introducing genetically modified male mosquitoes. Several models proposed to describe this technique present mathematical issues or rely on numerous parameters, making their application challenging to real-world situations. We propose a model describing the spatial population dynamics of the *Aedes aegypti* in the presence of genetically modified males. This model presents some mathematical improvements compared to the literature allowing deeper mathematical analysis. Moreover, this model relies on few parameters, which we show how to obtain or estimate from the literature. Through numerical simulations, we investigate the impacts of environmental heterogeneity, the periodicity of genetically modified male releases, and released genetically modified males quantity on the population dynamics of *Aedes aegypti*. The main results point to that the successful application of this vector control technique relies on releasing more than a critical amount of modified males with a frequency exceeding a specific critical value.

Mouse Trophoblast Cells Can Provide IFN-Based Antiviral Protection to Embryonic Stem Cells via Paracrine Signaling.

Fendereski, M., Neupane, B., Nazneen, F., Bai, F., Guo, Y.

01-06-2022

J Immunol

<https://pubmed.ncbi.nlm.nih.gov/35649628>

The blastocyst is the preimplantation stage embryo that consists of two major components: the inner cell mass (ICM) and the trophoctoderm (TE). The ICM gives rise to the fetus and some extraembryonic tissues whereas the TE contributes to development of the placenta. Previous studies have demonstrated that both human and mouse embryonic stem

cells (ESCs) derived from the ICM are deficient in expressing type I IFNs in response to viral infection. In this study, we investigated the IFN response in mouse trophoblast stem cells (TSCs) and their in vitro differentiated trophoblasts (TSC-TBs). In this study, we report that, unlike ESCs, TSCs have a functional IFN system. They can express type I IFNs in response to viral stimuli and express IFN-stimulated genes in response to type I IFNs. TSC-TBs have a further developed IFN system and acquired the ability to express specialized type III IFN- λ . Furthermore, TSCs and TSC-TBs can provide ESCs with antiviral activity against Chikungunya, West Nile, and Zika virus infection, as demonstrated with a novel coculture model that simulates the temporal and spatial relationship between the ICM and the TE in a blastocyst. Taken together, our data demonstrate that mouse ESCs can respond to type I IFNs and gain IFN-based antiviral protection from TSCs and TSC-TBs via paracrine signaling mechanisms even though they themselves are unable to express type I IFNs.

Intrinsic antiviral immunity of barrier cells revealed by an iPSC-derived blood-brain barrier cellular model.

Cheng, Y., Medina, A., Yao, Z., Basu, M., Natekar, J., Lang, J., Sanchez, E., Nkembo, M., Xu, C., Qian, X., Nguyen, P., Wen, Z., Song, H., Ming, G., Kumar, M., Brinton, M., Li, M., Tang, H.

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Cell Rep

<https://pubmed.ncbi.nlm.nih.gov/35649379>

Physiological blood-tissue barriers play a critical role in separating the circulation from immune-privileged sites and denying access to blood-borne viruses. The mechanism of virus restriction by these barriers is poorly understood. We utilize induced pluripotent stem cell (iPSC)-derived human brain microvascular endothelial cells (iBMECs) to study virus-blood-brain barrier (BBB) interactions. These iPSC-derived cells faithfully recapitulate a striking difference in in vivo neuroinvasion by two alphavirus isolates and are selectively permissive to neurotropic flaviviruses. A model of cocultured iBMECs and astrocytes exhibits high transendothelial electrical resistance and blocks non-neurotropic flaviviruses from getting across the barrier. We find that iBMECs constitutively express an interferon-induced gene, IFITM1, which preferentially restricts the replication of non-neurotropic flaviviruses. Barrier cells from blood-testis and blood-retinal barriers also constitutively express IFITMs that contribute to the viral resistance. Our application of a renewable human iPSC-based model for studying virus-BBB interactions reveals that intrinsic immunity at the barriers contributes to virus exclusion.

Efficacy of rupatadine in reducing the incidence of dengue haemorrhagic fever in patients with acute dengue: A randomised, double blind, placebo-controlled trial.

Malavige, G., Jeewandara, C., Wijewickrama, A., Gunasinghe, D., Mahapatna, S., Gangani, C., Vimalachandran, V., Jayaratne,

G., Perera, Y., Wanigatunga, C., Dissanayake, H., Prathapan, S., Narangoda, E., Idampitiya, D., Gomes, L., Wickramanayake, S., Sahabandu, P., Ogg, G.

01-06-2022

PLoS Negl Trop Dis

<https://doi.org/10.1371/journal.pntd.0010123>

Rupatadine was previously shown to reduce endothelial dysfunction in vitro, reduced vascular leak in dengue mouse models and to reduce the extent of pleural effusions and thrombocytopenia in patients with acute dengue. Therefore, we sought to determine the efficacy of rupatadine in reducing the incidence of dengue haemorrhagic fever (DHF) in patients with acute dengue. A phase 2, randomised, double blind, placebo controlled clinical trial was carried out in patients with acute dengue in Sri Lanka in an outpatient setting. Patients with ≤ 3 days since the onset of illness were either recruited to the treatment arm of oral rupatadine 40mg for 5 days ($n = 123$) or the placebo arm ($n = 126$). Clinical and laboratory features were measured daily to assess development of DHF and other complications. 12 (9.7%) patients developed DHF in the treatment arm compared to 22 (17.5%) who were on the placebo although this was not significant ($p = 0.09$, relative risk 0.68, 95% CI 0.41 to 1.08). Rupatadine also significantly reduced ($p = 0.01$) the proportion of patients with platelet counts $< 50,000$ cells/mm³ and significantly reduced ($p = 0.04$) persisting vomiting, headache and hepatic tenderness ($p < 0.0001$) in patients. However, there was no difference in the duration of illness and in the proportion of individuals who required hospital admission in both treatment arms. Only 2 patients on rupatadine and 3 patients on the placebo developed shock, while bleeding manifestations were seen in 6 patients on rupatadine and 7 patients on the placebo. Rupatadine appeared to be safe and well tolerated and showed a trend towards a reducing proportion of patients with acute dengue who developed DHF. Its usefulness when used in combination with other treatment modalities should be explored. International Clinical Trials Registration Platform: SLCTR/2017/024.

Additional considerations for assessing COVID-19 impact on dengue transmission.

Yek, C., Pacheco, A., Lon, C., Leang, R., Manning, J.

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Lancet Infect Dis

<https://pubmed.ncbi.nlm.nih.gov/35643097>

The application of environmental management methods in combating dengue: a systematic review.

Revue de littérature

Mahmud, M., Abdul Mutalip, M., Lodz, N., Muhammad, E., Yoep, N., Hasim, M., Abdul Rahim, F., Aik, J., Rajarethinam, J., Muhamad, N.

01-06-2022

Int J Environ Health Res

<https://doi.org/10.1080/09603123.2022.2076815>

Among several vector control methods commonly used, environmental management is one of the control measures to mitigate dengue in such vulnerable communities. Since there is no curative treatment for dengue yet, targeted environmental and ecosystem management is increasingly relevant. Hence, this review was conducted to identify the effectiveness of environmental management intervention strategy to reduce dengue cases. We searched PUBMED, CENTRAL, SCOPUS, Web of Science, CIJE, WHO ICTRP, and ClinicalTrials.gov up to January 2021. A total of 521 articles were screened. Only 16 studies were included in this review. There were 6 studies that applied all three types of environmental management interventions (manipulation, modification and behavior), 8 studies applied two types of interventions (manipulation and behavior) and 2 studies applied one type of intervention (manipulation or behavior). All included studies reported reduction of *Aedes* entomological indices. The studies showed reduction in dengue cases and density of *Aedes* population through environmental interventions. It is recommended for the health authority to incorporate environmental management intervention in dengue control activities and enhanced the community involvement to ensure sustainability with high impact on dengue reduction.

Drug repurposing against the RNA-dependent RNA polymerase domain of dengue serotype 3 by virtual screening and molecular dynamics simulations.

Gangopadhyay, A., Saha, A.

31-05-2022

J Biomol Struct Dyn

<https://doi.org/10.1080/07391102.2022.2080764>

Dengue is an arboviral disease caused by the dengue flavivirus. The NS5 protein of flaviviruses is a potential therapeutic target, and comprises an RNA-dependent RNA polymerase (RDRP) domain that catalyses viral replication. The aim of this study was to repurpose FDA-approved drugs against the RDRP domain of dengue virus serotype 3 (DENV3) using structure-based virtual screening and molecular dynamics (MD) simulations. The FDA-approved drugs were screened against the RDRP domain of DENV3 using a two-step docking-based screening approach with Glide SP and Glide XP. For comparison, four reported DENV3 RDRP inhibitors were docked as standards. The hitlist was screened based on the docking score of the inhibitor with the lowest docking score (PubChem ID: 118797902; reported IC₅₀ value: 0.34 μM). Five hits with docking scores and Molecular Mechanics/Generalized Born Surface Area (MM-GBSA) energy lower than those of 118797902 were selected. The stability of the hit-receptor complexes was investigated using 100ns MD simulations in an explicit solvent. The results of MD simulations demonstrated that polydatin and betiatide remained stably bound to the receptor, and formed stable interactions with the RDRP domain of DENV3. The hit-receptor interactions were comparable to those of 118797902. The average Prime MM-GBSA energy of polydatin and betiatide

was lower than that of 118797902 during simulation, indicating that their binding affinity to DENV3 RDRP was higher than that of the standard. The results of this study may aid in the development of serotype-selective drugs against dengue in the future. Communicated by Ramaswamy H. Sarma.

Myopericarditis associated with acute Zika virus infection: a case report.

Bôtto-Menezes, C., Safe, I., da Cunha Ferreira, A., do Nascimento Couceiro, K., Neto, A., Franca, R., Calvet, G., de Filippis, A., Kara, E., da Costa Castilho, M., Bastos, M., de Brito, C., Modjarrad, K., Broutet, N., Brasil, P., Hajjar, L., de Lacerda, M., ZIKABRA Study Team

31-05-2022

BMC Infect Dis

<https://doi.org/10.1186/s12879-022-07454-8>

Zika virus infection is commonly described as a mild and self-limiting illness. However, cardiac complications were associated with acute Zika virus infection. A 46-year-old woman without previous comorbidities with a 1-day history of symptoms tested positive for ZIKV by real time reverse transcriptase polymerase chain reaction (rRT-PCR). She was admitted two days after with clinical worsening, cardiac enzymes elevated, and cardiac imaging findings, and the diagnosis of myopericarditis was made. The patient was treated and presented significant clinical improvement after one year. Cardiac complication following ZIKV infection appears to be infrequent. Here, we report a rare case of viral myopericarditis caused by ZIKV infection.

Cardiovascular sequelae of dengue fever: a systematic review.

Rahim, A., Hameed, A., Ishaq, U., Malik, J., Zaidi, S., Khurshid, H., Malik, A., Satti, D., Naz, H.

02-06-2022

Expert Rev Cardiovasc Ther

<https://doi.org/10.1080/14779072.2022.2082945>

Dengue is one of the most important viral diseases globally and a majority of symptomatic infections result in a benign course. However, a small number of patients develop severe manifestations, including the cardiovascular (CV) manifestations, including myocardial impairment, arrhythmias, and fulminant myocarditis. Electronic databases, including PubMed/MEDLINE, EMBASE, Scopus, and CINAHL were searched for articles incorporating CV manifestations of dengue fever (DF). Included studies involved 6,773 patients, and 3,122 (46.1%) exhibited at least one cardiac manifestation. Electrocardiogram (ECG) abnormalities (30.6%) included sinus bradycardia (8.8%), nonspecific ST-T changes (8.6%), ST depression (7.9%), and T-wave inversion (2.3%). Mechanical sequelae were present in 10.4%, including left ventricular (LV) systolic dysfunction (5.7%), and myocarditis (2.9%). Pericardial involvement was noted as pericarditis (0.1%), pericardial effusion (1.3%), and pericardial tamponade (0.1%). Apart from that, the cardiac injury was depicted

through a rise in cardiac enzymes (4.5%). The spectrum of CV manifestations in dengue is broad, ranging from subtle ST-T changes to fulminant myocarditis and the use of contemporary techniques in diagnosing cardiac involvement should be employed for rapid diagnosis and treatment.

Retrospective Genomic Characterization of a 2017 Dengue Virus Outbreak, Burkina Faso.

Letizia, A., Pratt, C., Wiley, M., Fox, A., Mosore, M., Agbodzi, B., Yeboah, C., Kumordjie, S., Di Paola, N., Assana, K., Couliadiaty, D., Ouedraogo, C., Bonney, J., Ampofo, W., Tarnagda, Z., Sangaré, L.

Emerg Infect Dis

<https://doi.org/10.3201/eid2806.212491>

Knowledge of contemporary genetic composition of dengue virus (DENV) in Africa is lacking. By using next-generation sequencing of samples from the 2017 DENV outbreak in Burkina Faso, we isolated 29 DENV genomes (5 serotype 1, 16 serotype 2 [DENV-2], and 8 serotype 3). Phylogenetic analysis demonstrated the endemic nature of DENV-2 in Burkina Faso. We noted discordant diagnostic results, probably related to genetic divergence between these genomes and the Trioplex PCR. Forward and reverse primers had a single mismatch when mapped to the DENV-2 genomes, probably explaining the insensitivity of the molecular test. Although we observed considerable homogeneity between the Dengvaxia and TetraVax-DV-TV003 vaccine strains as well as B cell epitopes compared with these genomes, we noted unique divergence. Continual surveillance of dengue virus in Africa is needed to clarify the ongoing novel evolutionary dynamics of circulating virus populations and support the development of effective diagnostic, therapeutic, and preventive countermeasures.

Effects of Acute Dengue Infection on Sperm and Virus Clearance in Body Fluids of Men.

Mons, J., Mahé-Poiron, D., Mansuy, J., Lheureux, H., Nigon, D., Moinard, N., Hamdi, S., Pasquier, C., Dejuçq-Rainsford, N., Bujan, L.

Emerg Infect Dis

<https://doi.org/10.3201/eid2806.212317>

We investigated the effects of dengue virus (DENV) on semen using samples collected 7, 15, 30, 60, and 90 days after symptom onset from 10 infected volunteers on Réunion Island. We assessed characteristics of semen and reproductive hormones and isolated motile spermatozoa from semen. We assayed semen for DENV using reverse transcription PCR and searched for DENV RNA by virus isolation in Vero E6 cell cultures. Four volunteers had >1 DENV RNA-positive semen samples; 2 volunteers had DENV RNA-positive semen at day 15 and 1 at day 30. No motile sperm were DENV positive. After exposure to positive semen, few Vero E6 cells stained positive for DENV antigens, indicating low levels of replicative virus. We found DENV had shorter duration in semen than in blood. These findings support the possibilities that DENV is

sexually transmissible for a short period after acute dengue illness and that acute dengue induces reversible alterations in sperm.

Status of Vector Control Capabilities and Capacities in Florida and Texas, and its Potential Public Health Consequences.

Peper, S., Xue, R., Presley, S.

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J Am Mosq Control Assoc

<https://doi.org/10.2987/21-7053>

It has been reported that roughly 80% of vector control organizations throughout the southern USA lack critical capabilities to properly address potential vector populations and vector-borne diseases within their jurisdictions. This study further investigated current vector control capabilities and capacity within the states of Florida and Texas. It was reported that only 26% of jurisdictions in Florida and 14% in Texas reported that they were "fully capable." Both states are among the top 4 states relative to the number of human cases of mosquito-borne diseases, and both states have had local transmission of Zika virus. Respondents from Florida indicated that 88% of jurisdictions have vector control capabilities to some degree, with 65% of those reporting they had sufficient capabilities. Respondents from Texas indicated that 89% of jurisdictions have vector control capabilities to some degree, with 67% of those reporting they had sufficient capabilities. As the prioritization of resource commitment for vector control capabilities varies throughout the USA, it is imperative that each state evaluates their specific needs and current capabilities and capacity to best ensure the public health needs of their constituents.

Predation of *Aedes aegypti* Eggs By Foraging Ants *Solenopsis invicta*, *Myrmecaria brunnea*, *Diacamma rugosum*, and *Monomorium minimum*.

Muniaraj, M., Rajamannar, V., Venkatesh, A., Leo, S., Venkatasubramani, K., Paramasivan, R., Kumar, A.

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J Am Mosq Control Assoc

<https://doi.org/10.2987/22-7060>

The diseases transmitted by *Aedes* mosquitoes, such as dengue, chikungunya, yellow fever, and Zika, are ever-increasing. Rapid and unplanned urbanization adversely impacts various endemic species such as ants and facilitates the breeding of *Aedes* mosquitoes. We have observed the predatory potential of ants over *Aedes* eggs in urban breeding habitats, and their impact on *Aedes* mosquito breeding was determined by a field experiment that mimicked the natural breeding habitats. It was found that 99.4% of eggs were removed from the experimental containers by foraging ants in 4 days. The present study demonstrates the role of ants as a natural regulator, limiting *Aedes* mosquito breeding.

A Cross-Sectional Household Survey in the US Virgin Islands (2019) Reveals Cisterns as Challenging Peridomestic *Aedes aegypti* Habitats.

Seger, K., Day, C., Gaeddert, L., Rao, G., Kahler, A., Ellis, E., Ellis, B., Byrd, B.

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J Am Mosq Control Assoc

<https://doi.org/10.2987/21-7022>

Most residences in the United States Virgin Islands (USVI) rely on household rainwater-catchment systems and subterranean cisterns for long-term water storage that may provide suitable habitats for mosquitoes of public health relevance. We conducted a household cistern survey (n = 164) on the islands of St. Croix, St. John, and St. Thomas in 2019. The survey revealed that 45.7% (95% CI: 38.3-53.4%) of cisterns contained mosquitoes (adult and/or immature mosquitoes). *Aedes aegypti*, a vector of chikungunya, dengue, and Zika viruses in the USVI, was found in 27.4% (95% CI: 21.2-34.7%) of cisterns and accounted for 83.3% of the total mosquitoes identified in the study. The odds of detecting mosquitoes in a cistern were 5.45 times higher at locations where the residents reported that they had observed adult mosquitoes coming out of their cisterns (95% CI: 2.25-14.21), suggesting that vector control personnel should consider resident complaints about mosquitoes in their cistern as valid and likely reliable self-assessments. Resident mosquito management practices in cisterns did not correspond with decreased odds of mosquito detection. We conclude that cisterns in the USVI commonly provide habitat for immature and adult *Ae. aegypti*, which may decrease the effectiveness of area-wide mosquito control strategies. Additional studies are necessary to evaluate the importance of these cisterns as they relate to mosquito production and arbovirus transmission risk, and to assess physical and chemical control methods.

Identification of Algerian field-caught mosquito vectors by MALDI-TOF MS.

Abdellahoum, Z., Nebbak, A., Lafri, I., Kaced, A., Bouhenna, M., Bachari, K., Boumegoura, A., Agred, R., Boudchicha, R., Smadi, M., Maurin, M., Bitam, I.

25-04-2022

Vet Parasitol Reg Stud Reports

<https://pubmed.ncbi.nlm.nih.gov/35569916>

Vector-borne diseases represent a real threats worldwide, in reason of the lack of vaccine and cure for some diseases. Among arthropod vectors, mosquitoes are described to be the most dangerous animal on earth, resulting in an estimated 725,000 deaths per year due to their borne diseases. Geographical position of Algeria makes this country a high risk area for emerging and re-emerging diseases, such as dengue coming from north (Europe) and malaria from south (Africa). To prevent these threats, rapid and continuous surveillance of mosquito vectors is essential. For this purpose we aimed in this study to create a mosquito vectors locale database using MALDI-TOF mass spectrometry technology for rapid identification of these arthropods. This methodology was

validated by testing 211 mosquitoes, including four species (*Aedes albopictus*, *Culex pipiens*, *Culex quinquefasciatus*, and *Culiseta longiareolata*), in two northern wilayahs of Algeria (Algiers and Bejaia). Species determination by MALDI TOF MS was highly concordant with reference phenotypic and genetic methods. Using this MALDI-TOF MS tool will allow better surveillance of mosquito species able to transmit mosquito borne diseases in Algeria.

Anterior scleritis treated with systemic corticosteroids in Chikungunya infection.

Cruz, J., Moreno, C., Colombo-Barboza, G., Colombo-Barboza, M.

26-04-2022

Am J Ophthalmol Case Rep

<https://doi.org/10.1016/j.ajoc.2022.101555>

Chikungunya is a matter of grave concern in Brazil. This case report describes a rare ocular manifestation in a patient with chikungunya. A 49-year old male diagnosed with chikungunya one month previously was being treated and followed up by a rheumatologist. He presented with complaints of pain and hyperemia in both eyes over the preceding seven days. Biomicroscopy of both eyes revealed bulbar conjunctival hyperemia 3+/4+ with 360° of ciliary injection, and no other abnormalities. The patient was prescribed 1 drop of loteprednol etabonate every 4 h, tapering every three days, and nimesulide 100 mg every 12 hours for 7 days. One week later, however, scleritis was worse and the medial sclera was elevated, particularly in the right eye. Intraocular pressure remained normal, and hyperemia increased to 4+/4+ in the right eye. Supplementary tests revealed positive serology for chikungunya IgG and IgM antibodies and other etiologies were ruled out. Treatment was then changed to oral prednisone 60 mg/day, tapering every three days. The patient was pain-free three days later with all signs and symptoms having disappeared within five days. Ocular abnormalities resulting from chikungunya virus infection require careful monitoring even after the acute phase of chikungunya infection has passed. The fact that patients usually stop being followed-up after they have been symptomless for some time delays diagnosis and the appropriate treatment of ocular manifestations. Consequently, chikungunya should be included in the differential diagnosis of ocular pathologies wherever the infection is endemic or epidemic.

Tetravalent formulation of polymeric nanoparticle-based vaccine induces a potent immune response against dengue virus.

Khan, R., Ahmed, F., Afroz, S., Khan, N.

31-05-2022

Biomater Sci

<https://doi.org/10.1039/d2bm00167e>

Dengue is a mosquito-borne disease caused by the four serotypes of the dengue virus (DENV 1-4). It is growing at an alarming rate globally, which could be partly attributed to the

lack of an effective therapeutic regimen. Therefore, strategies for developing an effective vaccine have gained more significance in the given scenario. Failure of the existing live attenuated vaccine candidates to mount effective and broader protection against all the four serotypes of DENV has generated a new interest in exploring novel strategies for augmenting the efficacy of non-infectious, non-replicating subunit vaccines. In the current study, we employed a new strategy of encapsulating the immunodominant EDIII domain of Envelop protein of all the serotypes of DENV (1-4) into PLGA nanoparticles separately. All four nano formulations were physically mixed to develop a tetravalent nano formulation in combination with TLR agonists. Further, we examined its immunological efficacy using a mouse and *in vitro* infection model system. Interestingly, our results demonstrate that majority of EDIII protein loaded PLGA nanoparticles were polydispersed and less than 1 μm in size with optimal encapsulation efficacy. Tetravalent nanoformulation along with TLR agonists (MPLA + R837) enhanced the magnitude of antigen-specific polyfunctional T cell response. It triggered robust antibody responses in mice concurrent with the increased level of genes involved in the programming of memory B-cell formation and the maintenance and maturation of GCs, leading to the formation of long-lived plasma cells secreting antigen-specific antibodies. Further assessment revealed that tetravalent nanoformulation in combination with TLR ligands upon immunization in mice aids in the enhanced production of serotype-specific neutralizing antibodies, which can effectively neutralize all the four serotypes of DENV (DENV 1-4). The findings of this study reveal a new strategy for enhancing the immunogenicity of vaccine candidates and might pave the way for the development of a tetravalent vaccine against all the serotypes of Dengue Virus.

Backward bifurcation and optimal control in a co-infection model for SARS-CoV-2 and ZIKV.

Omame, A., Abbas, M., Onyenegecha, C.

09-04-2022

Results Phys

<https://doi.org/10.1016/j.rinp.2022.105481>

In co-infection models for two diseases, it is mostly claimed that, the dynamical behavior of the sub-models usually predict or drive the behavior of the complete models. However, under a certain assumption such as, allowing incident co-infection with both diseases, we have a different observation. In this paper, a new mathematical model for SARS-CoV-2 and Zika co-dynamics is presented which incorporates incident co-infection by susceptible individuals. It is worth mentioning that the assumption is missing in many existing co-infection models. We shall discuss the impact of this assumption on the dynamics of a co-infection model. The model also captures sexual transmission of Zika virus. The positivity and boundedness of solution of the proposed model are studied, in addition to the local asymptotic stability analysis. The model is shown to exhibit backward bifurcation caused by the disease-induced death rates and parameters associated with

susceptibility to a second infection by those singly infected. Using Lyapunov functions, the disease free and endemic equilibria are shown to be globally asymptotically stable for $R_0 < 1$, respectively. To manage the co-circulation of both infections effectively, under an endemic setting, time dependent controls in the form of SARS-CoV-2, Zika and co-infection prevention strategies are incorporated into the model. The simulations show that SARS-CoV-2 prevention could greatly reduce the burden of co-infections with Zika. Furthermore, it is also shown that prevention controls for Zika can significantly decrease the burden of co-infections with SARS-CoV-2.

Acute macular neuroretinopathy associated to dengue disease.

Translateur, A., Perez-Rueda, M.

31-03-2022

Am J Ophthalmol Case Rep

<https://doi.org/10.1016/j.ajoc.2022.101474>

To highlight an interesting case of Acute Macular Neuroretinopathy (AMN) in the context of dengue disease. A 70 year old woman from Ibagué, Colombia developed AMN during her hospitalization for dengue illness with warning signs. Her initial ophthalmic evaluation revealed a deep visual loss with no noticeable biomicroscopic findings and altered outer retinal layers in her macular optical coherence tomography (OCT). After a five year follow up, she maintains a poor visual acuity. There are few reported cases of AMN associated to dengue. This case report highlights the common physiopathological pathways between dengue and AMN, and the crossroads between vascular, infectious, and immune disorders.

Spatial dynamics of dengue fever spreading for the coexistence of two serotypes with an application to the city of São Paulo, Brazil.

Pereira, F., Schimit, P.

26-03-2022

Comput Methods Programs Biomed

<https://pubmed.ncbi.nlm.nih.gov/35398620>

Dengue fever is a disease in which individuals' spatial distribution and *Aedes aegypti* mosquitoes breeding places are important factors for the disease dynamics. Typically urban, dengue is a problem for least developed countries due to the ineffectiveness in controlling the vector and disorderly urbanization processes. The result is a composition of urban sanitation problems and areas with high demographic densities and intense flows of people. This paper explores the spatial distribution of vector breeding places to evaluate introducing a new dengue serotype to a population at equilibrium for a pre-existing serotype. The paper's objective is to analyze the spatial dynamics of dengue using variations of the basic reproduction number. A model based on probabilistic cellular automata is proposed to permitting the necessary flexibility to consider some spatial distributions of

vector breeding places. Then, ordinary differential equations are used as a mean-field approach of the model, and the basic reproduction number (R_0) is derived considering the next-generation matrix method. A spatial approach for R_0 is also proposed, and the model is tested in a neighbourhood from the city of São Paulo, Brazil, to examine the potential risks of vector breeding cells distribution. The results indicated that the more spread out these places, the higher are the values of R_0 . When the model is applied to a neighbourhood in São Paulo, residential areas may boost the infections and must be under public vigilance to combat vector breeding sites. Considering the mean-field approximation of the cellular automata model by ordinary differential equations, the basic reproduction number derived returned an estimative of the disease dynamics in the population. However, the spatial basic reproduction number was more assertive in showing areas with a higher disease incidence. Moreover, the model could be easily adapted to be used in real maps enabling simulations closer to real problems.

The endothelial glycocalyx in critical illness: A pediatric perspective.

Richter, R., Payne, G., Ambalavanan, N., Gaggar, A., Richter, J.
09-03-2022

Matrix Biol Plus

<https://doi.org/10.1016/j.mbplus.2022.100106>

The vascular endothelium is the interface between circulating blood and end organs and thus has a critical role in preserving organ function. The endothelium is lined by a glycan-rich glycocalyx that uniquely contributes to endothelial function through its regulation of leukocyte and platelet interactions with the vessel wall, vascular permeability, coagulation, and vasoreactivity. Degradation of the endothelial glycocalyx can thus promote vascular dysfunction, inflammation propagation, and organ injury. The endothelial glycocalyx and its role in vascular pathophysiology has gained increasing attention over the last decade. While studies characterizing vascular glycocalyx injury and its downstream consequences in a host of adult human diseases and in animal models has burgeoned, studies evaluating glycocalyx damage in pediatric diseases are relatively few. As children have unique physiology that differs from adults, significant knowledge gaps remain in our understanding of the causes and effects of endothelial glycocalyx disintegrity in pediatric critical illness. In this narrative literature overview, we offer a unique perspective on the role of the endothelial glycocalyx in pediatric critical illness, drawing from adult and preclinical data in addition to pediatric clinical experience to elucidate how marked derangement of the endothelial surface layer may contribute to aberrant vascular biology in children. By calling attention to this nascent field, we hope to increase research efforts to address important knowledge gaps in pediatric vascular biology that may inform the development of novel therapeutic strategies.

The data on molecular docking of cinnamic acid amide on dengue viral target NS2B/NS3.

Yusoff, N., Asari, A., Addis, S.

08-03-2022

Data Brief

<https://doi.org/10.1016/j.dib.2022.108036>

A natural occurring class compound, cinnamic acid is composed of a benzene ring, an alkene double bond and an acrylic acid functional group. Due to the feasibility of its structure modifications with a variety of compounds, cinnamic acids have been actively explored to improve their biological efficacy. Cinnamic acid derivatives have been reported to exhibit an antimicrobial property. Despite the beneficial properties of cinnamic acid derivatives, the antiviral activity of the amide derivatives especially against the dengue virus is poorly defined. Herein, the cinnamic amide derivatives were evaluated for their potential as an anti-dengue virus through the *in-silico* analysis of the derivatives. This data aimed to analyze the interactions of the derivatives against the non-structural protein of viral target, dengue virus type 2 (DENV-2) NS2B/NS3. The evaluation was based on binding affinity, interaction type (bond type and distance) and interaction with amino acids. Three derivatives (CAA15, CAA16 and CAA17) with the best docking score were reported. Enhanced understanding of the interaction acquired from this analysis provide a useful information on for the prediction of the binding behavior affinity of cinnamic amide derivatives and is ultimately useful in the rational design of drugs to synthesis new compounds with the potential benefits against DENV-2.

A systematic review of brain imaging findings in neurological infection with Japanese encephalitis virus compared with Dengue virus.

Revue de littérature

Pichl, T., Wedderburn, C., Hoskote, C., Turtle, L., Bharucha, T.
10-03-2022

Int J Infect Dis

<https://pubmed.ncbi.nlm.nih.gov/35283297>

Japanese encephalitis virus (JEV) and dengue virus (DENV) represent important causes of encephalitis in Asia. Brain imaging may provide diagnostic clues about the etiology of infectious encephalitis. We performed a systematic review of brain imaging findings in Japanese encephalitis (JE) and DENV neurological infection (dengue) to identify characteristic lesions. Five databases were searched. We included all study types and imaging techniques. Laboratory methods were categorized using diagnostic confidence levels. Imaging data were synthesized, and focal findings are presented as proportions for JE and dengue and for subgroups based on diagnostic confidence. Thalamic lesions were the most reported magnetic resonance imaging finding in both diseases but appeared to occur more often in JE (74% in 23 studies) than dengue (29.4% in 58 studies). In cases diagnosed with antigen or nucleic acid tests, thalamic lesions were reported frequently in both JE (76.5% in 17 studies) and dengue (65.2% in 23 studies). The results suggest that thalamic lesions

frequently occur in both JE and dengue encephalitis. No radiological findings were found to be pathognomonic of either disease. Although brain imaging may support a diagnosis, laboratory confirmation with highly specific tests remains crucial.

ChikvInt: a Chikungunya virus-host protein-protein interaction database.

Kusari, M., Dey, L., Mukhopadhyay, A.

11-03-2022

Lett Appl Microbiol

<https://doi.org/10.1111/lam.13677>

Chikungunya is a fast-mutating virus causing Chikungunya virus disease (ChikvD) with a significant load of disability-adjusted life years (DALY) around the world. The outbreak of this virus is significantly higher in the tropical countries. Several experiments have identified crucial viral-host protein-protein interactions (PPIs) between Chikungunya Virus (Chikv) and the human host. However, no standard database that catalogs this PPI information exists. Here we develop a Chikv-Human PPI database, ChikvInt, to facilitate understanding ChikvD disease pathogenesis and the progress of vaccine studies. ChikvInt consists of 109 interactions and is available at www.chikvint.com.

Simultaneous detection of Zika, chikungunya, dengue, yellow fever, West Nile, and Japanese encephalitis viruses by a two-tube multiplex real-time RT-PCR assay.

Xu, Z., Peng, Y., Yang, M., Li, X., Wang, J., Zou, R., Liang, J., Fang, S., Liu, Y., Yang, Y.

22-02-2022

J Med Virol

<https://doi.org/10.1002/jmv.27658>

Due to the concurrent prevalence and increasing risk of coinfection of the clinically important Arboviruses, timely and accurate differential diagnosis is important for clinical management and the epidemiological investigation. A two-tube multiplex real-time reverse transcription-polymerase chain reaction (RT-PCR) assay for the simultaneous detection of Zika virus (ZIKV), chikungunya virus (CHIKV), dengue virus (DENV), yellow fever virus (YFV), West Nile virus (WNV), and Japanese encephalitis virus (JEV) was developed and optimized with high specificity and sensitivity. The detection limit for all the six viruses could reach as low as five genome equivalent copies and 2.8×10^{-3} tissue culture infectious doses (TCID₅₀) for ZIKV, YFV, CHIKV and 2.8×10^{-2} TCID₅₀ for JEV per reaction, with high accuracy and precision ($R^2 > 0.99$). The coefficient of variation of intra-assay and inter-assay for our quantitative reverse transcription-polymerase chain reaction (qRT-PCR) assay was low, and the obtained positive rates and C_t values of this assay were comparable with singleplex commercial kits. Moreover, the multiplex qRT-PCR assay was able to detect possible co-infections without competitive inhibition of target viral genomes. In conclusion, our rapid,

sensitive, cost-effective multiplex qRT-PCR will be of great use for differential diagnosis in a clinical setting and epidemiological investigation during surveillance.

Anti-DENV-NS1 monoclonal antibody for the differential histopathological diagnosis of hemorrhagic fever caused by dengue.

Kanamura, C., Piazza, R., Iglézias, S., Borges, C., Sansone, M., Polatto, J., Teixeira, D., da Silva, M., Rocha, L., Nogueira, J., Maeda, A., da Silva Vasami, F.

07-02-2022

Braz J Microbiol

<https://doi.org/10.1007/s42770-022-00697-2>

Dengue is the most prevalent arboviral disease in humans in tropical and subtropical regions, especially in urban areas, and can cause major epidemics. Although a self-limiting illness, it may sometimes have serious hemorrhagic manifestations, and the outcome of dengue hemorrhagic fever has similar clinical manifestations as in other infections, which could result in death. Therefore, autopsy procedures are required under certain circumstances such as in hemorrhagic fevers, sometimes to confirm or to clarify the diagnosis that may have epidemiological consequences. Normally, the Immunohistochemistry Laboratory of the Pathology Center of Adolfo Lutz Institute receives autopsy samples from different hospitals in Sao Paulo State to confirm a previous diagnosis, especially hemorrhagic fever of infectious etiology. For this diagnosis, we have been using a mouse polyclonal antibody to dengue virus that often does not provide a clear conclusion, because of background staining or no relevant immunostaining, which hampers the histopathological analysis. Accordingly, in the present study, anti-DENV-NS1 monoclonal antibody (4H2) was tested to determine its accuracy in immunohistochemical analysis. Twenty-four autopsy cases of hemorrhagic febrile syndrome showing histopathological alterations compatible with dengue disease were studied: twenty cases were confirmed by RT-PCR for DENV-2 and in four by RT-PCR for yellow fever virus. Samples from autopsied cases of deaths caused by other infectious diseases (two meningitis C and two severe acute respiratory syndrome caused by influenza A H1N1) were included as negative control cases. Positive immunostaining for DENV-NS1 was detected in 16/20 (80%) liver samples and 11/15 (73%) spleen samples from autopsied hemorrhagic dengue patients, whereas the polyclonal antibody detected DENV antigens in 12/20 (60%) liver and in 6/15 (40%) spleen samples from the same cases. Positive results were not obtained with liver biopsy samples from yellow fever or *Neisseria meningitidis* and Flu-A cases. 4H2 mAb recognizes the native protein of the four DENV serotypes in infected cells and did not cross-react with native ZIKV- or CHIKV-infected cells by immunohistochemical assay, so it is a useful tool for differential histopathological conclusion of acute febrile hemorrhagic deaths.

Neglected Tropical Diseases in Lebanon.

Alam, W., Mobayed, T., Younis, N., Zarif, R., Bizri, N., Tamim, H., Musharrafieh, U., Bizri, A.

03-02-2022

Acta Parasitol

<https://doi.org/10.1007/s11686-021-00510-4>

Neglected tropical diseases (NTDs) are highly endemic and distributed within the Middle East and North Africa (MENA) region, affecting an estimated 65 million people. Lebanon suffers from several NTDs as they are either endemic in the country or imported via expats residing in endemic regions, refugees, and foreign labor force. The Syrian crisis and the displacement of refugees to Lebanon have made the country the largest host of refugees per capita right after the Syrian crisis in 2011, peaking in the year of 2013. Additionally, foreign labor in Lebanon come from different countries in Africa and Asia that are endemic with certain NTDs. The Lebanese diaspora is approximately twice the number of those residing in the country and is distributed throughout the continents carrying the risk of importing new NTDs. A descriptive study about the prevalence of NTDs in Lebanon, their distribution, and factors contributing to spread was performed. The Lebanese Ministry of Public Health (LMPH) database regarding reportable transmissible diseases was reviewed for reportable NTDs between 2002 and 2020 in relation to age, gender, prevalence, and geographical distribution. The medical literature was searched using several engines looking for all reports about NTDs in Lebanon, those relevant to regions hosting Lebanese diaspora, and countries where the refugees and migrant workers came from. Only leishmaniasis, leprosy, echinococcosis, schistosomiasis, and rabies are mandatorily reportable NTDs by the LMPH. Additionally, case reports about fasciolosis, ascariidiosis, and Dengue were reported from Lebanon. The presence of the Syrian refugees in the country affected the prevalence of leishmaniasis and rabies. The most prevalent NTD in Lebanon is cutaneous leishmaniasis. The Lebanese diaspora reside mainly in South America, Africa, and in some Arab states known to be endemic with certain NTDs. Little information is known about NTDs in Lebanon. The country is at an increased risk of experiencing several new NTDs due to refugee influx, foreign labor, economic crisis, and ever-growing number of Lebanese seeking work opportunities abroad. More information is needed to assess the true burden of NTDs in Lebanon and the future steps to contain and mitigate their effects.

Assessing *Aedes aegypti* candidate genes during viral infection and Wolbachia-mediated pathogen blocking.

Sigle, L., Jones, M., Novelo, M., Ford, S., Urakova, N., Lymeropoulos, K., Sayre, R., Xi, Z., Rasgon, J., McGraw, E.

14-02-2022

Insect Mol Biol

<https://doi.org/10.1111/imb.12764>

One approach to control dengue virus transmission is the

symbiont Wolbachia, which limits viral infection in mosquitoes. Despite plans for its widespread use in *Aedes aegypti*, Wolbachia's mode of action remains poorly understood. Many studies suggest that the mechanism is likely multifaceted, involving aspects of immunity, cellular stress and nutritional competition. A previous study from our group used artificial selection to identify a new mosquito candidate gene related to viral blocking; alpha-mannosidase-2a (alpha-Mann-2a) with a predicted role in protein glycosylation. Protein glycosylation pathways tend to be involved in complex host-viral interactions; however, the function of alpha-mannosidases has not been described in mosquito-virus interactions. We examined alpha-Mann-2a expression in response to virus and Wolbachia infections and whether reduced gene expression, caused by RNA interference, affected viral loads. We show that dengue virus (DENV) infection affects the expression of alpha-Mann-2a in a tissue- and time-dependent manner, whereas Wolbachia infection had no effect. In the midgut, DENV prevalence increased following knockdown of alpha-Mann-2a expression in Wolbachia-free mosquitoes, suggesting that alpha-Mann-2a interferes with infection. Expression knockdown had the same effect on the togavirus chikungunya virus, indicating that alpha-Mann-2a may have broad antiviral effects in the midgut. Interestingly, we were unable to knockdown the expression in Wolbachia-infected mosquitoes. We also provide evidence that alpha-Mann-2a may affect the transcriptional level of another gene predicted to be involved in viral blocking and cell adhesion; cadherin87a. These data support the hypothesis that glycosylation and adhesion pathways may broadly be involved in viral infection in *Ae. aegypti*.

Detection of Mayaro virus in *Aedes aegypti* mosquitoes circulating in Goiânia-Goiás-Brazil.

de Curcio, J., Salem-Izacc, S., Pereira Neto, L., Nunes, E., Anuniação, C., Silveira-Lacerda, E.

31-01-2022

Microbes Infect

<https://pubmed.ncbi.nlm.nih.gov/35108606>

The Arboviral diseases are caused by arthropod-borne viruses, such as Mayaro virus (MAYV), the etiological agent of Mayaro fever. This disease has been drawing the attention of the public health authorities for the increased number of cases likely due to virus adaptation for survival to urban areas as well as infection and multiplication in other vectors insects. Therefore, this work aimed to identify the MAYV infecting *Aedes aegypti* mosquitoes in Goiânia, the capital of state of Goiás, Brazil. For the development of study, the larvae of *A. aegypti* were collected in Basic Health Units from different regions of Goiânia then the larvae were grown to adult mosquitoes in controlled laboratory conditions. The female mosquitoes were submitted to the procedure of head and body separation. The RNAs obtained from these samples were analyzed by real-time PCR for identification of arboviruses. We only detect the presence of MAVY in the mosquitoes, in this sense our findings suggest that *A. aegypti* harbor MAVY in

different anatomical sites, and potentially the process of vertical transmission of MAYV can occur in this vector.

Detection of Zika virus disease in Thiruvananthapuram, Kerala, India 2021 during the second wave of COVID-19 pandemic.

Yadav, P., Niyas, V., Arjun, R., Sahay, R., Shete, A., Sapkal, G., D Pawar, S., Patil, D., Gupta, N., Abraham, P.
08-02-2022
J Med Virol
<https://doi.org/10.1002/jmv.27638>

Formulations of curcumin and d-mannitol as a photolarvicide against *Aedes aegypti* larvae: Sublethal photolarvicidal action, toxicity, residual evaluation, and small-scale field trial.

Garbuio, M., Dias, L., de Souza, L., Corrêa, T., Mezzacappo, N., Blanco, K., de Oliveira, K., Inada, N., Bagnato, V.
31-01-2022
Photodiagnosis Photodyn Ther
<https://pubmed.ncbi.nlm.nih.gov/35101624>

Dengue, Zika, chikungunya, and yellow fever are arboviruses transmitted by *Aedes aegypti* mosquito. In this regard, a number of techniques have emerged aiming to combat its proliferation. Elimination of *Aedes aegypti* larvae by photodynamic action has been reported as an efficient approach. In this regard, this study was aimed at synthesize and characterize formulations with different proportions (w/w) of the plant-based photolarvicidal curcumin and d-mannitol (CCD 1-4) and their evaluation on sublethal photolarvicidal efficiency, photodegradation profile, solubility, internalization, elimination time, persistence in simulated field, growth of microorganisms in water and the toxicity using an animal models (Zebrafish). CCD 3 (curcumin:d-mannitol 50:50 w/w) showed the best efficacy ($LC_{50-24h} = 0.01$ mg/L), and also presented the shortest internalization and longest elimination time, 60 min and 8 days, respectively. This formulation caused an extrusion into the intestine and peritrophic membrane. Moreover, CCD 3 showed a photodegradation of 50% (in 24 h) under white fluorescent lamps. In a small-scale field trial, CCD 3 had a residual time of 14 days and abnormal microbial growth was not observed. Finally, CCD 3 did not present any toxicity in Zebrafish, after exposition for 24 h at 100 mg/L. Overall, these results raise the possibility of reducing virus transmission through the controlled photoinactivation of *Aedes aegypti* larvae using a non-toxic plant-based formulated photolarvicide.

Using first-contact serum ferritin to predict severe thrombocytopenia in dengue patients: determination and validation in independent cohorts.

Lodha, A., Pillai, A., Reddy, P., Munshi, N.
26-01-2022
Infect Dis (Lond)

<https://doi.org/10.1080/23744235.2022.2032823>

Severe thrombocytopenia and associated haemorrhage are dreaded complications of dengue fever. The identification of a biomarker that can predict, or rule out, its subsequent development can help identify at-risk individuals. 200 dengue patients were included - the first 100 in the deterministic cohort and the latter, the validation cohort. Serum ferritin levels were measured at first presentation. Platelets were monitored serially. Data from the first cohort was used to determine the optimal ferritin level to predict significant thrombocytopenia ($<20,000/\mu\text{L}$). This threshold was validated in the second cohort. In the deterministic cohort, a ferritin threshold of 593 ng/mL predicted severe thrombocytopenia with a sensitivity of 93.33%, negative predictive value of 98.18% and negative likelihood ratio (LR-) of 0.10. In the validation cohort, the sensitivity and negative predictive value of this threshold were both 100%. The power of the study (determined post-hoc) for each cohort was 98.4% and 86.4% respectively. First-contact ferritin consistently identified at-risk individuals. Individuals with ferritin levels below 593 ng/mL were unlikely to develop severe thrombocytopenia independent of clinical presentation.

G-quadruplex ligands inhibit chikungunya virus replication.

Lv, L., Cui, H., Chen, Z., Zhou, Y., Zhang, L.
02-02-2022
J Med Virol
<https://doi.org/10.1002/jmv.27622>

Chikungunya virus (CHIKV) is a mosquito-transmitted alphavirus affecting human health globally. G-quadruplex secondary structures attract great attention as potential targets for antiviral strategy. In this study, we show that the CHIKV genome possesses several conserved potential G-quadruplex sequences. G-quadruplex ligands BRACO-19 and TMPyP4 could stabilize the CHIKV G-quadruplex and inhibit the transcription of constructs containing CHIKV G-quadruplex sequences. Importantly, BRACO-19 and TMPyP4 suppress CHIKV replication. Our study not only reinforces the presence of viral G-quadruplex sequences but also suggests that targeting G-quadruplex structure could represent a novel strategy to inhibit CHIKV.

Genetic characterization of Chikungunya virus circulating in individuals from Paraná, Brazil.

de Castro Moreira, D., Junior, F., Júnior, J., Jorge, F., Dos Santos Rando, F., Thomazella, M., Presibella, M., Riediger, I., Fernandez, M., Bertolini, D.
14-01-2022
Braz J Microbiol
<https://doi.org/10.1007/s42770-022-00680-x>

Phylogenetic analysis carried out in several Brazilian regions shows the circulation of the Asian and East-Central South African (ECSA) Chikungunya virus (CHIKV) genotypes in the country. Until now, there are no genetic studies about CHIKV

strains circulating in the South region. In this study, we sequenced 5 new partial sequences of the CHIKV Envelope 1 gene from strains detected in Paraná state during the years 2016-2017. Maximum likelihood and neighbor-joining trees grouped all sequences in Brazilian branches within ECSA genotype and comparative analysis did not show E1-A226V mutation. However, we identified E1-K211T amino acid substitution in a sample demonstrating the dispersion of mutant strains in the country.

Rapid screening of dengue fever using research parameters from new generation hematological analyzers.

Chhabra, G., Das, B., Mishra, S., Mishra, B.

22-12-2021

Int J Lab Hematol

<https://doi.org/10.1111/ijlh.13782>

The early diagnosis of dengue fever and its differentiation from other causes of acute febrile illness is essential for a better outcome. The new generation automated hematology analyzers provide parameters like high fluorescence lymphocyte count (HFLC) and leukocyte cell population data (CPD) representing various leukocytes. We tried to analyze the utility of these parameters in the rapid screening of dengue fever. The HFLC and the leukocytic CPD from the Sysmex XN1000 analyzer were obtained for 299 cases presenting with acute febrile illness, which included 97 dengue-positive and 202 cases dengue-negative controls. Additionally, 100 healthy controls were also included. The Receiver operative curves (ROC) were drawn to obtain a cut-off value for these parameters for discriminating among the dengue-positive and dengue-negative subgroups and healthy controls. The dengue-positive cases showed a significantly increased HFLC among the different groups of controls. The median (range) HFLC% was 1.9(0.30-6.55), 0.20(0.10-0.70), and 0.10(0.0-0.30) in the cases that were positive for dengue, negative for dengue, and healthy controls, respectively. The ROC analysis revealed HFLC% at a cut-off value of 1.75 which can discriminate between dengue-positive and dengue-negative patients, with 52% sensitivity, 90% specificity, 72% positive predictive value (PPV), and 80% negative predictive value (NPV). The regression analysis revealed LY-X, LY-Z, Ly-WX, LY-WZ, and MO-X as independent predictors for dengue fever. The HFLC and CPD obtained from Sysmex XN1000 hematology analyzer are valuable tools in rapidly screening dengue infection from other febrile illnesses in routine practice.

Integrated serological surveillance of acute febrile illness in the context of a lymphatic filariasis survey in Timor-Leste: a pilot study using dried blood spots.

Arkell, P., Angelina, J., do Carmo Vieira, A., Wapling, J., Marr, I., Monteiro, M., Matthews, A., Amaral, S., da Conceicao, V., Kim, S., Bailey, D., Yan, J., Fancourt's, N., Vaz Nery, S., Francis, J.

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Trans R Soc Trop Med Hyg

<https://doi.org/10.1093/trstmh/trab164>

Acute febrile illnesses (AFIs), including dengue, scrub typhus and leptospirosis, cause significant morbidity and mortality in Southeast Asia. Serological surveillance can be used to investigate the force and distribution of infections. Dried blood spot (DBS) samples are an attractive alternative to serum because they are easier to collect and transport and require less cold storage. We conducted a pilot study to determine the feasibility of integrating serological surveillance for dengue, scrub typhus and leptospirosis into a population-representative lymphatic filariasis seroprevalence survey in Timor-Leste using DBSs. A total of 272 DBSs were collected from healthy community participants. DBSs were analysed at the National Health Laboratory using commercially available enzyme-linked immunosorbent assays. To validate assays for DBSs, 20 anonymised serum samples of unknown serostatus were used to create dried serum spots (DSSs). These were analysed with optical densities compared with those of serum. Where low variance was observed (dengue assay) the published kit cut-offs for serum were applied to the analysis of DBSs. For the other assays (scrub typhus and leptospirosis), index values (IVs) were calculated and cut-offs were determined to be at 2 standard deviations (SDs) above the mean. Of the 272 samples analysed, 19 (7.0% [95% confidence interval {CI} 4.3 to 10.7]) were positive for dengue immunoglobulin G (IgG), 11 (4.0% [95% CI 2.1 to 7.1]) were positive for scrub typhus IgG and 16 (5.9% [95% CI 3.4 to 9.4%]) were positive for leptospira IgG. While dengue seroprevalence was lower than in nearby countries, results represent the first evidence of scrub typhus and leptospirosis transmission in Timor-Leste. Integrated programmes of serological surveillance could greatly improve our understanding of infectious disease epidemiology in remote areas and would incur minimal additional fieldwork costs. However, when planning such studies, the choice of assays, their validation for DBSs and the laboratory infrastructure and technical expertise at the proposed location of analysis must be considered.

Clinical manifestations, laboratory profile and outcomes of dengue virus infection in hospitalised older patients.

Ng, W., Ngim, C., Chow, K., Goh, S., Zaid, M., Dhanoa, A.

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Trans R Soc Trop Med Hyg

<https://doi.org/10.1093/trstmh/trab168>

Due to an ageing population, dengue among older patients is encountered more frequently in many countries. Our study aimed to explore the clinico-laboratory parameters and outcomes among dengue-infected older patients in comparison with younger patients. This retrospective chart review involved dengue patients with dengue non-structural protein 1 (NS1) antigen positivity admitted to a tertiary hospital in Malaysia from January to July 2015. A comparison was made between older people (aged ≥ 60 y) and others. Among 406 dengue patients, 43 (10.6%) were older people.

Older dengue patients were less likely to present with persistent vomiting (adjusted OR [AOR] 0.247, 95% CI 0.093 to 0.656, $p=0.005$), while restlessness and confusion were more common at presentation (AOR 3.356, 95% CI 1.024 to 11.003, $p=0.046$). Older patients had significantly lower albumin upon admission (38 vs 40 g/L, $p=0.036$) and during hospital stay (35 vs 37 g/L, $p=0.015$). Compared with younger patients, older patients were more likely to have experienced nadir platelet counts of $<50 \times 10^9/L$ (AOR 2.897, 95% CI to 1.176 to 7.137, $p=0.021$). They were also more likely to require an extended hospital stay (AOR 3.547, 95% CI 1.575 to 7.986, $p=0.002$). Diagnosis of dengue in older people may be challenging because of atypical presentations. Increased vigilance is necessary as there is an increased tendency to develop severe thrombocytopenia, hypoalbuminemia and prolonged hospitalisation in older people.

RAGE

RABIES IN ARCTIC FOX (*VULPES LAGOPUS*) AND REINDEER (*RANGIFER TARANDUS PLATYRHYNCHUS*) DURING AN OUTBREAK ON SVALBARD, NORWAY, 2011-2012.

Ørpetveit, I., Reiten, M., Benestad, S., Ropstad, E., Strandbygaard, B., Madslie, K., Stokke, E., Ytnehus, B.

06-06-2022

J Wildl Dis

<https://doi.org/10.7589/JWD-D-21-00112>

Rabies is an important zoonotic disease with high fatality rates in animals and humans. In the Arctic, the Arctic fox (*Vulpes lagopus*) is regarded as the principal reservoir, but there is considerable debate about how the disease persists at the low population densities that are typical for this species. We describe an outbreak of rabies among Arctic foxes and Svalbard reindeer (*Rangifer tarandus platyrhynchus*) during 2011-2012 on the remote Arctic archipelago of Svalbard, an area with a very low and relatively stable Arctic fox density. The aim of the research was to increase knowledge of Arctic rabies in this ecosystem and in the presumed spillover host, the Svalbard reindeer. Phylogenetic analysis of rabies virus (RABV) RNA isolates from Arctic fox and reindeer was performed, and clinical observations and histologic and immunohistochemical findings in reindeer were described. An ongoing capture-mark-recapture project allowed collection of serum samples from clinically healthy reindeer from the affected population for detection of rabies virus-neutralizing antibodies. The outbreak was caused by at least two different variants belonging to the RABV Arctic-2 and Arctic-3 clades, which suggests that rabies was introduced to Svalbard on at least two different occasions. The RABV variants found in Arctic fox and reindeer were similar within locations, suggesting that Arctic foxes and reindeer acquired the infection from the same source(s). The histopathologic and

immunohistochemical findings in 10 reindeer were consistent with descriptions in other species infected with RABV of non-Arctic lineages. Evidence of RABV was detected in both brain and salivary gland samples. None of 158 examined serum samples from clinically healthy reindeer had virus-neutralizing antibodies against RABV.

Risks related to a possible reduction of the waiting period for dogs after rabies antibody titration to 30 days compared with 90 days of the current EU legislative regime.

European Food Safety Authority (EFSA), Alvarez, J., Nielsen, S., Robardet, E., Stegeman, A., Van Gucht, S., Vuta, V., Antoniou, S., Aznar, I., Papanikolaou, A., Roberts, H.

02-06-2022

EFSA J

<https://doi.org/10.2903/j.efsa.2022.7350>

EFSA received a mandate from the European Commission to assess the risks related to a possible reduction of the waiting period after rabies antibody titration test to 30 days compared with 90 days of the current EU legislation, for dogs moving from certain non-EU countries to the EU. This Scientific Report assessed the probability of introduction of rabies into the EU through commercial and non-commercial movements of vaccinated dogs with a positive titration test ($\geq 0.5 IU/mL$) if the waiting period decreases from 90 to 30 days. Assuming that all the legal requirements are complied with, the risk of transmission of rabies through the movement of a vaccinated dog is related to the risk of introducing an animal incubating rabies that was infected before the day of vaccination or shortly after vaccination but before the development of immunity (21 days post-vaccination). Using published data on the incubation period for experimental and field cases in dogs and considering the rabies incidence data in certain countries, the aggregated probability for the annual introduction of rabies through dogs was assessed. Considering the uncertainty related to the duration of the incubation period, the number of imported dogs, and the disease incidence in some countries it was concluded with a 95% certainty that the maximum number of rabies-infected imported dogs complying with the regulations in a 20-year period could increase from 5 to 20 when decreasing the waiting period from 90 to 30 days. Nevertheless, the potential impact of even a small increase in probability means the risk is increased for a region like the EU where rabies has long been a focus for eradication, to protect human and animal health.

Knowledge, attitudes, and practices associated with zoonotic disease transmission risk in North Sulawesi, Indonesia.

Kusumaningrum, T., Latine, A., Martinez, S., Kalengkongan, J., Wiyatno, A., Dewantari, A., Kasenda, N., Bernadus, J., Jaya, U., Ma'roef, C., Francisco, L., Hagan, E., Miller, M., Myint, K., Daszak, P., Olival, K., Saputro, S., Pamungkas, J., Safari, D.

03-06-2022

One Health Outlook

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Hunters, vendors, and consumers are key actors in the wildlife trade value chain in North Sulawesi, Indonesia, and potentially face an elevated risk of exposure to zoonotic diseases. Understanding the knowledge, attitudes, and practices (KAP) associated with the risk of zoonotic disease transmission in these communities is therefore critical for developing recommendations to prevent or mitigate zoonotic outbreaks in the future. Qualitative and quantitative methods were combined to understand KAP associated zoonotic diseases transmission risk in communities involved in the wildlife trade in North Sulawesi. Qualitative data were collected through semi-structured ethnographic interviews and focus group discussions (FGDs) while quantitative data were collected using questionnaires. We conducted 46 ethnographic interviews and 2 FGDs in 2016, and 477 questionnaire administrations in 2017-2018 in communities from five districts in North Sulawesi. We also collected biological specimens, including nasal swab, oropharyngeal swab, and blood, from 254 participants. The study sites were targeted based on known wildlife consumption and trade activities. The participants for qualitative data collection were purposively selected while participants for quantitative data collection were randomly selected. Biological samples were tested for five viral families including Coronaviridae, Filoviridae, Flaviviridae, Orthomyxoviridae and Paramyxoviridae. Knowledge regarding disease transmission from animals to humans was similar across the participants in qualitative focus groups, including knowledge of rabies and bird flu as zoonotic diseases. However, only a small fraction of the participants from the quantitative group (1%) considered that contact with wild animals could cause sickness. Our biological specimen testing identified a single individual (1/254, 0.004%) who was sampled in 2018 with serological evidence of sarbecovirus exposure. Overall, participants were aware of some level of risk in working with open wounds while slaughtering or butchering an animal (71%) but most did not know what the specific risks were. However, significant differences in the attitudes or beliefs around zoonotic disease risk and health seeking behaviors were observed across our study sites in North Sulawesi. Our study showed variable levels of knowledge, attitudes, and practices associated with the risk of zoonotic disease transmission among study participants. These findings can be used to develop locally responsive recommendations to mitigate zoonotic disease transmission.

Divergent Rabies Virus Variant of Probable Bat Origin in 2 Gray Foxes, New Mexico, USA.

Condori, R., Aragon, A., Breckenridge, M., Pesko, K., Mower, K., Ettestad, P., Melman, S., Velasco-Villa, A., Orciari, L., Yager, P., Streicker, D., Gigante, C., Morgan, C., Wallace, R., Li, Y.

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Emerg Infect Dis

<https://doi.org/10.3201/eid2806.211718>

In the Western Hemisphere, bat-associated rabies viruses (RABVs) have established independent transmission cycles in

multiple mammal hosts, forming genetically distinct lineages. In New Mexico, USA, skunks, bats, and gray foxes are rabies reservoir hosts and represent a public health risk because of encounters with humans. During 2015 and 2019, two previously undescribed RABVs were detected in 2 gray foxes (*Urocyon cinereoargenteus*) in Lincoln County, New Mexico. Phylogenetic analysis of the nucleoprotein gene indicated that the isolates are a novel RABV variant. These 2 cases probably represent repeated spillover events from an unknown bat reservoir to gray foxes. Molecular analysis of rabies cases across New Mexico identified that other cross-species transmission events were the result of viral variants previously known to be enzootic to New Mexico. Despite a robust rabies public health surveillance system in the United States, advances in testing and surveillance techniques continue to identify previously unrecognized zoonotic pathogens.

Dual-Mode Immunosensor for Electrochemiluminescence Resonance Energy Transfer and Electrochemical Detection of Rabies Virus Glycoprotein Based on Ru(bpy)₃²⁺-Loaded Dendritic Mesoporous Silica Nanoparticles.

Li, J., Wang, C., Wang, W., Zhao, L., Han, H.

17-05-2022

Anal Chem

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Rabies is a serious zoonotic disease in almost all warm-blooded animals and causes fatal encephalitis. The detection of rabies virus (RABV) is critical and remains a significant challenge. Herein, an electrochemiluminescence resonance energy transfer (ECL-RET) and electrochemical (EC) dual-mode immunosensor was developed for highly sensitive detection of RABV glycoprotein. Dendritic mesoporous silica nanoparticles (DMSNs) were employed to load Ru(bpy)₃²⁺ and to obtain ECL probes (Ru@DMSNs). Ru@DMSNs were decorated on the electrode surface, followed by the modification of the RABV antibody (Ab₁). RABV was specifically recognized and captured by Ab₁, causing the decline of the ECL signal due to the obstruction of electron transfer. Additionally, manganese oxide nanoparticles (MnO_x) modified with Ab₂ can further quench the ECL signal of Ru@DMSNs via the RET between Ru@DMSNs and MnO_x. Meanwhile, MnO_x can catalyze the oxidation of *o*-phenylenediamine (*o*-PD), generating a significant differential pulse voltammetry (DPV) signal as a second signal to monitor RABV glycoprotein concentration. Consequently, an immunosensor was developed to achieve dual-signal detection of RABV and improve reliability. Under the optimal conditions, detection ranges of 0.10 pg·mL⁻¹ to 10 ng·mL⁻¹ for ECL (with an 88 fg·mL⁻¹ detection limit) and 1 pg·mL⁻¹ to 2 ng·mL⁻¹ for EC (with a 0.1 pg·mL⁻¹ detection limit) were obtained for RABV detection. The reliability of this immunoassay was validated by eight brain tissue samples. The results were found to be compatible with the results of the real-time reverse transcription-polymerase chain reaction (RT-PCR) assay, indicating the potential applicability of this method for RABV diagnosis.

Using causal loop analysis to explore pathways for zoonosis control in low-income setting: The case of dog rabies vaccination in Burkina Faso.

Savadogo, M., Renmans, D., Bada Alamedji, R., Tarnagda, Z., Antoine-Moussiaux, N.

24-03-2022

Prev Vet Med

<https://pubmed.ncbi.nlm.nih.gov/35390599>

Dog vaccination is an effective pathway to control rabies if a minimum of 70% dog vaccination coverage is achieved. For more than six decades, dog vaccination has been adopted as part of the rabies control measures in Burkina Faso. However, the required vaccination coverage in canine population remains challenging and rabies endemic. This study describes the use of systems thinking to explore the dynamics arising from dog vaccination complexity and explain the possible causes of low vaccination coverage in the dog population. In-depth interviews were conducted in three administrative regions and included various stakeholders. A thematic analysis was performed to analyze the obtained narratives. Subsequently, causal loop diagrams (CLDs) were developed, depicting the causes of low dog vaccination coverage. The CLDs were composed of reinforcing loops and balancing loops, visualizing how different variables including social, economic, technical, political and organizational factors that affect the implementation of rabies vaccination in the country are causally interrelated. Overall, the results revealed the importance of community awareness raising, strengthening the vaccination workforce, enhanced governance and leadership in the dynamics of dog vaccination. The study calls for wide consideration of all drivers and factors that may affect dog vaccination coverage, for the development of any rabies control strategy or vaccination program. Beyond the dog vaccination problem, the methods and findings from this study could be applied to other critical rabies-related questions such as postexposure prophylaxis, epidemiological surveillance, dog population management, laboratory diagnosis, and the One Health collaboration issues, to understand and improve rabies control.

Spatiotemporal heterogeneity and determinants of canine rabies evidence at Local Government Area Level in Nigeria: Implications for rabies prevention and control.

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04-03-2022

One Health

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Canine rabies poses a significant risk to humans and animals in Nigeria. However, the lack of reliable tools to evaluate the performance of existing canine rabies control programs to inform public health policy decisions poses a severe obstacle. We obtained canine rabies surveillance data from the National Veterinary Research Institute (NVRI) and supplemented these data with rabies diagnoses reported in the published studies

from Nigeria. To uncover contextual factors (i.e., environmental and sociodemographic) associated with canine rabies evidence at the Local Government Area (LGA) level, we classified LGAs in Nigeria into four categories based on evidence availability (i.e., LGAs with NVRI data or published studies, both, or no evidence). We described the geographical and temporal variation in coverage. We fitted a multinomial regression model to examine the association between LGA level canine rabies evidence and potential sociodemographic and ecological determinants of canine rabies evidence. The effective annual testing during the 19 years was less than one dog/100,000 Nigerian resident-year. Our results showed that 58% of Nigerian LGAs (450/774) had not been targeted by the existing national rabies surveillance or studies on rabies, including ten states capitals with high human populations. While 16% (122/774) of Nigerian LGAs concentrated in Taraba, Adamawa, and Abia had canine rabies evidence from published studies, none of these LGAs was represented in the NVRI rabies surveillance data. We also observed an increasing trend in rabies evidence over time towards the eastern part of Nigeria. Our multinomial regression model indicated that education level, poverty, population density, land use and temperature were significantly associated with canine rabies evidence at the LGA level. This study underscores the value of combining canine rabies evidence from different sources to better understand the current disease situation for targeted intervention.

Mitochondrial Dysfunction in Rabies Virus-Infected Human and Canine Brains.

Harsha, P., Ranganayaki, S., Yale, G., Dey, G., Mangalparthi, K., Yarlagadda, A., Chandrasekhar Sagar, B., Mahadevan, A., Srinivas Bharath, M., Mani, R.

28-02-2022

Neurochem Res

<https://doi.org/10.1007/s11064-022-03556-6>

Rabies is a fatal encephalitis caused by the Rabies lyssavirus (RABV). The presence of minimal neuropathological changes observed in rabies indicates that neuronal dysfunction, rather than neuronal death contributes to the fatal outcome. The role of mitochondrial changes has been suggested as a possible mechanism for neuronal dysfunction in rabies. However, these findings are mostly based on studies that have employed experimental models and laboratory-adapted virus. Studies on brain tissues from naturally infected human and animal hosts are lacking. The current study investigated the role of mitochondrial changes in rabies by morphological, biochemical and proteomic analysis of RABV-infected human and canine brains. Morphological analysis showed minimal inflammation with preserved neuronal and disrupted mitochondrial structure in both human and canine brains. Proteomic analysis revealed involvement of mitochondrial processes (oxidative phosphorylation, cristae formation, homeostasis and transport), synaptic proteins and autophagic pathways, with over-expression of subunits of mitochondrial respiratory complexes. Consistent with these findings, human and canine brains displayed elevated activities of complexes I

($p < 0.05$), IV ($p < 0.05$) and V ($p < 0.05$). However, this did not result in elevated ATP production ($p < 0.0001$), probably due to lowered mitochondrial membrane potential as noted in RABV-infected cells in culture. These could lead to mitochondrial dysfunction and mitophagy as indicated by expression of FKBP8 ($p < 0.05$) and PINK1 ($p < 0.001$)/PARKIN ($p > 0.05$) and ensuing autophagy, as shown by the status of LCIII ($p < 0.05$), LAMP1 ($p < 0.001$) and pertinent ultrastructural markers. We propose that altered mitochondrial bioenergetics and cristae architecture probably induce mitophagy, leading to autophagy and consequent neuronal dysfunction in rabies.

Accounting for animal movement improves vaccination strategies against wildlife disease in heterogeneous landscapes.

McClure, K., Bastille-Rousseau, G., Davis, A., Stengel, C., Nelson, K., Chipman, R., Wittemyer, G., Abdo, Z., Gilbert, A., Pepin, K.
31-03-2022

Ecol Appl

<https://doi.org/10.1002/eap.2568>

Oral baiting is used to deliver vaccines to wildlife to prevent, control, and eliminate infectious diseases. A central challenge is how to spatially distribute baits to maximize encounters by target animal populations, particularly in urban and suburban areas where wildlife such as raccoons (*Procyon lotor*) are abundant and baits are delivered along roads. Methods from movement ecology that quantify movement and habitat selection could help to optimize baiting strategies by more effectively targeting wildlife populations across space. We developed a spatially explicit, individual-based model of raccoon movement and oral rabies vaccine seroconversion to examine whether and when baiting strategies that match raccoon movement patterns perform better than currently used baiting strategies in an oral rabies vaccination zone in greater Burlington, Vermont, USA. Habitat selection patterns estimated from locally radio-collared raccoons were used to parameterize movement simulations. We then used our simulations to estimate raccoon population rabies seroprevalence under currently used baiting strategies (actual baiting) relative to habitat selection-based baiting strategies (habitat baiting). We conducted simulations on the Burlington landscape and artificial landscapes that varied in heterogeneity relative to Burlington in the proportion and patch size of preferred habitats. We found that the benefits of habitat baiting strongly depended on the magnitude and variability of raccoon habitat selection and the degree of landscape heterogeneity within the baiting area. Habitat baiting improved seroprevalence over actual baiting for raccoons characterized as habitat specialists but not for raccoons that displayed weak habitat selection similar to radiocollared individuals, except when baits were delivered off roads where preferred habitat coverage and complexity was more pronounced. In contrast, in artificial landscapes with either more strongly juxtaposed favored habitats and/or higher proportions of favored habitats, habitat baiting performed better than actual baiting, even when raccoons displayed weak habitat preferences and where baiting was

constrained to roads. Our results suggest that habitat selection-based baiting could increase raccoon population seroprevalence in urban-suburban areas, where practical, given the heterogeneity and availability of preferred habitat types in those areas. Our novel simulation approach provides a flexible framework to test alternative baiting strategies in multiclass landscapes to optimize bait-distribution strategies.

Neglected Tropical Diseases in Lebanon.

Alam, W., Mobayed, T., Younis, N., Zarif, R., Bizri, N., Tamim, H., Musharrafieh, U., Bizri, A.

03-02-2022

Acta Parasitol

<https://doi.org/10.1007/s11686-021-00510-4>

Neglected tropical diseases (NTDs) are highly endemic and distributed within the Middle East and North Africa (MENA) region, affecting an estimated 65 million people. Lebanon suffers from several NTDs as they are either endemic in the country or imported via expats residing in endemic regions, refugees, and foreign labor force. The Syrian crisis and the displacement of refugees to Lebanon have made the country the largest host of refugees per capita right after the Syrian crisis in 2011, peaking in the year of 2013. Additionally, foreign labor in Lebanon come from different countries in Africa and Asia that are endemic with certain NTDs. The Lebanese diaspora is approximately twice the number of those residing in the country and is distributed throughout the continents carrying the risk of importing new NTDs. A descriptive study about the prevalence of NTDs in Lebanon, their distribution, and factors contributing to spread was performed. The Lebanese Ministry of Public Health (LMPH) database regarding reportable transmissible diseases was reviewed for reportable NTDs between 2002 and 2020 in relation to age, gender, prevalence, and geographical distribution. The medical literature was searched using several engines looking for all reports about NTDs in Lebanon, those relevant to regions hosting Lebanese diaspora, and countries where the refugees and migrant workers came from. Only leishmaniasis, leprosy, echinococcosis, schistosomiasis, and rabies are mandatorily reportable NTDs by the LMPH. Additionally, case reports about fasciolosis, ascariidiosis, and Dengue were reported from Lebanon. The presence of the Syrian refugees in the country affected the prevalence of leishmaniasis and rabies. The most prevalent NTD in Lebanon is cutaneous leishmaniasis. The Lebanese diaspora reside mainly in South America, Africa, and in some Arab states known to be endemic with certain NTDs. Little information is known about NTDs in Lebanon. The country is at an increased risk of experiencing several new NTDs due to refugee influx, foreign labor, economic crisis, and ever-growing number of Lebanese seeking work opportunities abroad. More information is needed to assess the true burden of NTDs in Lebanon and the future steps to contain and mitigate their effects.

TRACHOME

ULCERE DE BURULI

PIAN

Yaws in the Philippines: A clinico-seroprevalence study of selected communities in Mindanao.

Dofitas, B., Kalim, S., Toledo, C., Richardus, J.

01-06-2022

PLoS Negl Trop Dis

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Yaws is a chronic, highly contagious skin and bone infection affecting children living in impoverished, remote communities. It is caused by *Treponema pallidum* subsp. *pertenue*. We report the prevalence of active yaws among elementary schoolchildren based on clinical and serological criteria in selected municipalities of Southern Philippines. From January to March 2017, exploratory cross-sectional surveys and screening of skin diseases were conducted in the Liguasan Marsh area of the provinces Maguindanao, Sultan Kudarat, and Cotabato. We included 9 municipalities and randomly selected one public elementary school per municipality. Members of students' households and the communities were also examined and treated. Yaws suspects and contacts had blood tests for treponemal and non-treponemal antibodies using Dual Pathway Platform and *Treponema pallidum* particle agglutination (TPPA) tests. A total of 2779 children and adults were screened for any skin disease: 2291 students, 393 household members, and 95 community members. Among 210 yaws suspects and contacts, 150 consented to serologic tests. The estimated prevalence of active yaws among schoolchildren screened was 1 out of 2291 (0.04%). Among 2532 children who were 14 years old and younger, 4 (0.2%) had active yaws. Eight adult household contacts and community members had latent yaws and 2 had past yaws. Five out of 9 municipalities were endemic for yaws. This study confirmed that the Philippines is endemic for yaws but at a low level in the schools surveyed. This is an under-estimation due to the limited sampling. The lack of proper disease surveillance after the eradication campaign in the 1960's has made yaws a forgotten disease and has led to its resurgence. Yaws surveillance is needed to determine the extent of yaws in the Philippines and to help develop a strategy to eradicate yaws by 2030.

LEPRE

Beneficial Effect of Minocycline as Additional Treatment to Prednisone for Pustular Erythema Nodosum Leprosum.

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31-05-2022

Int Med Case Rep J

<https://doi.org/10.2147/IMCRJ.S368213>

Pustular erythema nodosum leprosum (ENL) is an atypical manifestation associated with chronic ENL. The use of corticosteroid alone might not be sufficient for this condition, and addition of another anti-inflammatory drug is often necessary. Minocycline is a tetracycline antibiotic with anti-neutrophilic properties, which may accelerate the treatment of pustular ENL. This case report aimed to elaborate on the beneficial effect of minocycline for pustular ENL. We report a case of pustular ENL in a 23-year-old male who had been released from treatment (RFT) of lepromatous leprosy (LL). The patient had been on prednisone for six months as treatment for ENL. The condition recurred when prednisone was tapered to 10 mg daily. Eventually, pustules developed on the erythematous nodules, and the lesions did not improve despite seven weeks of treatment with 40-60 mg prednisone. Later, 100 mg minocycline once daily was given in addition to 60 mg prednisone once daily and improvement was rapidly observed on the ninth day after minocycline administration. This condition was sustained for four weeks with prednisone tapering, and no side effects were reported during the treatment. Minocycline is an antibiotic with anti-inflammatory properties. Only a few studies have been conducted regarding the use of minocycline in chronic ENL, but there was no reported case of minocycline use for pustular ENL in RFT patient. The addition of minocycline to prednisone may accelerate the improvement of pustular ENL. We observed an improvement after the ninth day of minocycline administration compared to seven weeks of prednisone monotherapy. No new ENL lesions occurred during four weeks of minocycline administration therapy. Pustular ENL is an atypical manifestation of chronic ENL, and the addition of minocycline to prednisone may accelerate its therapeutic effect on the patient.

Time-to-Disability Determinants Among Leprosy Patients Enrolled for Treatment at ALERT Center, Addis Ababa, Ethiopia: A Survival Analysis.

Masresha, B., Biresaw, H., Moyehodie, Y., Mulugeta, S.

30-05-2022

Infect Drug Resist

<https://doi.org/10.2147/IDR.S361799>

Mycobacterium leprae causes leprosy, which is a long-term or recurrent infection. The causative agent's collusion with Schwann cells results in the irreversible loss of fringe nerve tissue; followed by incapacity, which includes not just actual impotence but also mental incapacity, creates a bad image of

the transformed, resulting in segregation and societal humiliation of leprosy patients, as well as their families. This study's survival analysis includes a sample of 205 patients who were taking leprosy medication and had all essential data from January 2015 to December 2019 G.C. at the All African TB and Leprosy Rehabilitation and Training Centre. The Cox proportional hazard model was used to figure out what factors influence leprosy patients' survival status during treatment. Among the 205 leprosy patients, 71 (34.63%) had at least one type of impairment grade during treatment. The Cox proportional model revealed that the most significant variables of impairment among leprosy patients were age, symptom duration, treatment category, living place, and sensory loss. The study investigated and revealed characteristics associated with the survival status of leprosy patients in ALRT centers using survival analysis. Patients' risk of worsening disability grade increased with age, was greater for patients with a long duration of symptom, was higher for defaulter patients, and was lower for patients who did not lose their sensibility throughout therapy. The existence of a difference in the survival curves between two or more groups of factors for the patient's survival function was also discovered in this inquiry. Female patients, particularly those who were new to the medication, were shown to be more in their survival.

Case of borderline leprosy presenting with urticaria-like eruptions and limbs swelling: A lesson to be learned for dermatologists.

Chen, H., Zhang, G., Zhang, P., Long, H.

06-06-2022

J Dermatol

<https://doi.org/10.1111/1346-8138.16483>

National Health Survey reveals high percentage of signs and symptoms of leprosy in Brazil.

Penna, G., Pontes, M., Nobre, M., Pinto, L.

18-09-2021

Cien Saude Colet

<https://pubmed.ncbi.nlm.nih.gov/35649013>

Leprosy is a debilitating, infectious, systemic or localized dermatoneurological disease caused by *Mycobacterium lepra*. In Brazil, the magnitude and high disabling power keep the disease as a public health problem. Skin spotting and numbness are pathognomonic signs and symptoms in leprosy. The Instituto Brasileiro de Geografia e Estatística (IBGE) 2019 National Health Survey (PNS-2019) considered the following question as a proxy to estimate its magnitude in the country. "Do you have a spot with numbness or part of the skin with numbness?". In Brazil, 1,921,289 adults reported having a patch or part of the skin with numbness, with no regional differences. As for the age group, the older, the higher the prevalence, for example, between 18 to 29 years old (235,445) and 30 to 39 years old (236,485), 0.7% had the condition, between 40 to 59 years old (827,887), 1.5% and among the elderly, 1.8% (621,472). Being able to estimate, in

population-based surveys, with statistical representativeness, a reported morbidity such as leprosy is essential to support the formulation of public policies, notably those related to primary health care actions. In this way, the IBGE fulfills its constitutional role of portraying the reality of the Brazilian population and today it is the main external evaluator of the Unified Health System (SUS) and of public policies developed by the federal level.

Mycobacterium leprae induces Schwann cell proliferation and migration in a denervated milieu following intracutaneous excision axotomy in nine-banded armadillos.

Ebenezer, G., Pena, M., Daniel, A., Truman, R., Adams, L., Duthie, M., Wagner, K., Zampino, S., Tolf, E., Tsottles, D., Polydefkis, M.

24-03-2022

Exp Neurol

<https://pubmed.ncbi.nlm.nih.gov/35341747>

Nine-banded armadillos develop peripheral neuropathy after experimental *Mycobacterium leprae* infection that recapitulates human disease. We used an intracutaneous excision axotomy model to assess the effect of infection duration by *M. leprae* on axonal sprouting and Schwann cell density. 34 armadillos (17 naïve and 17 *M. leprae*-infected) underwent 3 mm skin biopsies to create an intracutaneous excision axotomy followed by a concentric 4-mm overlapping biopsy 3 and 12-months post *M. leprae* inoculation. A traditional distal leg biopsy was obtained at 15mo for intraepidermal nerve fiber (IENF) density. Serial skin sections were immunostained against axons (PGP9.5, GAP43), and Schwann cells (p75, s100) to visualize regenerating nerves. Regenerative axons and proliferation of Schwann cells was measured and the rate of growth at each time point was assessed. Increasing anti-PGL antibody titers and intraneural *M. leprae* confirmed infection. 15mo following infection, there was evidence of axon loss with reduced distal leg IENF versus naïve armadillos, $p < 0.05$. This was associated with an increase in Schwann cell density ($11,062 \pm 2905$ vs. 7561 ± 2715 cells/mm³, $p < 0.01$). Following excisional biopsy epidermal reinnervation increased monotonically at 30, 60 and 90 days; the regeneration rate was highest at 30 days, and decreased at 60 and 90 days. The reinnervation rate was highest among animals infected for 3mo vs those infected for 12mo or naïve animals (mean \pm SD, 27.8 ± 7.2 vs. 16.2 ± 5.8 vs. 15.3 ± 6.5 mm/mm³, $p < 0.05$). The infected armadillos displayed a sustained Schwann cell proliferation across axotomy time points and duration of infection (3mo: 182 ± 26 , 12mo: 256 ± 126 , naïve: 139 ± 49 cells/day, $p < 0.05$). *M. leprae* infection is associated with sustained Schwann cell proliferation and distal limb nerve fiber loss. Rates of epidermal reinnervation were highest 3mo after infection and normalized by 12 mo of infection. We postulate that excess Schwann cell proliferation is the main pathogenic process and is deleterious to sensory axons. There is a compensatory initial increase in regeneration rates that may be an attempt to compensate for the injury, but it is not sustained and

eventually followed by axon loss. Aberrant Schwann cell proliferation may be a novel therapeutic target to interrupt the pathogenic cascade of *M. leprae*.

Neglected Tropical Diseases in Lebanon.

Alam, W., Mobayed, T., Younis, N., Zarif, R., Bizri, N., Tamim, H., Musharrafieh, U., Bizri, A.

03-02-2022

Acta Parasitol

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Neglected tropical diseases (NTDs) are highly endemic and distributed within the Middle East and North Africa (MENA) region, affecting an estimated 65 million people. Lebanon suffers from several NTDs as they are either endemic in the country or imported via expats residing in endemic regions, refugees, and foreign labor force. The Syrian crisis and the displacement of refugees to Lebanon have made the country the largest host of refugees per capita right after the Syrian crisis in 2011, peaking in the year of 2013. Additionally, foreign labor in Lebanon come from different countries in Africa and Asia that are endemic with certain NTDs. The Lebanese diaspora is approximately twice the number of those residing in the country and is distributed throughout the continents carrying the risk of importing new NTDs. A descriptive study about the prevalence of NTDs in Lebanon, their distribution, and factors contributing to spread was performed. The Lebanese Ministry of Public Health (LMPH) database regarding reportable transmissible diseases was reviewed for reportable NTDs between 2002 and 2020 in relation to age, gender, prevalence, and geographical distribution. The medical literature was searched using several engines looking for all reports about NTDs in Lebanon, those relevant to regions hosting Lebanese diaspora, and countries where the refugees and migrant workers came from. Only leishmaniasis, leprosy, echinococcosis, schistosomiasis, and rabies are mandatorily reportable NTDs by the LMPH. Additionally, case reports about fasciolosis, ascariidiosis, and Dengue were reported from Lebanon. The presence of the Syrian refugees in the country affected the prevalence of leishmaniasis and rabies. The most prevalent NTD in Lebanon is cutaneous leishmaniasis. The Lebanese diaspora reside mainly in South America, Africa, and in some Arab states known to be endemic with certain NTDs. Little information is known about NTDs in Lebanon. The country is at an increased risk of experiencing several new NTDs due to refugee influx, foreign labor, economic crisis, and ever-growing number of Lebanese seeking work opportunities abroad. More information is needed to assess the true burden of NTDs in Lebanon and the future steps to contain and mitigate their effects.

Leprosy: what is new.

Randhawa, A., Kapila, R., Schwartz, R.

26-11-2021

Int J Dermatol

<https://doi.org/10.1111/ijd.15998>

Leprosy, also known as Hansen's disease, is an age-old chronic granulomatous infection characterized by prominent cutaneous and neurologic findings. Long known to be caused by *Mycobacterium leprae*, a new etiologic species was identified and linked in 2008, *Mycobacterium lepromatosis*. The BCG vaccine with highly variable efficacy may soon be replaced by the first leprosy-specific subunit vaccine LepVax, which has recently moved forward in human trials. Recent evidence supporting theories of zoonotic transmission from armadillos and the less-discussed Eurasian red squirrels has emerged. Knowledge on genetic polymorphisms that may increase leprosy susceptibility, such as the newly uncovered mitochondrial ribosomal protein S5 (MRPS5) polymorphism in the Chinese population, has provided a fresh perspective and direction. Further, we will delineate the latest information on leprosy, including the possible effects of leprosy coinfection with COVID-19, HIV, and HTLV-1, and the shift to newer leprosy therapies and treatment regimens.

Role of shear wave elastography in treatment follow-up of leprosy neuropathy.

Meghashyam, K., Prakash, M., Narang, T., Sinha, A., Sandhu, M.
06-05-2021

J Ultrasound

<https://doi.org/10.1007/s40477-021-00583-x>

Grayscale ultrasonography when complemented with shear wave elastography helps in better evaluation of treatment response of leprosy neuropathy and in guiding appropriate management of the patient. There is limited literature regarding the use of shear wave elastography in ulnar nerve neuropathy. Our purpose was to evaluate the role of shear wave elastography in assessing stiffness changes within the ulnar nerve during treatment of leprosy. This was a prospective study which included 30 patients diagnosed with leprosy neuropathy. Recruited patients were followed up, during the course of treatment, i.e. for 1 year. Serial ultrasonography of these patients was done at 0, 3, 6 and 12 months interval. Significant ($P < 0.05$) decrease in elastography parameters was seen in transverse imaging plane between first and third, as well as first and fourth visits (mean stiffness and velocity pretreatment $\sim 25.78 \pm 18$ kPa and 2.74 ± 0.98 m/s, mean stiffness and velocity post-treatment 15.67 ± 5.89 kPa and 2.24 ± 0.428 m/s). Although elastography parameters decreased during these visits in the long-axis imaging plane, they were not found to be statistically significant. However, gross morphology and cross-sectional area of the nerve did not change significantly across visits. Interestingly, elastography values were higher in patients with neuritis, though not statistically significant. Shear wave elastography is a novel, upcoming modality in musculoskeletal imaging especially in the evaluation of peripheral neuropathy. It can act as an adjunct to grey-scale imaging, which can help in early diagnosis and in guiding treatment of leprosy neuropathy.

TRYPANOSOMES (TRYPANOSOMIASE ET MALADIE DE CHAGAS)

Trypanosoma cruzi modulates lipid metabolism and highjacks phospholipids from the midgut of Rhodnius prolixus.

Atella, T., Bittencourt-Cunha, P., Araujo, M., Silva-Cardoso, L., Maya-Monteiro, C., Atella, G.

04-06-2022

Acta Trop

<https://pubmed.ncbi.nlm.nih.gov/35671784>

Chagas disease is potentially life-threatening and caused by the protozoan parasite *Trypanosoma cruzi*. The parasite cannot synthesize some lipids and depends on the uptake of these lipids from its vertebrate and invertebrate hosts. To achieve this, *T. cruzi* may need to modify the physiology of the insect host for its own benefit. In this study, we investigated the interaction of *T. cruzi* (Y strain) with its insect vector *Rhodnius prolixus* and how it manipulates the vector lipid metabolism. We observed a physiological change in lipid flux in infected insects. In the fat body of infected insects, triacylglycerol levels decreased by 80.6% and lipid storage droplet-1(LSD-1) mRNA levels were lower, when compared to controls. Lipid sequestration by infected midguts led to increased levels of 5' AMP-activated protein kinase (AMPK) phosphorylation and activation in the fat body, inhibiting the synthesis of fatty acids and stimulating their oxidation. This led to reduced lipid levels in the fat body of infected insects, despite the fact that *T. cruzi* does not colonize this tissue. There was a 3-fold increase, in lipid uptake and synthesis in the midgut of infected insects. Finally, our results suggest that the parasite modifies the lipid flux and metabolism of its vector *R. prolixus* through the increase in lipid delivery from the fat body to midgut that are then scavenged by *T. cruzi*.

Potential of sulfur-selenium isosteric replacement as a strategy for the development of new anti-chagasic drugs.

Revue de littérature

Rubio-Hernández, M., Alcolea, V., Pérez-Silanes, S.

03-06-2022

Acta Trop

<https://pubmed.ncbi.nlm.nih.gov/35667455>

Current treatment for Chagas disease is based on only two drugs: benznidazole and nifurtimox. Compounds containing sulfur (S) in their structure have shown promising results in vitro and in vivo against *Trypanosoma cruzi*, the parasite causing Chagas disease. Notably, some reports show that the isosteric replacement of S by selenium (Se) could be an interesting strategy for the development of new compounds for the treatment of Chagas disease. To date, the activity against *T. cruzi* of three Se-containing groups has been compared with their S counterparts: selenosemicarbazones, selenoquinones, and selenocyanates. More studies are needed to confirm the positive results of Se compounds.

Therefore, we have investigated S compounds described in the literature tested against *T. cruzi*. We focused on those tested in vivo that allowed isosteric replacement to propose their Se counterparts as promising compounds for the future development of new drugs against Chagas disease.

Comparison of Anxiety and Depression Symptoms in Individuals According to their Sex, Type of Cardiac Device, and Diagnosis of Chagas Disease.

Dessotte, C., Grotti, E., Ignacio, I., Fernandes, P., Maier, S., Rossi, L., Dantas, R.

03-06-2022

Braz J Cardiovasc Surg

<https://doi.org/10.21470/1678-9741-2021-0392>

Implantable cardiac pacemakers or cardioverter defibrillators are alternatives for the treatment of arrhythmias, however, their use has caused changes in the emotional state of patients. The objective of this study was to compare the measures of anxiety and depression symptoms in individuals according to their sex, type of cardiac device, and diagnosis of Chagas disease. This is an observational and cross-sectional study conducted with adults with implantable cardiac pacemakers or cardioverter defibrillators. Data was collected using a sociodemographic and clinical questionnaire and the Hospital Anxiety and Depression Scale. We used the Student's t-test for independent samples and the Chi-squared test, with a significance level of 0.05. Two hundred forty-four patients participated in the study, 168 with cardiac pacemakers and 76 with implantable cardioverter defibrillators; 104 had Chagas cardiomyopathy (85 with cardiac pacemakers and 19 with implantable cardioverter defibrillators). No statistically significant differences were found in measures of anxiety and depression symptoms according to device type ($P=0.594$ and $P=0.071$, respectively) and the presence of Chagas etiology ($P=0.649$ and $P=0.354$, respectively). Women had higher mean scores for anxiety ($P=0.002$) and depression symptoms ($P<0.001$). In the comparison between the groups, according to the type of implanted device and the diagnosis of Chagas disease, no significant differences were found in the measures of anxiety and depression symptoms. Women showed higher means when compared to men, indicating the need to test and implement interventions to minimize these symptoms in this population.

Spatial epidemiology and adaptive targeted sampling to manage the Chagas disease vector *Triatoma dimidiata*.

Case, B., Young, J., Penados, D., Monroy, C., Hébert-Dufresne, L., Stevens, L.

02-06-2022

PLoS Negl Trop Dis

<https://doi.org/10.1371/journal.pntd.0010436>

Widespread application of insecticide remains the primary form of control for Chagas disease in Central America, despite only temporarily reducing domestic levels of the endemic

vector *Triatoma dimidiata* and having little long-term impact. Recently, an approach emphasizing community feedback and housing improvements has been shown to yield lasting results. However, the additional resources and personnel required by such an intervention likely hinders its widespread adoption. One solution to this problem would be to target only a subset of houses in a community while still eliminating enough infestations to interrupt disease transfer. Here we develop a sequential sampling framework that adapts to information specific to a community as more houses are visited, thereby allowing us to efficiently find homes with domiciliary vectors while minimizing sampling bias. The method fits Bayesian geostatistical models to make spatially informed predictions, while gradually transitioning from prioritizing houses based on prediction uncertainty to targeting houses with a high risk of infestation. A key feature of the method is the use of a single exploration parameter, α , to control the rate of transition between these two design targets. In a simulation study using empirical data from five villages in southeastern Guatemala, we test our method using a range of values for α , and find it can consistently select fewer homes than random sampling, while still bringing the village infestation rate below a given threshold. We further find that when additional socioeconomic information is available, much larger savings are possible, but that meeting the target infestation rate is less consistent, particularly among the less exploratory strategies. Our results suggest new options for implementing long-term *T. dimidiata* control.

An Updated View of the *Trypanosoma cruzi* Life Cycle: Intervention Points for an Effective Treatment.

Revue de littérature

Martín-Escolano, J., Marín, C., Rosales, M., Tsaousis, A., Medina-Carmona, E., Martín-Escolano, R.

02-06-2022

ACS Infect Dis

<https://doi.org/10.1021/acscinfecdis.2c00123>

Chagas disease (CD) is a parasitic, systemic, chronic, and often fatal illness caused by infection with the protozoan *Trypanosoma cruzi*. The World Health Organization classifies CD as the most prevalent of poverty-promoting neglected tropical diseases, the most important parasitic one, and the third most infectious disease in Latin America. Currently, CD is a global public health issue that affects 6-8 million people. However, the current approved treatments are limited to two nitroheterocyclic drugs developed more than 50 years ago. Many efforts have been made in recent decades to find new therapies, but our limited understanding of the infection process, pathology development, and long-term nature of this disease has made it impossible to develop new drugs, effective treatment, or vaccines. This Review aims to provide a comprehensive update on our understanding of the current life cycle, new morphological forms, and genetic diversity of *T. cruzi*, as well as to identify intervention points in the life cycle where new drugs and treatments could achieve a parasitic cure.

Genomic Occupancy of the Bromodomain Protein Bdf3 Is Dynamic during Differentiation of African Trypanosomes from Bloodstream to Procyclic Forms.

Ashby, E., Paddock, L., Betts, H., Liao, J., Miller, G., Porter, A., Rolloson, L., Saada, C., Tang, E., Wade, S., Hardin, J., Schulz, D.
01-06-2022

mSphere

<https://doi.org/10.1128/msphere.00023-22>

Trypanosoma brucei, the causative agent of human and animal African trypanosomiasis, cycles between a mammalian host and a tsetse fly vector. The parasite undergoes huge changes in morphology and metabolism during adaptation to each host environment. These changes are reflected in the different transcriptomes of parasites living in each host. However, it remains unclear whether chromatin-interacting proteins help mediate these changes. Bromodomain proteins localize to transcription start sites in bloodstream parasites, but whether the localization of bromodomain proteins changes as parasites differentiate from bloodstream to insect stages remains unknown. To address this question, we performed cleavage under target and release using nuclease (CUT&RUN) against bromodomain protein 3 (Bdf3) in parasites differentiating from bloodstream to insect forms. We found that Bdf3 occupancy at most loci increased at 3h following onset of differentiation and decreased thereafter. A number of sites with increased bromodomain protein occupancy lie proximal to genes with altered transcript levels during differentiation, such as procyclins, procyclin-associated genes, and invariant surface glycoproteins. Most Bdf3-occupied sites are observed throughout differentiation. However, one site appears *de novo* during differentiation and lies proximal to the procyclin gene locus housing genes essential for remodeling surface proteins following transition to the insect stage. These studies indicate that occupancy of chromatin-interacting proteins is dynamic during life cycle stage transitions and provide the groundwork for future studies on the effects of changes in bromodomain protein occupancy. Additionally, the adaptation of CUT&RUN for *Trypanosoma brucei* provides other researchers with an alternative to chromatin immunoprecipitation (ChIP). **IMPORTANCE** The parasite *Trypanosoma brucei* is the causative agent of human and animal African trypanosomiasis (sleeping sickness). Trypanosomiasis, which affects humans and cattle, is fatal if untreated. Existing drugs have significant side effects. Thus, these parasites impose a significant human and economic burden in sub-Saharan Africa, where trypanosomiasis is endemic. *T. brucei* cycles between the mammalian host and a tsetse fly vector, and parasites undergo huge changes in morphology and metabolism to adapt to different hosts. Here, we show that DNA-interacting bromodomain protein 3 (Bdf3) shows changes in occupancy at its binding sites as parasites transition from the bloodstream to the insect stage. Additionally, a new binding site appears near the locus responsible for remodeling of parasite surface proteins during transition to the insect stage. Understanding the mechanisms behind host adaptation is important for understanding the life cycle of the parasite.

Lizards as Silent Hosts of *Trypanosoma cruzi*.

Botto-Mahan, C., Correa, J., Araya-Donoso, R., Farías, F., San Juan, E., Quiroga, N., Campos-Soto, R., Reyes-Olivares, C., González-Acuña, D.

Emerg Infect Dis

<https://doi.org/10.3201/eid2806.220079>

We assessed 4 lizard species in Chile for *Trypanosoma cruzi*, the causative agent of Chagas disease, and 1 species for its ability to transmit the protozoan to uninfected kissing bugs. All lizard species were infected, and the tested species was capable of transmitting the protozoan, highlighting their role as *T. cruzi* reservoirs.

A novel metabarcoded deep amplicon sequencing tool for disease surveillance and determining the species composition of *Trypanosoma* in cattle and other farm animals.

Yasein, G., Zahid, O., Minter, E., Ashraf, K., Rashid, I., Shabbir, M., Betson, M., Sargison, N., Chaudhry, U.

19-03-2022

Acta Trop

<https://pubmed.ncbi.nlm.nih.gov/35317999>

The World Health Organization (WHO) and the Food and Agriculture Organization (FAO) have developed strategies to control trypanosomiasis in humans and livestock in endemic areas. These require a better understanding of the distribution of different *Trypanosoma* species and improved predictions of where they might appear in the future, based on accurate diagnosis and robust surveillance systems. Here, we describe a metabarcoding deep amplicon sequencing method to identify and determine the *Trypanosoma* species in co-infecting communities. First, four morphological verified *Trypanosoma* species (*T. brucei*, *T. congolense*, *T. vivax* and *T. theileri*) were used to prepare test DNA pools derived from different numbers of parasites to evaluate the method's detection threshold for each of the four species and to assess the accuracy of their proportional quantification. Having demonstrated the accurate determination of species composition in *Trypanosoma* communities, the method was applied to determine its detection threshold using blood samples collected from cattle with confirmed *Trypanosoma* infections based on a PCR assay. Each sample showed a different *Trypanosoma* species composition based on the proportion of MiSeq reads. Finally, we applied the assay to field samples to develop new insight into the species composition of *Trypanosoma* communities in cattle, camels, buffalo, horses, sheep, and goat in endemically infected regions of Pakistan. We confirmed that *Trypanosoma evansi* is the major species in Pakistan and for the first time showed the presence of *Trypanosoma theileri*. The metabarcoding deep amplicon sequencing method and bioinformatics pathway have several potential applications in animal and human research, including evaluation of drug treatment responses, understanding of the emergence and spread of drug resistance, and description of species interactions during co-

infections and determination of host and geographic distribution of trypanosomiasis in humans and livestock.

The hormonal and neural control of egg production in the historically important model insect, *Rhodnius prolixus*: A review, with new insights in this post-genomic era.

Revue de littérature

Lange, A., Leyria, J., Orchard, I.

19-03-2022

Gen Comp Endocrinol

<https://pubmed.ncbi.nlm.nih.gov/35317995>

Rhodnius prolixus, the blood gorging kissing bug, is a model insect, extensively used by Sir Vincent Wigglesworth and others, upon which the foundations of insect physiology, endocrinology, and development are built. It is also medically important, being a principal vector of *Trypanosoma cruzi*, the causative agent of Chagas disease in humans. The blood meal stimulates and enables egg production, and since an adult mated female can take several blood meals, each female can produce hundreds of offspring. Understanding the reproductive biology of *R. prolixus* is therefore of some critical importance for controlling the transmission of Chagas disease. The *R. prolixus* genome is available and so the post-genomic era has arrived for this historic model insect. This review focuses on the female reproductive system and coordination over the production of eggs, emphasizing the classical (neuro)endocrinological studies that led to a model describing inputs from feeding and mating, and the neural control of egg-laying. We then review recent insights brought about by molecular analyses, including transcriptomics, that confirm, support, and considerably extends this model. We conclude this review with an updated model describing the events leading to full expression of egg production, and also provide a consideration of questions for future exploration and experimentation.

Isolation and molecular characterization of circulating extracellular vesicles from blood of chronic Chagas disease patients.

Madeira, R., Meneghetti, P., de Barros, L., de Cassia Buck, P., Mady, C., Ianni, B., Fernandez-Becerra, C., Torrecilhas, A.

31-03-2022

Cell Biol Int

<https://doi.org/10.1002/cbin.11787>

Extracellular vesicles (EVs) are lipid bilayer envelopes that encase several types of molecules. Their contents mostly reflect their cell origin and possible targets at other locations in the organism and can be modified in pathological conditions to interfere with intercellular communication, thus promoting disease establishment and development. These characteristics, in addition to their presence in virtually all body fluids, make such vesicles ideal for biomarker discovery in human diseases. Here, we describe the effect of different anticoagulants and the combination of two purification methods for isolation and characterization of circulating EVs

from blood of chronic Chagas disease (CCD) patients. We illustrated this procedure by studying a population of patients with Chagas disease at the indeterminate chronic stage, in which the *Trypanosoma cruzi* is very scarce in circulation. EVs were harvested from blood collected without or with different anticoagulants. Protein and nanoparticle tracking analysis was used to measure EVs size and concentration. The EVs were purified by ultracentrifugation, followed by size-exclusion chromatography and characterized by chemiluminescent enzyme-linked immunosorbent assay and dot blot using antibodies that recognized parasite-derived EVs, such as hyperimmune sera, polyclonal and monoclonal antibodies against trans-sialidase and mucins. In parallel, antibodies against classical human EV markers CD9, CD63, CD81, and CD82, were also analyzed. The results showed that anticoagulants did not interfere with the analyzed parameters and circulating EVs from CCD patients contain *T. cruzi* antigens and classical human exosomal markers. Overall, our protocol is adequate for the isolation of the total circulating EVs and can serve as an important basis for further studies on biomarker discovery in Chagas' disease.

Evaluation of the Re-emergence Risk of Human African Trypanosomiasis in the Southwestern Burkina Faso, A Gold-Bearing Mutation Area.

Somda, M., Kaboré, J., Karambiri, S., Dama, E., Dabiré, D., Compaoré, C., Salou, E., Ilboudo, H., Houaga, I., Courtin, F., Belem, A., Jamonneau, V., Bengaly, Z.

14-01-2022

Acta Parasitol

<https://doi.org/10.1007/s11686-021-00512-2>

The boom in Burkina Faso's artisanal gold mining since 2007 has attracted populations from Côte d'Ivoire and Guinea, which are the West African countries most affected by human African trypanosomiasis (HAT) and therefore increases its risk of re-emergence. Our aim was to update the HAT data in Burkina Faso in the risk of the re-emergence context with the advent of artisanal gold mining. The study was carried out in the southwestern Burkina Faso where entomological surveys were conducted using biconical traps in March 2017. Follow by an active medical survey in April 2017, which was targeted the gold panners in 7 villages closer to artisanal gold sites, using CATT, mini-anion exchange centrifugation technique, trypanolysis test (TL) and ELISA test to measure human/tsetse contacts. The buffy coat technique and the TL were also applied in pigs to check their reservoir role of human trypanosomes. Our results have shown no case of HAT among 958 individuals tested and all the 50 pigs were also negative, but the level of antibodies against tsetse saliva evidenced by ELISA revealed low human/tsetse contact. Moreover, gold panners practise agriculture and breeding in an infected tsetse area, which are increased the risk. Our results illustrate that the risk of re-emergence is low. The passive surveillance system implemented in 2015 in southwestern Burkina Faso is needed to increase the sentinel sites to better cover this area by taking into account the gold mining. Finally, awareness-raising activities are needed among populations about HAT.

Infections and Coinfections by Trypanosomatid Parasites in a Rural Community of Venezuela.

Herrera, L., Morocoima, A., Lozano-Arias, D., García-Alzate, R., Vietri, M., Lares, M., Ferrer, E.

11-01-2022

Acta Parasitol

<https://doi.org/10.1007/s11686-021-00505-1>

Trypanosoma cruzi, *Trypanosoma rangeli* and *Leishmania* spp. are parasites that coexist in several endemic areas. The identification of these parasites in hosts is important for the control programs. 216 samples from human blood (101), blood of other mammals (45) and triatomine intestinal content and hemolymph (70), from an endemic area of Venezuela, were analysed. The samples were evaluated by; serology (only humans) and PCR for *T. cruzi* in human, other mammals and triatomines, PCR for *T. rangeli* in mammals-including human and triatomines and PCR for *Leishmania* in mammals-including human. The 9.9% of the human samples were positive for *T. cruzi* by serology, 11.9% by PCR, 4% for *T. rangeli* PCR and none for *Leishmania* spp. PCR. 60% of the samples of other mammals showed DNA amplification for *T. cruzi*, 42.2% for *T. rangeli* and 4.4% for *Leishmania* spp. 61.4% of the triatomine samples showed DNA amplification for *T. cruzi* and 10% for *T. rangeli*. High *T. cruzi* infection was detected in mammals and triatomines compared with *T. rangeli*. Low leishmanial infection was detected in other mammals. It is the first time that *T. cruzi*/*T. rangeli* coinfection, in humans, *Canis familiaris* (dog), and *Bos Taurus* (cow), were reported world-wide, and that this coinfection was described in *Tamandua tetradactyla* (anteater) from Venezuela. The coinfection *T. cruzi*/*T. rangeli* in mammals-including humans and triatomines, and coinfection *T. cruzi*/*Leishmania* spp. in non-human mammals, show the risk for trypanosomic zoonoses in this endemic area.

Deaths related to Chagas disease and HIV/AIDS coinfection in Brazil: a nationwide population-based analysis.

Martins-Melo, F., Castro, M., Werneck, G., Heukelbach, J.

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Trans R Soc Trop Med Hyg

<https://doi.org/10.1093/trstmh/trab183>

Trypanosoma cruzi/HIV coinfection has been described as a relevant clinical event and an emerging public health problem. Here, we describe the epidemiological patterns of deaths related to Chagas disease and HIV/AIDS coinfection in Brazil from 2000 to 2019. We performed a nationwide population-based study using mortality data obtained from the Brazilian Mortality Information System. We included all deaths recorded in Brazil from 2000 to 2019 in which Chagas disease and HIV/AIDS were mentioned on the same death certificate, either as underlying or as associated causes of death. Chagas disease and HIV/AIDS were mentioned on 196/22 663 092 death certificates. HIV/AIDS was the underlying cause in 58.2% (114/196) of deaths and Chagas disease in 33.2% (65/196). The average annual mortality rate was 0.05 deaths/1 000 000

inhabitants (95% CI 0.03 to 0.09). The highest death rates were found among males, those aged 60-69 y, Afro-Brazilians, those with 1-3 y of schooling/study and residents in Chagas disease-endemic regions/states. Respiratory, infectious/parasitic and cardiovascular diseases/disorders were the associated causes of death most commonly mentioned. Mortality due to Chagas disease and HIV/AIDS coinfection may be largely underestimated in Brazil. Our data further reinforce the importance of screening for *T. cruzi* infection in HIV-infected patients from Chagas disease-endemic areas. Appropriate clinical management should be ensured for Chagas disease and HIV coinfecting patients.

Control of pyrethroid-resistant populations of *Triatoma infestans*, the main vector of *Trypanosoma cruzi*, by treating dogs with fluralaner in the Argentine Chaco.

Laiño, M., Cardinal, M., Gaspe, M., Enriquez, G., Alvedro, A., Macchiaverna, N., Gürtler, R.

06-12-2021

Med Vet Entomol

<https://doi.org/10.1111/mve.12561>

We assessed whether fluralaner administered to outbred healthy dogs reduced or suppressed site infestation and abundance of pyrethroid-resistant populations of *Triatoma infestans* Klug (Heteroptera: Reduviidae). We conducted a placebo-controlled before-and-after efficacy trial in 28 infested sites in Castelli (Argentine Chaco) over 10 months. All 72 dogs initially present received either an oral dose of fluralaner (treated group) or placebo (control group) at month 0 posttreatment (MPT). Preliminary results justified treating all 38 control-house dogs with fluralaner 1 month later, and 71 of 78 existing dogs at 7 MPT. Site-level infestation and triatomine abundance were evaluated using timed manual searches with a dislodging aerosol. In the fluralaner-treated group, infestation dropped significantly from 100% at baseline to 19% over 6-10 MPT whereas mean abundance fell highly significantly from 5.5 to 0.8-0.9 triatomines per unit effort. In the placebo group, site infestation and mean abundance remained stable between 0 and 1 MPT, and strongly declined after fluralaner administration from 13.0-14.7 triatomines at 0-1 MPT to 4.0-4.2 over 6-10 MPT. Only one of 81 noninfested sites before fluralaner treatment became infested subsequently. Fluralaner significantly reduced the site-level infestation and abundance of pyrethroid-resistant *T. infestans* and should be tested more widely in Phase III efficacy trials.

Association of HLA-B*35 and moderate or severe cutaneous reactions secondary to benznidazole treatment in chronic chagas disease.

Bosch-Nicolau, P., Salvador, F., Sánchez-Montalvá, A., Franco-Jarava, C., Arrese-Muñoz, I., Sulleiro, E., Roure, S., Valerio, L., Oliveira-Souto, I., Serre-Delcor, N., Pou, D., Treviño, B., Aznar, M., Espinosa-Pereiro, J., Molina, I.

01-12-2021

Clin Microbiol Infect

<https://pubmed.ncbi.nlm.nih.gov/34863919>

Benznidazole is the first-line treatment for Chagas disease. Adverse events appear in more than 50% of patients, leading to discontinuation in approximately 15%. Cutaneous reactions are one of the most frequent adverse events. Human leucocyte antigen (HLA) genotyping studies identified an association between cutaneous reactions to benznidazole and carrying the specific allele HLA-B*35:05. We designed the present study to prospectively confirm this association. This is a prospective observational study including Chagas disease patients aged 18 years or more who accepted to receive benznidazole treatment following current guidelines. Allele genotyping of HLA-B was determined in all patients. Clinical and analytical follow up was performed at days 0, 7, 14, 30 and 60 of treatment. Two-hundred and seven individuals were included. Seventy per cent were female with a mean age of 45.1 (SD ± 9.86) years mainly from Bolivia (92.8%). In 102 (49.3%) cases a cutaneous reaction was diagnosed. Forty-eight (46.6%) were classified as mild, 37 (35.9%) as moderate and 18 (17.5%) as severe. Thirty-two (15.4%) patients had to definitively interrupt the treatment because of a cutaneous reaction. Female sex (OR 4.49; 95% CI 1.62-12.47), new-onset eosinophilia before cutaneous symptoms (OR 2.55; 95% CI 1.2-5.43) and carrying the HLA-B*35 allelic group (OR 2.58; 95% CI 1.2-5.51) were all predictors of moderate to severe cutaneous reactions. No statistical significance was found when the specific allele HLA-B*35:05 was analysed. Patients carrying the HLA-B*35 allelic group are at higher risk of moderate to severe reactions when taking benznidazole treatment.

LEISHMANIOSE

Use of light emitting diodes (LEDs) are effective and useful for sand fly ecoepidemiology studies in an Amazonian environment.

da Silva, M., Júnior, A., Costa, N., Costa, G., Rodrigues, M., Medeiros, J.

04-06-2022

Acta Trop

<https://pubmed.ncbi.nlm.nih.gov/35671783>

One strategy to identify transmission foci is based on vector monitoring, and efficient methods are important for vector control. Our study evaluated different light sources (red, green, ultraviolet, blue, and incandescent light) to capture sand fly in Porto Velho, Brazil. We also evaluated *Leishmania* and blood meal sources in females. A total of 1,943 individuals were identified in 45 species level-taxa, with *Trichophoromyia ubiquitalis* (Mangabeira) (n=364), *Nyssomyia antunesi* (n=241), *Bichromomyia flaviscutellata* (Mangabeira) (n=222), and *Psychodopygus davisii* (Root) (n=148) being the most abundant. Incandescent light captured most individuals (n=589), followed by blue (n=471), green (n=452), ultraviolet

(n=281) and red (n=150). No significant difference was observed between the species composition and lights (PERMANOVA: Pseudo F = 1.29, p = 0.14, NMDS: Stress 0.18). The Shannon and Simpson indices demonstrated a high diversity captured using all lights. Our data demonstrated that LEDs are alternative devices for sand fly capture, with blue and green LEDs presenting similar results to incandescent light. 53 pools were analyzed, only one pool was positive for kDNA and hsp70 targets [*Nyssomyia fraihai* (Martins, Falão & Silva)] and identified as *Endotrypanum* spp., suggesting that other trypanosomatids may circulate in the locality. *Choloepus hoffmanni* (two-toed sloth) Peters, *Homo sapiens* Linnaeus, *Proechimys gardneri* (Gardner's spiny rat) Da Silva, and *Tamandua tetradactyla* (lesser anteater) (Linnaeus) were blood meal sources identified in females, increasing the knowledge about sources used by these insects.

Seropositivity of main vector-borne pathogens in dogs across Europe.

Miró, G., Wright, I., Michael, H., Burton, W., Hegarty, E., Rodón, J., Buch, J., Pantchev, N., von Samson-Himmelstjerna, G.
06-06-2022

Parasit Vectors

<https://doi.org/10.1186/s13071-022-05316-5>

Background: Canine vector-borne disease (CVBD) has been an area of increasing interest in Europe over the last few decades, and there have been changes in the prevalence and distribution of many of these diseases. Monitoring CVBD infections in Europe is often done by individual countries, but aggregated data for the European countries are helpful to understand the distribution of CVBDs. **Methods:** We used an extensive retrospective database of results from point-of-care rapid enzyme-linked immunosorbent assay (ELISA) tests on dogs across Europe to identify distribution and seropositivity in animals tested for selected CVBDs (*Anaplasma* spp., *Ehrlichia* spp., *Borrelia burgdorferi*, *Leishmania* spp., and *Dirofilaria immitis*) from 2016 through 2020. Geographic distribution of positive tests and relative percent positive values were mapped by the Nomenclature of Territorial Units for Statistics classification for regions with sufficient test results for reporting. **Results:** A total of 404,617 samples corresponding to 1,134,648 canine results were available from dogs tested in 35 countries over the 5-year study period. Over this period the number of test results per year increased whereas test positivity decreased. *Leishmania* spp. had the largest increase in total test results from 25,000 results in 2016 to over 60,000 results in 2020. Test positivity for *Leishmania* spp. fell from 13.9% in 2016 to 9.4% in 2020. Test positivity fell for *Anaplasma* spp. (7.3 to 5.3%), *Ehrlichia* spp. (4.3 to 3.4%), and *Borrelia burgdorferi* (3.3 to 2.4%). *Dirofilaria immitis* test positivity trended down with a high of 2.7% in 2016 and low of 1.8% in 2018. *Leishmania* spp. test positivity was highest in endemic areas and in several non-endemic countries with low numbers of test results. Co-positivity rates were significantly higher than expected for all pathogen test positive pairs except for *Ehrlichia* spp. with *Borrelia burgdorferi* and *D. immitis* with *Borrelia burgdorferi*.

Conclusions: This study represents the largest data set on CVBD seropositivity in Europe to date. The increase in the number of test results and decreasing test positivity over the study period may reflect changes in testing behavior and increased screening of healthy animals. The Europe-wide mapping of CVBD provides expected test positivity that can help inform veterinarians' decisions on screening and improve prevention and identification of these important, sometimes zoonotic, diseases.

Pre-clinical evaluation of LASSBio-1491: From in vitro pharmacokinetic study to in vivo leishmanicidal activity.

de Queiroz, A., Barbosa, G., de Oliveira, V., de Mattos Alves, H., Alves, M., Carregaro, V., Santana da Silva, J., Barreiro, E., Alexandre-Moreira, M., Lima, L.
06-06-2022

PLoS One

<https://doi.org/10.1371/journal.pone.0269447>

Leishmaniasis is a public health issue. It is among the top five parasitic illnesses worldwide and is one of the most neglected diseases. The current treatment disease includes limitations of toxicity, variable efficacy, high costs and inconvenient doses and treatment schedules. LASSBio-1736 was described as antileishmanial drug-candidate to cutaneous leishmaniasis, displaying plasma stability and with no preliminary signals of hepatic or renal toxicity. In this paper, we described the in vitro pharmacokinetic study of LASSBio-1491 (a less lipophilic isostere of LASSBio-1736) and it is in vitro and in vivo leishmanicidal activities. Our results demonstrated that LASSBio-1491 has high permeability, satisfactory aqueous solubility, long plasma and microsomal half-lives and low in vitro systemic clearance, suggesting a pharmacokinetic profile suitable for its use in a single daily dose. The antileishmanial effect of LASSBio-1491 was confirmed in vitro and in vivo. It exhibited no cytotoxic effect to mammalian cells and displayed good in vivo effect against BALB/c mice infected with *Leishmania major* LV39 substrain, being 3 times more efficient than glucantime.

Regulatory role of Transcription factor-EB (TFEB) in parasite control through alteration of antigen presentation in visceral leishmaniasis.

Ghosh, R., Jawed, J., Roy, N., Mandal, S., Majumdar, S., Majumdar, S.
02-06-2022

Exp Parasitol

<https://pubmed.ncbi.nlm.nih.gov/35660529>

Leishmania donovani, an obligate intracellular parasite, the causative agent of visceral leishmaniasis is known to subvert the host immune system for its own survival. Although the precise mechanism is still unknown, emerging evidences indicate that *L. donovani* efficiently suppress MHC I mediated antigen presentation, rendering inadequate CD8⁺T cell activation and weakening host defense against parasite. The

role of transcription factor EB (TFEB) was recognized in modulating antigen presentation besides its role in lysosomal biogenesis and function. Here, we investigated the regulatory role of TFEB in the modulation of presentation of Leishmania antigen in host tissue. Our results showed an increased expression of TFEB after Leishmania infection both in vitro and in vivo and there was a decrease in the expression of Th-1 cytokine IFN γ along with MHC class I and CD8⁺T cells indicating attenuation of cell mediated immunity and possibly MHC I restricted antigen presentation. Silencing of TFEB resulted in increased expression of IFN γ and MHC I along with increased CD8⁺T cells population without any significant change in CD4⁺T cell number. We also observed a decreased parasite burden in TFEB silenced condition which indicates enhanced parasite clearance by alteration of immunological response possibly through induction of presentation of Leishmania antigen through MHC I. The present study explains the role of TFEB silencing in parasite clearance through regulating the antigen presentation of Leishmania antigen thereby promises to formulate a potential therapeutic strategy against visceral leishmaniasis.

A novel rapid LAMP test for identification of cutaneous leishmaniasis: An evaluation and comparative analysis of three molecular methods.

Salari, S., Taghdiri, A., Bamorovat, M., Sharifi, I., Ghasemi Nejad Almani, P.

31-05-2022

Microb Pathog

<https://pubmed.ncbi.nlm.nih.gov/35660477>

Leishmaniasis is a neglected and widespread parasitic disease that can lead to serious health problems. The conventional method in diagnostic health clinics is direct smear preparation of the lesion and staining with standard Giemsa to visualize the amastigote stage and by culturing the organism in an NNN (Novy-MacNeal-Nicolle) to observe the promastigote form of the parasite. In the case of urban-type leishmaniasis, microscopic diagnosis is sometimes not possible due to the reduction of amastigotes in patients' wounds. Because most endemic areas are located in regions that do not have access to laboratories equipped with molecular tools, access to a rapid test to diagnose the disease is essential. In this study, for the first time for DNA extraction, the scalpel used for sampling was washed and extracted by boiling method. Also, the LAMP technique in this study was modified so that the test can be performed in 10 minutes and the results can be recognized by color. We used four microscopic methods, conventional PCR, real-time PCR, and LAMP, to diagnose urban-type leishmaniasis and compared the results of these methods with each other. The sensitivity and specificity of LAMP were higher than other techniques used. Therefore, it allows rapid diagnosis for timely treatment of the disease to control the primary reservoir host more quickly in ACL as humans are the principal source of infection. This test is performed at a high-speed and is cost-effective. For its convenience, this test is highly recommended to be used in endemic areas.

Evaluation of prime and prime-boost immunization strategies in BALB/c mice inoculated with Leishmania infantum transfected with toxic plasmids.

Augusto Sanches Roque, G., Esteves Zorzi, N., Janaína Soares Rocha, F., Flóro E Silva, M., Fernanda Araújo, T., Ruiz Abánades, D., Giorgio, S.

02-06-2022

Vaccine

<https://pubmed.ncbi.nlm.nih.gov/35660330>

The etiologic agents of visceral leishmaniasis are *Leishmania infantum* and *Leishmania donovani*. Despite the variety of drugs available to treat leishmaniasis, most lead to serious adverse effects, and resistance to these drugs has been reported. Currently, no leishmaniasis vaccine is available for humans. That is why the group developed transgenic *L. infantum* promastigote lines, which express toxic proteins after differentiation into amastigotes. That is why group developed the pFL-AMA plasmid and transfected it into *L. infantum* promastigotes. This plasmid was expressed only in the amastigote form of the parasite. Sequences encoding toxic proteins (active bovine trypsin and egg avidin) were inserted in this plasmid, and the transfected parasites died after the differentiation process. In this study, two immunization protocols were performed in BALB/c mice: prime and prime-boost immunization prior to challenge with the wild-type *L. infantum* (WT). The parasite burdens in the spleen, liver, and bone marrow were evaluated to verify immunological protection. Histopathological analysis of the spleen and liver and the humoral immune response were also performed. The data showed that the parasite burden was reduced in prime-boosted mice in the spleen, liver, and bone marrow, indicating that mice immunized with two doses of the transfected parasites were satisfactorily protected. High levels of IgG, IgG1, and IgG2a antibodies were observed, as well as the presence of anti-inflammatory cytokine Interleukine-10 and pro-inflammatory cytokine Tumor Necrosis Factor- α (TNF- α) and Interferon- γ (IFN - γ) suggesting a Th1/Th2 mix response, in addition to the presence of multinucleated giant cells in the spleen and lymphocyte infiltration in the liver. Therefore, *L. infantum* transfected with a toxic plasmid is an excellent vaccine candidate against visceral leishmaniasis and the application of a boost before the challenge promotes greater protection against WT *L. infantum* infection.

Establish an allele-specific real-time PCR for Leishmania species identification.

Wu, Y., Jiang, M., Li, S., Waterfield, N., Yang, G.

02-06-2022

Infect Dis Poverty

<https://doi.org/10.1186/s40249-022-00992-y>

Leishmaniasis is a serious neglected tropical disease that may lead to life-threatening outcome, which species are closely related to clinical diagnosis and patient management. The current *Leishmania* species determination method is not appropriate for clinical application. New *Leishmania* species

identification tool is needed using clinical samples directly without isolation and cultivation of parasites. A probe-based allele-specific real-time PCR assay was established for *Leishmania* species identification between *Leishmania donovani* and *L. infantum* for visceral leishmaniasis (VL) and among *L. major*, *L. tropica* and *L. donovani/L. infantum* for cutaneous leishmaniasis (CL), targeting hypoxanthine-guanine phosphoribosyl transferase (HGPRT) and spermidine synthase (SPDSYN) gene with their species-specific single nucleotide polymorphisms (SNPs). The limit of detection of this assay was evaluated based on 8 repeated tests with intra-assay standard deviation <0.5 and inter-assay coefficients of variability <5%. The specificity of this assay was tested with DNA samples obtained from *Plasmodium falciparum*, *Toxoplasma gondii*, *Brucella melitensis* and *Orientia tsutsugamushi*. Total 42 clinical specimens were used to evaluate the ability of this assay for *Leishmania* species identification. The phylogenetic tree was constructed using HGPRT and SPDSYN gene fragments to validate the performance of this assay. This new method was able to detect 3 and 12 parasites/reaction for VL and CL respectively, and exhibited no cross-reaction with *P. falciparum*, *T. gondii*, *B. melitensis*, *O. tsutsugamushi* and non-target species of *Leishmania*. Twenty-two samples from VL patients were identified as *L. donovani* (n=3) and *L. infantum* (n=19), and 20 specimens from CL patients were identified as *L. major* (n=20), providing an agreement of 100% compared with sequencing results. For further validation, 29 sequences of HGPRT fragment from nine *Leishmania* species and 22 sequences from VL patients were used for phylogenetic analysis, which agreed with the results of this new method. Similar results were obtained with 43 sequences of SPDSYN fragment from 18 *Leishmania* species and 20 sequences from CL patients. Our assay provides a rapid and accurate tool for *Leishmania* species identification which is applicable for species-adapted therapeutic schedule and patient management.

Prevalence of antinuclear antibodies and rheumatoid factor titers in dogs with arthritis secondary to leishmaniosis (*Leishmania infantum*).

Tsoulofi, T., Theodorou, K., Day, M., Oikonomidis, I., Kasabalis, D., Mylonakis, M., Saridomichelakis, M., Kritsepi-Konstantinou, M., Soubasis, N.

02-06-2022

J Vet Diagn Invest

<https://doi.org/10.1177/10406387221099030>

Dogs with infectious arthritis may occasionally exhibit positive serum antinuclear antibody (ANA) and rheumatoid factor (RF) titers; however, relevant data are sparse for arthritis secondary to canine leishmaniosis (CanL) caused by *Leishmania infantum*. We determined the prevalence of positive serum ANA and RF titers in dogs with arthritis secondary to CanL. Blood samples from adult, client-owned dogs with purulent arthritis secondary to CanL, without any comorbidities, were collected for diagnostic purposes. Serum ANA titers were measured by immunoperoxidase test and RF titers by the Rose-Waaler latex test. Twelve of 23 dogs

enrolled prospectively in our study had clinical arthritis, and 11 of 23 had subclinical arthritis. Based on LeishVet clinical staging, 7 dogs had clinical stage II disease, 11 had clinical stage III disease, and 5 had stage IV. None of the 23 dogs was seropositive for ANA; 3 of 23 were positive for RF. ANA and/or RF seropositivity, in dogs with CanL-associated arthritis, appears to be weak, if present at all. Based on our results, positive serum ANA and RF titers should not be expected in dogs with arthritis secondary to CanL.

Contribution of researchers in Arab countries to scientific publications on neglected tropical diseases (1971 - 2020).

Sweileh, W.

01-06-2022

Trop Dis Travel Med Vaccines

<https://doi.org/10.1186/s40794-022-00173-7>

The neglected tropical diseases (NTDs) are endemic in several Arab countries. The purpose of the current study was to assess the contribution of researchers in Arab countries to the knowledge base on NTDs using bibliometric indicators. Keywords related to all 20 NTDs were obtained from previously published bibliometric studies and were combined with the names of Arab countries listed as country affiliation. The search strategy was implemented in the Scopus database and bibliometric indicators were generated for the study period from 1971 to 2020. RESULTS: The search strategy generated 6542 documents; representing less than 4% of the global research in the field. Scientific research on NTDs from researchers in Arab countries (a) has experienced slow growth; (b) generated a relatively inadequate number of publications over the study period; (c) was disseminated mainly through journals in the field of parasitology or tropical medicine; (d) was contributed by researchers from the 22 Arab countries, but mainly by researchers from Egypt, Saudi Arabia, and Sudan; (e) has fragmented author networks with weak collaboration between active authors in the field; (f) was characterized by strong cross-country research collaboration with researchers in the US and the UK; (g) has focused on three main diseases, specifically, schistosomiasis, leishmaniasis, and onchocerciasis, and (h) showed less emphasis on soil-transmitted helminthiasis infections despite high prevalence. Arab countries cannot achieve the 2030 global agenda without control and elimination of prevalent NTDs. Researchers in Arab countries need to establish strong research networks to exchange expertise on all NTDs.

Exploring novel nitrofuranyl sulfonohydrazides as anti-Leishmania and - cancer agents: Synthesis, in vitro efficacy and hit identification.

Kannigadu, C., Aucamp, J., N'Da, D.

01-06-2022

Chem Biol Drug Des

<https://doi.org/10.1111/cbdd.14097>

Leishmaniasis and cancer are two deadly diseases that plague

the human population. There are a limited number of drugs available for the treatment of these diseases; however, their overuse has resulted in pathogenic resistance. Recent studies have indicated the repurposing of nitro-containing compounds to be a new avenue into finding new treatments. In this study, new nitrofuranyl sulfonohydrazide derivatives were synthesized and evaluated for their *in vitro* antileishmanial and anticancer activities. The analogue 2h, featuring biphenyl moiety exhibited selective ($SI > 10$) submicromolar activity (IC_{50} 0.97 μ M) against acute promyelocytic leukemia cells hence was identified anticancer hit. This study revealed no antileishmanial hit. However, several promising analogues were uncovered and are worthy of further structural modifications to improve their toxicity and bioactivity profiles.

Design, synthesis and evaluation of novel phenanthridine triazole analogs as potential antileishmanial agents.

Nandikolla, A., Singireddi, S., Banoth, K., Murugesan, S., Aggarwal, H., Balaña-Fouce, R., Estela, M., Chandra Sekhar Kondapalli, V.

01-06-2022

Future Med Chem

<https://doi.org/10.4155/fmc-2021-0354>

Aim: To synthesize and screen phenanthridine and 1,2,3-triazole derivatives for antileishmanial activity. **Methodology:** Synthesized analogs were tested for antileishmanial activity against transgenic strain of *Leishmania infantum* promastigotes and *ex vivo* infections. **Results:** Compounds **T01**, **T08** and **T11** revealed significant activity with $EC_{50} < 30 \mu$ m and lacked toxicity in mouse spleen and HepG2 cells. **T01** with EC_{50} 3.07 μ m is four-fold more potent than the drug miltefosine (EC_{50} 12.6 μ M) against *L. infantum* promastigotes. *In silico* studies indicate that the analogs are nontoxic. A molecular docking analysis was also carried out on the **T01** and **T08** to investigate the binding pattern at the active site of the chosen target trypanothione reductase. **Conclusion:** The results of this study reveal that phenanthridine triazoles exhibit antileishmanial activity.

Acute kidney injury as initial presentation of visceral leishmaniasis in a young patient- A case report.

Mohamed, A., Bashir, A.

18-05-2022

Ann Med Surg (Lond)

<https://doi.org/10.1016/j.amsu.2022.103821>

Visceral leishmaniasis is endemic in Somalia and in East Africa at large. Clinically, patients present with recurrent fever, weight loss, hepatosplenomegaly and pancytopenia. Sometimes, patients in low resource countries with no properly functioning primary healthcare facilities may present with complications. Here, we report a case of 19 years old male patient who presented with impaired renal function.

After diagnosing with VL and starting Sodium Stibogluconate, patient developed acute pancreatitis, that compelled us to shift to liposomal amphotericin B, which he responded well and finally was discharged within a good condition. Early diagnosis and proper treatment is necessary to restore the renal function. This case report elaborates some of the clinical presentations of VL, complications of treatment and encouraging physicians in endemic areas to keep VL into their list of differential diagnosis in patients with fever and hepatosplenomegaly.

Geographic Origin and Vertical Transmission of Leishmania infantum Parasites in Hunting Hounds, United States.

Franssen, S., Sanders, M., Berriman, M., Petersen, C., Cotton, J.

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Emerg Infect Dis

<https://doi.org/10.3201/eid2806.211746>

Vertical transmission of leishmaniasis is common but is difficult to study against the background of pervasive vector transmission. We present genomic data from dogs in the United States infected with *Leishmania infantum* parasites; these infections have persisted in the apparent absence of vector transmission. We demonstrate that these parasites were introduced from the Old World separately and more recently than *L. infantum* from South America. The parasite population shows unusual genetics consistent with a lack of meiosis: a high level of heterozygous sites shared across all isolates and no decrease in linkage with genomic distance between variants. Our data confirm that this parasite population has been evolving with little or no sexual reproduction. This demonstration of vertical transmission has profound implications for the population genetics of *Leishmania* parasites. When investigating transmission in complex natural settings, considering vertical transmission alongside vector transmission is vital.

Identification of blood source preferences and Leishmania infection in sand flies (Diptera: Psychodidae) in north-eastern Algeria.

Messahel, N., Benallal, K., Halada, P., Lafri, I., Manseur, H., Hakem, A., Houali, K., Harrat, Z., Volf, P., Dvorak, V.

15-04-2022

Vet Parasitol Reg Stud Reports

<https://pubmed.ncbi.nlm.nih.gov/35569914>

Leishmaniasis are among the most neglected vector-borne diseases, infecting humans as well various animal hosts with clinical outcomes varying from cutaneous disorders to visceral and life-threatening disease. In Algeria, canine leishmaniasis (CanL) caused by *Leishmania infantum* is endemic mainly throughout the northern regions of the country with the Mediterranean climate that favours the occurrence of *Larrousius* sand flies, the vectors of the parasite. This study conducted in Bougaa and Kherrata, two regions located in north-eastern Algeria and endemic for CanL, focuses on: i)

composition of sand fly fauna, ii) screening of *Leishmania* parasites and iii) the blood sources of engorged females. Entomological surveys were conducted between June and September 2019 using CDC light-traps in rural areas of both regions. Sand fly specimens were morphologically identified, females were screened for *Leishmania* DNA using kDNA and ITS1 primers, blood meals in engorged females were identified by peptide mass mapping (PMM)-based MALDI-TOF mass spectrometry and confirmed by DNA sequencing analysis. Overall, 1940 specimens (844 males, 1096 females) were collected, all belonging to the subgenus *Larrousius*: *Phlebotomus perniciosus*, (94.64%), *Ph. perfiliewi* (4.74%) and *Ph. longicuspis* (0.62%). No *Leishmania* DNA was detected in the evaluated pools (n = 106) (1096 females). PMM-based MALDI-TOF MS successfully identified a source of blood in 92% (141/154) of engorged females (135 *Ph. perniciosus* and 6 *Ph. perfiliewi*). All blood meals were taken from domestic cattle (*Bos taurus*) except for one originating from a dog (*Canis lupus familiaris*) and one from sheep (*Ovis aries*). Sequencing of host cytochrome B gene confirmed these identifications but showed lower success rate of 58% (29/50), demonstrating the high effectivity of peptide mass mapping (PMM)-based MALDI-TOF mass spectrometry for routine identification of blood meals of varying degree of digestion. Our findings represent first record of cattle and dog blood in sand flies in Algeria and striking feeding preference of local sand fly population at domestic sites of studied regions for cattle which may play an important role in parasite transmission. Further studies are needed to better understand potential contribution of cattle to ecology of sand flies and epidemiology of leishmaniasis in north-eastern Algeria.

Synthesis, bio-physical and anti-leishmanial studies of some novel indolo[3,2-a]phenanthridine derivatives.

Banerjee, J., Bhattacharjee, A., Biswas, A., Chattopadhyay, S.
26-03-2022

Bioorg Chem

<https://pubmed.ncbi.nlm.nih.gov/35367783>

Eight indolo[3,2-a]phenanthridine derivatives have been synthesized in a regioselective manner involving intramolecular Heck-type arylation as a key step. The compounds display interesting photophysical properties and hence evaluated for their ability to interact with ct-DNA. Preliminary biophysical studies via UV and Fluorescence spectrophotometric titration with ct-DNA, and dye displacement studies with well known intercalator ethidium bromide and the groove binder Hoechst 33,258 reveal that the binding mode is probably minor groove binding. The prepared indolophenanthridine derivatives have also been evaluated as anti-leishmanial agents for the first time. MTT-assays for cell cytotoxicity against *Leishmania* promastigotes and *Leishmania* amastigotes were studied with the compounds 10b-f, 12-14 for the determination of their IC₅₀ values. Cytotoxicity was determined using a murine RAW 264.7 cell line and human embryonic kidney cell line HEK 293. In *L. donovani* amastigote assay, compounds 10e, 10f and 12

showed good activity with relatively low cytotoxicity against RAW 264.7, resulting in acceptable selectivity indices. Selectivity index determination indicated compounds to be potent anti-leishmanial agents while 10b, 10c and 14 showed moderate selectivity index. Moreover, cell-cycle analysis of four different compounds 10b, 12, 13 and 14, representative of each group, was performed by FACS as an attempt to understand the mechanism of actions of these different subclasses of the compounds on *Leishmania*.

Histological evaluation of skin lesions induced by *Leishmania braziliensis* treated by PACT using Laser light and 1.9 dimethyl-methylene blue.

Fagnani, S., de Oliveira, S., Monteiro, J., Sampaio, F., Crugeira, P., Dos Santos, J., Pinheiro, A.

17-03-2022

Photodiagnosis Photodyn Ther

<https://pubmed.ncbi.nlm.nih.gov/35306211>

This study aimed to perform a histological evaluation in skin lesions caused by *Leishmania braziliensis* after PACT treatment using Laser associated with 1.9. dimethyl methylene blue BALB/c mouse ear infection model was used. A total of 40 animals were assigned into two groups considering time intervals at 5 and 10 weeks and subdivided into four subgroups: Control, Photosensitizer, Laser and PACT. Two therapeutic interventions were performed after the 5th week of infection at 48 h intervals. 1.9 Dimethyl methylene blue was used as a photosensitizer at the concentration of 7 ng/mL, with a non-invasive topical administration method associated with Laser ($\lambda = 660$ nm, 40 mW, 12 J/cm²). Sample collection occurred 5 or 10 weeks after therapeutic interventions. The main histological findings were observed in the laser and PACT groups at the 10-week evaluation. The Laser group showed reduced lymphoplasmacytic inflammation and histiocytes ($p = 0.0079$). The PACT group showed reductions in lymphoplasmacytic inflammation at 5 and 10 weeks, discrete reduction of histiocytes and a higher percentage of tissue remodeling. PACT with non-invasive topical administration of the photosensitizer was able to reduce lymphoplasmacytic inflammation and increase tissue remodeling in leishmaniasis skin lesions. This protocol may be easily used in humans and clinical trial shall be carried out to confirm the animal's findings.

A recombinant *Leishmania* amastigote-specific protein, rLiHyG, with adjuvants, protects against infection with *Leishmania infantum*.

Machado, A., Lage, D., Vale, D., Freitas, C., Linhares, F., Cardoso, J., Pereira, I., Ramos, F., Tavares, G., Ludolf, F., Oliveira-da-Silva, J., Bandeira, R., Simões, A., Duarte, M., Oliveira, J., Christodoulides, M., Chávez-Fumagalli, M., Roatt, B., Martins, V., Coelho, E.

16-03-2022

Acta Trop

<https://pubmed.ncbi.nlm.nih.gov/35305943>

Vaccination against visceral leishmaniasis (VL) should be

considered as a control measure to protect against disease, and amastigote-specific proteins could help to develop such vaccines, since this parasite form is in contact with the host immune system during the active disease. In this study, a *Leishmania* amastigote-specific protein, LiHyG, was evaluated as recombinant protein (rLiHyG) as vaccine candidate against *Leishmania infantum* infection in BALB/c mice. The protein was associated with saponin (rLiHyG/Sap) or Poloxamer 407-based polymeric micelles (rLiHyG/Mic) as adjuvants, and animals receiving saline, saponin or micelle as controls. Immunological and parasitological analyses were performed before ($n = 8$ per group; as primary endpoint) and after ($n = 8$ per group; as secondary endpoint) infection. Results showed that, in both endpoints, rLiHyG/Sap and rLiHyG/Mic induced higher levels of IFN- γ , IL-12 and GM-CSF in spleen cell cultures from vaccinated animals, besides elevated presence of IgG2a isotype antibodies. Decreased hepatotoxicity and 'positive lymphoproliferative response were also found after challenge. Such findings reflected in significantly lower levels of parasite load found in their spleens, livers, bone marrows and draining lymph nodes. In conclusion, rLiHyG associated with Th1-type adjuvant could be considered for future studies as vaccine candidate to protect against VL.

Leishmania (Viannia) braziliensis replicates in mouse bone marrow.

Floro E Silva, M., Roque, G., Machado, D., Rocha, F., Giorgio, S.
16-03-2022

Acta Trop

<https://pubmed.ncbi.nlm.nih.gov/35304124>

Leishmaniasis is a neglected disease caused by species of the protozoan *Leishmania*. *Leishmania (Viannia) braziliensis* causes the cutaneous and mucocutaneous forms of the disease. Experimental cutaneous infection of mice is one of the most important preclinical research models of leishmaniasis. Here, we investigated the course of infection in mice inoculated with two reference strains of *L. (V.) braziliensis* (MHOM/BR/00/BA788 strain [BA] and MHOM/BR/94/H-3227 strain [CE]). Although both parasite strains induced detectable footpad lesions, BA-infected mice developed small non-ulcerated lesions that self-healed, whereas CE-infected mice developed small non-ulcerated lesions that did not regress. The parasites were detected in the footpad lesions, lymph nodes draining the site of inoculation, spleen, and bone marrow of mice infected with BA or CE parasites at 6 and 25 weeks post-inoculation. These data indicate that *L. (V.) braziliensis*-infected mice harbor parasites that spread, even when these animals do not display overt lesions. In addition, this is the first report of the presence of the parasite in the bone marrow of mice inoculated with *L. (V.) braziliensis*.

Population dynamics of phlebotomine sand flies (Diptera: Psychodidae) in cutaneous leishmaniasis endemic areas of Kurunegala District, Sri Lanka.

Wijerathna, T., Gunathilaka, N., Gunawardena, K., Rodrigo, W.

13-03-2022

Acta Trop

<https://pubmed.ncbi.nlm.nih.gov/35296392>

Sand flies are the primary vectors of leishmaniasis. Disease management with effective vector control depends on the knowledge of vector population dynamics. In Sri Lanka, despite few isolated entomological collections, long-term studies are not reported to date. In the reported study, monthly entomological surveillance was conducted from May 2017 to December 2018 in Polpithigama, Maho, and Galgamuwa Medical Officer of Health (MOH) areas using standard entomological techniques. Climatic data were collected from the Department of Meteorology, Sri Lanka. Patient records were collected from each MOH office. A total of 38,339 sand flies were collected. The majority were *Phlebotomus argentipes* (99.50%, $n = 38,147$), while the rest was *Sergentomyia punjabensis* (0.50%, $n = 192$). Wind speed reduces sand fly abundance ($r = -0.519$, $P < 0.05$) evidently by limiting the movement. Rainfall increases sand fly abundance ($r = 0.842$, $P < 0.05$, lag = 6 months) probably by improving favorable conditions in breeding sites. The actual effect of humidity is not conclusive without further research. The observed higher prevalence of leishmaniasis in the study sites could be due to the higher sand fly density in these areas. The number of patients shows a strong positive correlation ($r = 0.516$, $P < 0.05$) to the sand fly abundance with a lag of 7 months. Systematic surveillance of sand flies as a part of general healthcare services is strongly recommended to identify and prevent possible outbreaks through timely planned vector control measures.

Climate Change Influences on the Potential Distribution of the Sand Fly *Phlebotomus sergenti*, Vector of *Leishmania tropica* in Morocco.

Daoudi, M., Outammassine, A., Amane, M., Hafidi, M., Boussaa, S., Boumezzough, A.

16-03-2022

Acta Parasitol

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Leishmaniasis are a vector-borne disease, re-emerging in several regions of the world posing a burden on public health. As other vector-borne diseases, climate change is a crucial factor affecting the evolution of leishmaniasis. In Morocco, anthroponotic cutaneous leishmaniasis (ACL) is widespread geographically as many foci across the country, mainly in central Morocco. The objective of this study is to evaluate the potential impacts of climate change on the distribution of ACL due to *Leishmania tropica*, and its corresponding vector *Phlebotomus sergenti* in Morocco. Using Ecological Niche Modeling (ENM) tool, the estimated geographical range shift of *L. tropica* and *P. sergenti* by 2050 was projected under two Representative's Concentration's Pathways (RCPs) to be 2.6 and RCP 8.5 respectively. *P. sergenti* records were obtained from field collections of the laboratory team and previously published entomological observations, while, epidemiological data for *L. tropica* were obtained from Moroccan Ministry of

Health reports. Our models under present-day conditions indicated a probable expansion for *L. tropica* as well as for its vector in Morocco, *P. sergenti*. It showed a concentrated distribution in the west-central and northern area of Morocco. Future predictions anticipate expansion into areas not identified as suitable for *P. sergenti* under present conditions, particularly in northern and southeastern areas of Morocco. *L. tropica* is also expected to have high expansion in southern areas for the next 30 years in Morocco. This indicates that *L. tropica* and *P. sergenti* will continue to find suitable climate conditions in the future. A higher abundance of *P. sergenti* may indeed result in a higher transmission risk of ACL. This information is essential in developing a control plan for ACL in Morocco. However, future investigations on *L. tropica* reservoirs are needed to confirm our predictions.

A Convenient and Sensitive kDNA-PCR for Screening of Leishmania infantum Latent Infection Among Blood Donors in a Highly Endemic Focus, Northwestern Iran.

Asfaram, S., Fakhar, M., Mohebbali, M., Ziaei Hezarjaribi, H., Mardani, A., Ghezelbash, B., Akhoundi, B., Zarei, Z., Moazeni, M.

16-03-2022

Acta Parasitol

<https://doi.org/10.1007/s11686-022-00528-2>

Recent global evidences showed that asymptomatic blood donor carriers of *Leishmania* infection will appear as a threat for blood transfusions recipients in endemic areas. As yet, there is no appropriate diagnostic procedure for detecting infection of blood donors in blood banks. The present study was aimed to apply various current diagnostic tests among blood donors in an endemic area of visceral leishmaniasis (VL), Ardabil Province, northwestern Iran. Blood samples were gathered from 860 blood donors in endemic areas of the province between 2017 and 2018, at eight blood donation centers. These samples were assessed using microculture, serological (DAT and rK39-ICT) and molecular based (conventional kDNA-PCR and HRM-PCR) tests. Of 860 eligible donors, 24 (2.8%) were seropositive for VL by DAT, and 388 (45%) were positive by kDNA-PCR. Moreover, 19 (19/860) were positive for both of them. Out of 19 subjects, 5.3% (1/19) was positive by rK39-ICT, 10.5% (2/19), and 79% (15/19) were detected positive in microculture and HRM-PCR methods, respectively. Nineteen donors were followed up for 2 years, of which 16 (84.2%) had a serological conversion, and 4 (21%) were positive by kDNA-PCR. The sensitivity of kDNA-PCR, and HRM-PCR procedures in detecting *Leishmania* parasite was found to be 98.7%, and 79%, respectively. Our findings justify the use of kDNA-PCR as a convenient and sensitive tool for screening subjects with leishmanial latent infection in blood banks at least in endemic regions. In these areas, however, a PCR-based test should be used to validate *Leishmania* infection among seropositive donors.

The Prospective Effects of Climate Change on Neglected Tropical Diseases in the Eastern Mediterranean Region: a Review.

Revue de littérature

Al-Delaimy, A.

14-03-2022

Curr Environ Health Rep

<https://doi.org/10.1007/s40572-022-00339-7>

An increase in the annual daily temperature is documented and predicted to occur in the coming decades. Climate change has a direct effect and adverse impact on human health, as well as on multiple ecosystems and their species. The purpose of this paper is to review the effect of climate change on neglected tropical diseases including leishmaniasis, schistosomiasis, and lymphatic filariasis in the Eastern Mediterranean Region (EMR). A list of engine web searches was done; 280 full-text records were assessed for eligibility. Only 48 original records were included within the final selection for the review study. Most research results show an alteration of neglected diseases related to climate change influencing specifically the Eastern Mediterranean Region, in addition to the expectation of more effects at the level of vectors and reservoir whether its vector transmission route or its egg hatching and replication or even the survival of adult worms in the coming years. At the same time, not all articles related to the region interpret the direct or indirect effect of climate variations on these specific diseases. Although few studies were found describing some of climate change effects on neglected tropical diseases in the region, still, the region lacks research funding, technical, and mathematical model expertise regarding the direct effect of climate change on the ecosystems of these neglected tropical diseases.

Urea, salts, and Tween 20 influence on adsorption of IgG and Leishmania rNTPDase2 to nitrocellulose.

Castro, R., de Souza, A., Pavione, N., Badaró de Moraes, J., Ribeiro, I., Agripino, J., Bressan, G., Vasconcellos, R., Silva-Júnior, A., Fietto, J.

09-03-2022

Anal Biochem

<https://pubmed.ncbi.nlm.nih.gov/35276071>

Lateral flow immunochromatography is a widely used technique for immunological assays. Construction of test and control lines is mostly done by antigen adsorption to nitrocellulose membranes, a process not fully understood. This study aimed to evaluate the influence of urea, salts, and Tween 20, on adsorption. The performance of canine IgG in water and in buffer containing urea and salts (pH 8.3) were compared to observe if the interferents would lead to protein stripping when challenged with increasing concentrations of Tween 20 in the lateral flow buffer. Immobilization of the rLNTPDase2, an antigen for Canine Leishmaniasis diagnosis, was evaluated and compared to the rLbNTPDase2 by the same method. There were no differences between adsorption coefficients of IgG in water and in buffer, but high salt and urea concentrations seems to stabilize and enhance IgG

immobilization. Adsorption performance between canine IgG and rNTPDases had different patterns, but was highly similar between rNTPDases, indicating that protein identity may have an important role. Also, low concentrations of Tween 20 in the flow solution may aid the maintenance of rNTPDase2 on the strips. Our results bring insights about protein adsorption and perspectives about the influence of urea, salts and Tween 20 on this process.

Involvement of trypanothione reductase (TryR) and trypanothione peroxidase (TryP) in antimony unresponsive of *Leishmania tropica* clinical isolates of Iran.

Nateghi-Rostami, M., Tasbihi, M., Darzi, F.

08-03-2022

Acta Trop

<https://pubmed.ncbi.nlm.nih.gov/35276060>

Clinical resistance to pentavalent antimonial compounds has long been recognized as a major problem in the treatment of human leishmaniasis. Trypanothione metabolism, the main form of thiol, has shown to play a central role in antimony resistance of laboratory-generated resistant *Leishmania* spp. and field-isolated resistant *L. donovani*; but the mechanism of antimony resistance in the clinical isolates of *L. tropica* causing anthroponotic cutaneous leishmaniasis (ACL) is less studied. Patients were selected among confirmed positive ACL cases who referred to Pasteur Institute of Iran, Tehran, from endemic regions of north-east and south of Iran. *L. tropica* clinical isolates were collected from patients who were either treatment-responsive (MAS=S1 to S5) or unresponsive (MAR=R1 to R4) to Glucantime® (meglumine antimoniate=MA). Isolates were tested for sensitivity to trivalent antimony (SbIII) in promastigotes and to pentavalent antimony (SbV) in intracellular amastigotes stages. Intracellular thiol levels were assayed and trypanothione-dependent components, including trypanothione reductase (TR) and trypanothione peroxidase I (TryP) were analysed at protein level and enzymatic activity in isolates. The MAR isolates had an approximate two fold increase in the levels of intracellular thiols ($P < 0.05$) accompanied by an average 5-10 fold increase in *in vitro* resistance to antimony. TryP was amplified at the protein level in all MAR strains as compared to the MAS strains (range: 2.8-5.6 fold). All MAR isolates metabolized H_2O_2 at higher rates than MAS isolates (8.55 ± 0.75 nmol/min/mg vs. 3.14 ± 0.36 nmol/min/mg) ($P < 0.05$). In addition, levels of TryR protein were also markedly elevated in 3 out of 4 MAR isolates (range: 2.2-4.1 fold). This was accompanied by overexpressed TryR activity (mean level of 46.83 ± 2.43 for extracts of MAR vs. 20.98 ± 3.02 for MAS strains) ($P < 0.05$). Elevated levels of TryP, active enzyme in peroxide detoxification, were observed in MAR parasites resulting in an increased metabolism of H_2O_2 . TryR activity was overexpressed on average in extracts of MAR strains, but not in all isolates. Enhanced anti-oxidant defenses through thiol metabolism may play a significant role in clinical resistance of ACL patients to Glucantime.

Autochthonous transmission of *Leishmania donovani* and *Leishmania major* with all the components of infection cycle at Europe's doorstep.

Özbilgin, A., Tunalı, V., Akar, Ş., Yıldırım, A., Şen, S., Çavuş, İ., Zorbozan, O., Gündüz, C., Turgay, N., İnanır, İ.

01-03-2022

Acta Trop

<https://pubmed.ncbi.nlm.nih.gov/35245491>

Leishmaniasis is a vector-borne disease and dogs may act as urban reservoirs. Turkey and most of the Mediterranean basin countries are endemic for leishmaniasis. In this study, it is aimed to report the autochthonous leishmaniasis cases, with all the components of the infection cycle (reservoir, vector, and the host) in a region close to Europe. Nine human and four canine autochthonous leishmaniasis cases were included in the study. Direct microscopy, culture methods, serological, and molecular tests were applied to the samples obtained from the cases. VL and CL patients consisted of 2 *L. infantum*, 1 *L. donovani*, 2 *L. tropica*, and 2 *L. tropica*, 1 *L. major*, 1 *L. infantum* infected patients respectively. CanL cases were infected with *L. infantum*, *L. donovani*, *L. tropica*, and *L. major*. All the cases were autochthonous cases located in Manisa province. As Greece and all the Mediterranean basin countries in Europe share competent vectors, it is concluded that the detection of all 4 species of *Leishmania* parasites in such proximity to Europe poses an important public health threat for Europe. This study reports all four species of *Leishmania* spp., including *L. major* and *L. donovani* in close proximity to continental Europe.

***Leishmania* survives by exporting miR-146a from infected to resident cells to subjugate inflammation.**

Ganguly, S., Ghoshal, B., Banerji, I., Bhattacharjee, S., Chakraborty, S., Goswami, A., Mukherjee, K., Bhattacharyya, S.

24-02-2022

Life Sci Alliance

<https://pubmed.ncbi.nlm.nih.gov/35210329>

Leishmania donovani, the causative agent of visceral leishmaniasis, infects and resides within tissue macrophage cells. It is not clear how the parasite infected cells crosstalk with the noninfected cells to regulate the infection process. During infection, *Leishmania* adopts a dual strategy for its survival by regulating the intercellular transport of host miRNAs to restrict inflammation. The parasite, by preventing mitochondrial function of host cells, restricts the entry of liver cell derived miR-122-containing extracellular vesicles in infected macrophages to curtail the inflammatory response associated with miR-122 entry. On contrary, the parasite up-regulates the export of miR-146a from the infected macrophages. The miR-146a, associated with the extracellular vesicles released by infected cells, restricts miR-122 production in hepatocytes while polarizing neighbouring naïve macrophages to the M2 state by affecting the cytokine expression. On entering the recipient macrophages, miR-146a dominates the miRNA antagonist RNA-binding protein HuR to inhibit the expression of proinflammatory cytokine mRNAs

having HuR-interacting AU-rich elements whereas up-regulates anti-inflammatory IL-10 by exporting the miR-21 to polarize the recipient cells to M2 stage.

Exploration of potential inhibitors for autophagy-related protein 8 as antileishmanial agents.

Rahman, F., Ali, R., Tabrez, S., Mobeen, A., Akand, S., Arish, M., AlAsmari, A., Ali, N., Rub, A.

22-02-2022

Chem Biol Drug Des

<https://doi.org/10.1111/cbdd.14029>

Leishmaniasis is considered a tropical neglected disease, which is caused by an intramacrophagic parasite, *Leishmania*. It is endemic in 89 different countries. Autophagy-related protein 8 (Ldatg8) is responsible for the transformation of parasites from promastigote to amastigote differentiation. Ldatg8 is one of the key drug targets of *Leishmania donovani* (*L. donovani*) responsible for the defense of parasites during stress conditions. Virtual screening of natural ligand library had been performed against Ldatg8 to identify novel and potent inhibitors. Molecular docking and molecular dynamics simulation studies showed that urolithin A stably blocked Ldatg8. Urolithins are combinations of coumarin and isocoumarin. Further, we evaluated the antileishmanial effects of urolithin A by antileishmanial assays. Urolithin A inhibited the growth and proliferation of *L. donovani* promastigotes with an IC_{50} value of $90.3 \pm 6.014 \mu\text{M}$. It also inhibited the intramacrophagic parasite significantly with an IC_{50} value of $78.67 \pm 4.62 \mu\text{M}$. It showed limited cytotoxicity to the human THP-1 differentiated macrophages with a CC_{50} value of $190.80 \pm 16.89 \mu\text{M}$. Further, we assayed reactive oxygen species (ROS) generation and annexin V/PI staining upon urolithin A treatment of parasites to have an insight into the mechanism of its action. It induced ROS significantly in a dose-dependent manner, which caused apoptosis partially in parasites. The potential inhibitors for Ldatg8, identified in this study, would provide the platform for the development of an effective and affordable antileishmanial drug.

Atomic structure of the *Leishmania* spp. Hsp100 N-domain.

Mercado, J., Lee, S., Chang, C., Sung, N., Soong, L., Catic, A., Tsai, F.

18-02-2022

Proteins

<https://doi.org/10.1002/prot.26310>

Hsp100 is an ATP-dependent unfoldase that promotes protein disaggregation or facilitates the unfolding of aggregation-prone polypeptides marked for degradation. Recently, new Hsp100 functions are emerging. In *Plasmodium*, an Hsp100 drives malaria protein export, presenting a novel drug target. Whether Hsp100 has a similar function in other protists is unknown. We present the 1.06 Å resolution crystal structure of the Hsp100 N-domain from *Leishmania* spp., the causative agent of leishmaniasis in humans. Our structure reveals a

network of methionines and aromatic amino acids that define the putative substrate-binding site and likely evolved to protect Hsp100 from oxidative damage in host immune cells.

Neglected Tropical Diseases in Lebanon.

Alam, W., Mobayed, T., Younis, N., Zarif, R., Bizri, N., Tamim, H., Musharrafieh, U., Bizri, A.

03-02-2022

Acta Parasitol

<https://doi.org/10.1007/s11686-021-00510-4>

Neglected tropical diseases (NTDs) are highly endemic and distributed within the Middle East and North Africa (MENA) region, affecting an estimated 65 million people. Lebanon suffers from several NTDs as they are either endemic in the country or imported via expats residing in endemic regions, refugees, and foreign labor force. The Syrian crisis and the displacement of refugees to Lebanon have made the country the largest host of refugees per capita right after the Syrian crisis in 2011, peaking in the year of 2013. Additionally, foreign labor in Lebanon come from different countries in Africa and Asia that are endemic with certain NTDs. The Lebanese diaspora is approximately twice the number of those residing in the country and is distributed throughout the continents carrying the risk of importing new NTDs. A descriptive study about the prevalence of NTDs in Lebanon, their distribution, and factors contributing to spread was performed. The Lebanese Ministry of Public Health (LMPH) database regarding reportable transmissible diseases was reviewed for reportable NTDs between 2002 and 2020 in relation to age, gender, prevalence, and geographical distribution. The medical literature was searched using several engines looking for all reports about NTDs in Lebanon, those relevant to regions hosting Lebanese diaspora, and countries where the refugees and migrant workers came from. Only leishmaniasis, leprosy, echinococcosis, schistosomiasis, and rabies are mandatorily reportable NTDs by the LMPH. Additionally, case reports about fasciolosis, ascariidiosis, and Dengue were reported from Lebanon. The presence of the Syrian refugees in the country affected the prevalence of leishmaniasis and rabies. The most prevalent NTD in Lebanon is cutaneous leishmaniasis. The Lebanese diaspora reside mainly in South America, Africa, and in some Arab states known to be endemic with certain NTDs. Little information is known about NTDs in Lebanon. The country is at an increased risk of experiencing several new NTDs due to refugee influx, foreign labor, economic crisis, and ever-growing number of Lebanese seeking work opportunities abroad. More information is needed to assess the true burden of NTDs in Lebanon and the future steps to contain and mitigate their effects.

Host-Parasite Interactions: Regulation of *Leishmania* Infection in Sand Fly.

Revue de littérature

Omondi, Z., Arserim, S., Töz, S., Özbek, Y.

02-02-2022

Acta Parasitol

<https://doi.org/10.1007/s11686-022-00519-3>

Sand flies are the only proven vectors of leishmaniasis, a tropical neglected disease endemic in at least 92 countries. Vector-parasite interactions play a significant role in vector-borne disease transmission. There are various bottlenecks to *Leishmania* colonization of the sand fly midgut. Such bottlenecks include the production of innate immune-related molecules, digestive proteases, parasite impermeable peritrophic membrane, and resident gut microbiota. These barriers determine the parasite load transmitted and, consequently, the disease outcome in mammalian host. Therefore, it is important to understand the molecular responses of both sand fly and *Leishmania* during infection. Here, we reviewed the published literature on sand fly-*Leishmania* interactions bringing together earlier and current findings to highlight new developments and research gaps in the field. Recent research studies on sand fly-*Leishmania* interaction have revealed contrasting observations to past studies. However, how *Leishmania* parasites evade the sand fly immune response still needs further research. Sand fly response to *Leishmania* infection can be best understood by analyzing its tissue transcriptome. Better characterization of the role of midgut components could be a game changer in development of transmission-blocking strategies for leishmaniasis.

Military Dogs and Their Soldier Companions: The More-than-human Biopolitics of Leishmaniasis in Conflict-torn Colombia.

Pinto-García, L.

02-02-2022

Med Anthropol Q

<https://doi.org/10.1111/maq.12694>

Cutaneous leishmaniasis is a vector-borne disease that produces growing skin ulcers. In Colombia, the transmitting phlebotomine sandfly is native to the same jungles that have been the primary theater of war. Although combatants are the most affected by leishmaniasis, military landmine detection dogs are also significantly impacted. This article draws on ethnographic field research with human and canine members of the Colombian military. While their leishmaniasis ulcers constitute a shared expression of violence that makes evident the closeness of the human-dog bond, differences in their state-provided health care reveal the production of shifting species hierarchies. I argue that war scrambles both human-dog affective relationships and biopolitically configured interspecies hierarchies in ways that produce suffering, not just for humans and dogs separately, but also for the bonds they forge together. Building peace through health care demands repairing the ways in which armed violence has rendered the bonds between humans and nonhumans pathological.

Multiplex qPCR assay to determine *Leishmania infantum* load in *Lutzomyia longipalpis* sandfly samples.

Mota, T., Brodskyn, C., Morello, L., Marchini, F., Krieger, M., de Cássia Pontello Rampazzo, R., Fraga, D.

28-01-2022

Med Vet Entomol

<https://doi.org/10.1111/mve.12564>

The study aimed to develop a multiplex qPCR to detect *Leishmania infantum* load in different sandfly sample settings using *Leishmania* kDNA and sandfly vacuolar ATPase (VATP) subunit C as internal control gene. The amplification of *Lutzomyia longipalpis* VATP gene was evaluated together with *Leishmania infantum* kDNA in a multiplex reaction. The concentration of VATP gene oligonucleotides was adjusted until no statistically significant difference was observed between all multiplex standard curves and singleplex curves, that is, only kDNA amplification. Limit of detection (LoD) was measured using a probit model and a cut-off defined by receiver operating characteristic analysis. Limit of quantification (LoQ) was assessed by a linear model using the coefficient of variation threshold of 25%. After assuring VATP gene amplification, its primer-probe concentrations were best at 100nM/10 nM, respectively. The cut-off C_q value for *L. infantum* kDNA was defined as 35.46 with 100% of sensitivity and specificity. A total of 95% LoD was determined to be of 0.162 parasites while LoQ was 5.858. Our VATP/kDNA multiplex qPCR assay shows that it can be used to evaluate both DNA integrity and determine *L. infantum* load in *L. longipalpis* even for low yielded samples, that is, individual midguts.

Designing, Optimization and Characterization of Trifluralin Transfersomal Gel to Passively Target Cutaneous Leishmaniasis.

Khan, A., Jamshaid, H., Ud Din, F., Zeb, A., Khan, G.

23-01-2022

J Pharm Sci

<https://pubmed.ncbi.nlm.nih.gov/35081406>

Herein, Trifluralin (TFL) laden transfersomes (TFS) were investigated against Cutaneous Leishmaniasis (CL), via localized and targeted dermal delivery of TFL. Designed TFL-TFS were optimized utilizing 2^3 full factorial design on the basis of desired response factors including Particle size (P.S), Polydispersity index (PDI), TFL entrapment (%EE) and deformability index (DI). Optimized formulation was found to display P.S of 140.3 ± 2.3 , PDI of 0.006 ± 0.002 , %EE of 86 ± 0.5 and 43.5 ± 1.0 DI. Results of TEM and XRD analysis have shown intact spherical structure of TFL-TFS and alteration in TFL crystallinity, respectively. Moreover, the optimized TFL-TFS were loaded in Carbopol-940 gel to attain protracted skin retention. TFL-TFS were found to exhibit sustain TFL release profile for up to 24 h. Ameliorated skin permeation of TFL-TFS, even in absence of permeation enhancers, has shown its suitability for cutaneous application. Macrophage uptake assay demonstrated higher intracellular

penetration, evidenced by intense reddish fluorescence of rhodamine loaded TFS in comparison to rhodamine-solution. In vitro anti-leishmanial assessment was showing 2.86-folds and 3.07-folds decrement in IC₅₀-value of TFL-TFS against *L. tropica* KWH23 amastigotes and promastigotes, respectively. Percent inhibition assay against intra-macrophage amastigotes demonstrated that 90.87% amastigotes were assassinated at 50 µg/ml concentration of TFL-TFS, in comparison to the plain TFL-solution, exhibiting 54% parasitic killing.

An In-depth Proteomic Map of *Leishmania donovani* Isolate from Post Kala-azar Dermal Leishmaniasis (PKDL) Patient.

Routaray, C., Kumar, A., Sundar, S., Sathe, G., Pawar, H., Pai, K.
12-01-2022

Acta Parasitol

<https://doi.org/10.1007/s11686-021-00511-3>

The trypanosomatid protozoan parasite *Leishmania donovani* is the etiological agent of visceral leishmaniasis (VL) or kala-azar. The patients that have undergone treatment may still harbor the parasite and in a small fraction of the patients the disease re-erupts in the form of post kala-azar dermal leishmaniasis (PKDL). PKDL is a pathological condition found to be intermediate between VL and complete cure of VL. The PKDL disease progression is determined by the host immune response to *L. donovani*. The majority of the proteomic studies on *L. donovani* till date have been undertaken on parasites either isolated from kala-azar patients or on established laboratory strains of *L. donovani*. However, no proteomic information is available on the cutaneous localized isolates of *L. donovani* from PKDL patients. The promastigote stage of *L. donovani* isolate from PKDL patient was cultured and harvested. The cell lysates were trypsin digested, followed by liquid chromatography-tandem mass spectrometry (LC-MS/MS) analysis. The LC-MS/MS raw data were analyzed on Proteome Discoverer. Further bioinformatics analysis was carried out. In the present, we have used high-resolution mass spectrometry to map the global proteome of a *L. donovani* isolate from PKDL patient. This in-depth study resulted in the identification of 5537 unique proteins from PKDL isolate of *L. donovani* which covered 64% of its proteome. This study also identified proteins previously shown to be upregulated in PKDL *L. donovani*. This is the most in-depth proteome of *Leishmania donovani* parasite till date.

Infections and Coinfections by Trypanosomatid Parasites in a Rural Community of Venezuela.

Herrera, L., Morocoima, A., Lozano-Arias, D., García-Alzate, R., Vietri, M., Lares, M., Ferrer, E.

11-01-2022

Acta Parasitol

<https://doi.org/10.1007/s11686-021-00505-1>

Trypanosoma cruzi, *Trypanosoma rangeli* and *Leishmania* spp. are parasites that coexist in several endemic areas. The identification of these parasites in hosts is important for the

control programs. 216 samples from human blood (101), blood of other mammals (45) and triatomine intestinal content and hemolymph (70), from an endemic area of Venezuela, were analysed. The samples were evaluated by; serology (only humans) and PCR for *T. cruzi* in human, other mammals and triatomines, PCR for *T. rangeli* in mammals-including human and triatomines and PCR for *Leishmania* in mammals-including human. The 9.9% of the human samples were positive for *T. cruzi* by serology, 11.9% by PCR, 4% for *T. rangeli* PCR and none for *Leishmania* spp. PCR. 60% of the samples of other mammals showed DNA amplification for *T. cruzi*, 42.2% for *T. rangeli* and 4.4% for *Leishmania* spp. 61.4% of the triatomine samples showed DNA amplification for *T. cruzi* and 10% for *T. rangeli*. High *T. cruzi* infection was detected in mammals and triatomines compared with *T. rangeli*. Low leishmanial infection was detected in other mammals. It is the first time that *T. cruzi*/*T. rangeli* coinfection, in humans, *Canis familiaris* (dog), and *Bos Taurus* (cow), were reported world-wide, and that this coinfection was described in *Tamandua tetradactyla* (anteater) from Venezuela. The coinfection *T. cruzi*/*T. rangeli* in mammals-including humans and triatomines, and coinfection *T. cruzi*/*Leishmania* spp. in non-human mammals, show the risk for trypanosomic zoonoses in this endemic area.

Investigation of *Leishmania (Viannia) braziliensis* Infection in Wild Mammals in Brazil.

Venial, H., Montoya, A., Checa, R., Miró, G., Uzai, G., da Silva, M., de Carvalho Nunes, L., Silveira, R., de Carvalho, E.
06-01-2022

Acta Parasitol

<https://doi.org/10.1007/s11686-021-00498-x>

Leishmaniasis are infectious and zoonotic diseases and present in cutaneous and visceral forms. Cutaneous leishmaniasis is endemic and widely distributed throughout the state of Espírito Santo, Brazil. Several cases of cutaneous leishmaniasis in humans and dogs associated with *Leishmania (Viannia) braziliensis* have been reported in the state. This study aimed to investigate the occurrence of natural infection by *Leishmania (Viannia) braziliensis* in wild mammals found dead (by trampling or natural death) in the Sooretama Biological Reserve, Espírito Santo State. From January 2018 to December 2019, 60 animals were collected. Of these, 47 animals from 12 different species were analyzed. The results were demonstrated using descriptive analysis of the observations to calculate the absolute and relative frequencies of the data. In the PCR, using specific primers for the genus *Leishmania* (D1, D2, and D3) and the species *Leishmania (Viannia) braziliensis* (ISVB/ISVC), 4 positive animals (8.5%) were detected: 1 *Cuniculus paca* (*paca*) (25%) and 3 *Callithrix geoffroyi* (white-faced marmoset) (25%). In the histopathological analysis, the parasitic amastigote form was not observed. The natural infection, detected by PCR, by *Leishmania (Viannia) braziliensis* in *Cuniculus paca* (*paca*) and *Callithrix geoffroyi* (white-faced marmoset) constitutes the first report of infection of this rodent and primate species in the literature. Despite the confirmation of *Leishmania*

(*Viannia*) *braziliensis* infection in rodents and primates, the role of these species in the transmission of this zoonosis still needs further observational studies to identify their seasonal variation, transmissibility, infection stability, and the effects of a given parasite on the population and/or individual.

Epidemiological and clinical features of cutaneous leishmaniasis and its time trend model in a high-endemic focus of disease in the southwest of Iran from 2014 to 2019.

Khosrotaj, M., Rakhshani, T., Nazari, M., Gheibi, Z., Soltani, A.

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Trans R Soc Trop Med Hyg

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Cutaneous leishmaniasis (CL) is a tropical infection with a relatively high incidence rate in Iran. The present study aimed to explore the time trend and associated factors of CL in Dezful, in southwest Iran. This case series study was conducted on all CL patients registered from 2014 to 2019. The descriptive analysis of the data was done using SPSS 20 software and the time series model on the number of cases was run through Interactive Time Series Modeling software. A total of 5349 leishmaniasis cases were identified in the study area during 2014-2019. The highest incidence rate was 35 840 per 100 000 in 2014. The fitted time series model revealed a decreasing trend with an annual periodic pattern. The mean age of infection was 19.82 y (standard deviation 21.87). The infection was most frequent in the 1-10 y age group (41.7%). Also, females were more prone to leishmaniasis (54.7%). Most lesions were located on the hand (23.1%), face (19.7%), and forearm (17.75%) and 48.5% of patients had only one lesion. The results revealed a decreasing trend of leishmaniasis in Dezful. It has been predicted that this infection will reach a minimum rate (300 per 100 000) in the winter of 2021.

Ultrasound patterns of localized cutaneous leishmaniasis and clinical correlations.

Sechi, A., Neri, I., Patrizi, A., Di Altobrando, A., Clinca, R., Caro, R., Leuzzi, M., Misciali, C., Gaspari, V.

01-02-2021

J Ultrasound

<https://doi.org/10.1007/s40477-020-00537-9>

A single-center retrospective study reviewed the following sonographic features of 18 confirmed cases of localized cutaneous leishmaniasis to identify shared presentation patterns: echotexture, lesion borders, hypodermal involvement, soft-tissue changes, and vascular pattern. A second objective was to correlate these patterns with clinical characteristics, including sex, age, anatomical location, nodule vs. plaque presentation, raised borders, granulation tissue, swelling, hyperkeratotic crusting, disease onset, and healing time. Two main patterns were identified with high-frequency ultrasonography. The first pattern was characterized by a high level of inflammation and deep hypodermal involvement, while the second variant showed involvement limited to the

dermis, with minimal inflammation. The "inflammatory pattern" showed ill-defined borders, mixed echotexture, prominent vascularity with central distribution, and was correlated with clinical signs of ulceration, granulation tissue, raised borders, and longer healing time ($p < 0.05$). The "pauci-inflammatory pattern" presented a well-defined structure with decreased echogenicity, reduced or absent vascularity with minimal soft-tissue changes, and was associated with a shorter healing time ($p < 0.05$).

CYSTICERCOSIS

Neurocysticercosis: an update on diagnosis, treatment, and prevention.

Pineda-Reyes, R., White, A.

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Curr Opin Infect Dis

<https://doi.org/10.1097/QCO.0000000000000831>

Neurocysticercosis (NCC) is an important cause of neurological disease worldwide, including imported cases in nonendemic countries. The purpose of this review is to update information on diagnosis, management, and prevention of neurocysticercosis. WHO and Infectious Diseases Society of America/American Society of Tropical Medicine and Hygiene guidelines emphasize the importance of corticosteroids and antiparasitic drugs for viable parenchymal disease and single enhancing lesions. Subarachnoid NCC is associated with a high fatality rate unless optimally treated. Advances in subarachnoid NCC include use of prolonged antiparasitic and anti-inflammatory courses and the increasing use of antigen-detection and quantitative PCR assays in diagnosis and follow-up. Emerging data support the safety and efficacy of minimally invasive surgery in ventricular cases. Calcified neurocysticercosis continues to be associated with a high burden of disease. Field studies are demonstrating the feasibility of eradication using a combination of mass chemotherapy for human tapeworms and vaccination/treatment of porcine cysticercosis. NCC remains an important and challenging cause of neurological disease with significant morbidity despite advances in treatment and prevention.

Taenia solium taeniasis/cysticercosis in Guatemala: a prevalent public health problem?

Hernández-Chea, R., Morales-Ramírez, P., Hernández, M., Toledo, A., Hun, A., Sciotto, E., Fleury, A.

03-06-2022

Pathog Glob Health

<https://doi.org/10.1080/20477724.2022.2083757>

In Guatemala, neurocysticercosis (NCC) was first recognized in 1940; since then, cases of NCC have been reported in all Guatemalan departments. However, epidemiological studies

on *Taenia solium* infections are scarce and most information remains unpublished. This study aims to provide evidence of *T. solium* infections as a public health problem in Guatemala. All information available, either published or unpublished, on *T. solium* infections in the country was compiled. Official data from the Ministry of Health for the period 2002-2019 were reviewed and analyzed, and all cases of *T. solium* infections were classified and counted. In total, 5246 cases of taeniasis and 454 cases of human cysticercosis were recorded. On the other hand, 44 studies were identified, mostly from local journals, which included 1591 cases of taeniasis, 543 cases of human cysticercosis, and 2590 cases of porcine cysticercosis. Cases were classified by geographic region, patient sex, and *Taenia* species in taeniasis cases when information was available, and the departments with the highest number of taeniasis and cysticercosis cases were identified. Meanwhile, in Zacapa, a northeastern department of Guatemala with one of the highest number of taeniasis cases, a young man diagnosed with a severe form of NCC and two cases of porcine cysticercosis (both confirmed by necropsy) were identified. Taken together, the data herein reported indicate that *T. solium* infections are a major health problem in Guatemala that needs to be addressed.

Porcine model of neurocysticercosis by intracarotid injection of *Taenia solium* oncospheres: Dose assessment, infection outcomes and serological responses.

Arroyo, G., Toribio, L., Vargas-Calla, A., Calcina, J., Bernal, E., Chile, N., Zambrano, M., Gomez-Puerta, L., Chacaltana, J., Marzal, M., Bustos, J., Verastegui, M., Gilman, R., O'Neal, S., Gonzalez, A., Garcia, H., Cysticercosis Working Group in Peru

02-06-2022

PLoS Negl Trop Dis

<https://doi.org/10.1371/journal.pntd.0010449>

Neurocysticercosis (NCC) is the infection of the human central nervous system (CNS) by *Taenia solium* larvae that cause significant neurological morbidity. Studies on NCC pathophysiology, host-parasite interactions or therapeutic agents are limited by the lack of suitable animal models. We have previously reported that carotid injection of activated *T. solium* oncospheres directs parasites into the CNS and consistently reproduces NCC. This study assessed the minimal dose required to consistently obtain NCC by intracarotid oncosphere injection and compared antigen and antibody response profiles by dose-group. Three groups of pigs were infected with either 2500 ($n = 10$), 5000 ($n = 11$), or 10000 ($n = 10$) oncospheres. Two pigs died during the study. Necropsy exam at day 150 post-infection (PI) demonstrated viable NCC in 21/29 pigs (72.4%), with higher NCC rates with increasing oncosphere doses (4/9 [44.4%], 9/11 [81.8%] and 8/9 [88.9%] for 2500, 5000, and 10000 oncospheres respectively, P for trend = 0.035). CNS cyst burden was also higher in pigs with increasing doses (P for trend = 0.008). Viable and degenerated muscle cysticerci were also found in all pigs, with degenerated cysticerci more frequent in the 2500 oncosphere dose-group. All pigs were positive for circulating parasite antigens on ELISA

(Ag-ELISA) from day 14 PI; circulating antigens markedly increased at day 30 PI and remained high with plateau levels in pigs infected with either 5000 or 10000 oncospheres, but not in pigs infected with 2500 oncospheres. Specific antibodies appeared at day 30 PI and were not different between dose-groups. Intracarotid injection of 5000 or more oncospheres produces high NCC rates in pigs with CNS cyst burdens like those usually found in human NCC, making this model appropriate for studies on the pathogenesis of NCC and the effects of antiparasitic treatment.

On Hazardous Pills for Weight Loss and Cysticercosis.

Galán-Puchades, M., Fuentes, M.

31-05-2022

Am J Trop Med Hyg

<https://doi.org/10.4269/ajtmh.22-0196>

Annexin in *Taenia crassiceps* ORF Strain is Localized in the Osmoregulatory System.

Rios-Valencia, D., Mompala-García, Y., Marquez-Navarro, A., Tirado-Mendoza, R., Ambrosio, J.

03-02-2022

Acta Parasitol

<https://doi.org/10.1007/s11686-022-00526-4>

Annexins are proteins with important roles in parasites, some of which are related to excretion-secretion processes, protein traffic, and microvesicle functionality. The participation of annexins in osmoregulation has been reported in tapeworms, including *Taenia solium*. This study aimed to investigate the localization and expression of annexin in cysticerci of *Taenia crassiceps*, used as a model of cysticercosis. We used an antibody made with a protein, previously employed on *Schistosoma bovis*, to detect annexin in *T. crassiceps* proteins extracts used Western blot assay. The histological distribution of annexin was studied with immunofluorescence and confocal microscopy. The antibody against annexin recognized a band at a molecular weight of 40.9 kDa. The histological distribution of annexin showed that the protein is mainly localized in the tegument and the protonephridia ducts. In our study, annexin was detected at a molecular weight similar to that described for *Schistosoma bovis*. In addition, its principal localization entailed structures of the osmoregulatory system one of the most important by the survival of the parasites. This confirms and solidifies previous reports concerning the role of annexins in *T. crassiceps* and this will be interesting by the development of new compounds against this protein.

DRACUNCULOSE

ECHINOCOCCOSE

Immunodiagnosis of cystic echinococcosis in livestock: Development and validation dataset of an ELISA test using a recombinant B8/2 subunit of *Echinococcus granulosus sensu lato*.

Poggio, T., Gómez, J., Boado, L., Vojnov, A., Larrieu, E., Mujica, G., Jensen, O., Gertiser, M., Prada, J., Basáñez, M.

11-05-2022

Data Brief

<https://doi.org/10.1016/j.dib.2022.108255>

The accuracy of screening tests for detecting cystic echinococcosis (CE) in livestock depends on characteristics of the host-parasite interaction and the extent of serological cross-reactivity with other taeniid species. The AgB8 kDa protein is considered to be the most specific native or recombinant antigen for immunodiagnosis of ovine CE. A particular DNA fragment coding for rAgB8/2 was identified, that provides evidence of specific reaction in the serodiagnosis of metacestode infection. We developed and validated an IgG Enzyme Linked Immunosorbent Assay (ELISA) test using a recombinant antigen B sub-unit EgAgB8/2 (rAgB8/2) of *Echinococcus granulosus sensu lato* (*s.l.*) to estimate CE prevalence in sheep. A 273 bp DNA fragment coding for rAgB8/2 was expressed as a fusion protein (~30 kDa) and purified by affinity chromatography. Evaluation of the analytical and diagnostic performance of the ELISA followed the World Organisation for Animal Health (OIE) manual, including implementation of serum panels from: uninfected lambs ($n = 79$); experimentally infected (with 2,000 *E. granulosus s.l.* eggs each) sheep with subsequent evidence of *E. granulosus* cysts by necropsy ($n = 36$), and animals carrying other metacestode/trematode infections ($n = 20$). The latter were used to assess the cross-reactivity of rAgB8/2, with these animals being naturally infected with *Taenia hydatigena*, *Thysanosoma actinioides* and/or *Fasciola hepatica*. EgAgB8/2 showed cross-reaction with only one serum sample from a sheep infected with *Ta. hydatigena* out of the 20 animals tested. Furthermore, the kinetics of the humoral response over time in five 6-month old sheep, each experimentally infected with 2,000 *E. granulosus s.l.* eggs, was evaluated up to 49 weeks (approximately one year) post infection ($n = 5$). The earliest detectable IgG response against rAgB8/2 was observed in sera from two and four sheep, 7 and 14 days after experimental infection, respectively. The highest immune response across all five animals was found 16 to 24 weeks post infection.

Understanding pathogen-host interplay by expression profiles of lncRNA and mRNA in the liver of *Echinococcus multilocularis*-infected mice.

Nian, X., Li, L., Ma, X., Li, X., Li, W., Zhang, N., Ohiolei, J., Li, L., Dai, G., Liu, Y., Yan, H., Fu, B., Xiao, S., Jia, W.

31-05-2022

PLoS Negl Trop Dis

<https://doi.org/10.1371/journal.pntd.0010435>

Almost all *Echinococcus multilocularis* (Em) infections occur in the liver of the intermediate host, causing a lethal zoonotic helminthic disease, alveolar echinococcosis (AE). However, the long non-coding RNAs (lncRNAs) expression profiles of the host and the potential regulatory function of lncRNA during Em infection are poorly understood. In this study, the profiles of lncRNAs and mRNAs in the liver of mice at different time points after Em infection were explored by microarray. Thirty-one differentially expressed mRNAs (DEMs) and 68 differentially expressed lncRNAs (DELs) were found continuously dysregulated. These DEMs were notably enriched in "antigen processing and presentation", "Th1 and Th2 cell differentiation" and "Th17 cell differentiation" pathways. The potential predicted function of DELs revealed that most DELs might influence Th17 cell differentiation and TGF- β /Smad pathway of host by trans-regulating SMAD3, STAT1, and early growth response (EGR) genes. At 30 days post-infection (dpi), up-regulated DEMs were enriched in Toll-like and RIG-I-like receptor signaling pathways, which were validated by qRT-PCR, Western blotting and downstream cytokines detection. Furthermore, flow cytometric analysis and serum levels of the corresponding cytokines confirmed the changes in cell-mediated immunity in host during Em infection that showed Th1 and Th17-type CD4⁺ T-cells were predominant at the early infection stage whereas Th2-type CD4⁺ T-cells were significantly higher at the middle/late stage. Collectively, our study revealed the potential regulatory functions of lncRNAs in modulating host Th cell subsets and provide novel clues in understanding the influence of Em infection on host innate and adaptive immune response.

Cystic echinococcosis of ruminant livestock in Namibia.

Aschenborn, J., Schneider, C., Addy, F., Aschenborn, O., Kern, P., Romig, T., Deplazes, P., Wassermann, M.

01-04-2022

Vet Parasitol Reg Stud Reports

<https://pubmed.ncbi.nlm.nih.gov/35569909>

Cystic echinococcosis (CE) is widespread and locally frequent in southern Africa where it affects humans, livestock, and wild mammals. However, most data from the region are old and do not provide information on the causative *Echinococcus* species. For Namibian livestock only anecdotal records were available prior to this preliminary survey. Our retrospective analysis of slaughterhouse records of CE in cattle from the commercial farming area in central and southern Namibia resulted in 1.65% CE prevalence among 35,143 slaughtered cattle in the period 2015-2016. For comparison, carcasses of ruminant livestock were prospectively examined in the communal farming areas of northern Namibia, resulting in three CE cases among only 12 cattle, and no cases among nine goats. To determine the *Echinococcus* species affecting Namibian livestock, a total of 53 cysts were collected from all parts of the country and analysed for species and genotype by amplification and sequencing of the nad1 gene. All 50 cattle cysts (isolated from 40 cattle), both from the commercial and communal farming areas, were *Echinococcus ortleppi* (all

fertile, and 42/50 from the lungs), while three opportunistically collected cysts from three sheep in southern Namibia were *E. canadensis* G7. Our data suggest that *E. ortleppi* is the only CE agent that is relevant for cattle infection in Namibia, and that low prevalence in the commercial farming areas contrasts with high CE burden in the northern traditional husbandry systems. The present data provide baseline information to stimulate epidemiological studies on the transmission pathways of various CE agents in livestock, wildlife, and humans in Namibia and neighbouring countries.

Spinal hydatid cyst as cause of neurological injury in a patient from Brazilian amazon region.

Santos, R., Danda, G., Junior, A., Gepp, R.

21-04-2022

Radiol Case Rep

<https://doi.org/10.1016/j.radcr.2022.03.102>

Echinococcus granulosus infection is the primary cause of spinal hydatidosis. We describe the case of a 22-year-old man from the Brazilian Amazon region with crural spastic paraparesis and back pain. Radiological examinations showed multilocular lesions involving compression of the thoracic spine and rib injury. The patient underwent vertebrectomy with spinal stabilization and thoracoplasty with resectioning of the costal arch. Subsequently, the patient was prescribed oral treatment with albendazole. Marked recovery of the neurological status was achieved. Bone hydatid disease is rare, accounting for 0.5%-0.4% of all hydatid cysts, affecting the spine in 50% of cases. The treatment of choice is surgery accompanied by antiparasitic medication.

Dispersal of taeniid eggs: Experimental faecal contamination of forest environment followed by DNA detection in wild berries.

Malkamäki, S., Oksanen, A., Näreaho, A., Sukura, A.

11-04-2022

Food Waterborne Parasitol

<https://doi.org/10.1016/j.fawpar.2022.e00152>

To understand Taeniidae epidemiology, the principles of egg-dispersion dynamics under natural conditions must be known. In this study, non-zoonotic *Taenia laticollis* was used as a model parasite for the family Taeniidae (including *Echinococcus* spp.). An experiment to investigate dispersion from contaminated faeces to the surroundings was performed both with bilberries (*Vaccinium myrtillus*) and lingonberries (*Vaccinium vitis-idaea*), both of which are commercially harvested wild berries in Finland. For this experiment, 30 g of fox faeces was inoculated with 30,000 *T. laticollis* eggs for the bilberry experiment and 100,000 eggs for the lingonberry experiment. The faecal material was placed in the middle of good berry growth areas in four locations for bilberries and eight locations for lingonberries. After 41-42 days, berries at different distances (0-15 m) from the original contamination spot were collected and delivered to our laboratory. DNA was extracted from washed and sieved material and analysed

using *T. laticollis*-specific semi-quantitative SYBR Green real-time polymerase chain reaction (qPCR). *Taenia laticollis*-specific DNA was recovered from 67% (8/12) of bilberry samples but not reliably from any of the lingonberry samples 0% (0/24), although the exposure dose was higher for those. The qPCR results suggest that under natural conditions, taeniid egg dispersion from the contamination spot is demonstrated but attachment is berry specific. The surface of bilberries may be more adhesive for taeniid eggs than the waxier and harder pericarp of the lingonberries or there might be a difference in the dispersal mechanism caused by different biotopes.

Unraveling post-translational modifications in *Echinococcus granulosus sensu lato*.

Miles, S., Magnone, J., García-Luna, J., Dematteis, S., Mourglia-Ettlin, G.

15-03-2022

Acta Trop

<https://pubmed.ncbi.nlm.nih.gov/35300939>

Echinococcus granulosus sensu lato (s.l.) is the helminth parasite responsible for cystic echinococcosis, a neglected tropical disease currently affecting millions of people worldwide. Incomplete knowledge on the parasite biochemistry contributes, at least partially, to the limited development of useful biotechnological advances for the infection control. In this sense, little information is available regarding post-translational modifications (PTMs) occurring in *E. granulosus* s.l. proteins, which ultimately may affect the performance of biotechnological products to be developed. Therefore, we report here a proteomic analysis of the parasite PTMs identified through FindMod software applied to a set of tegumental proteins previously characterized by mass spectrometry (MALDI-TOF/TOF) analysis of protein spots from a 2D electrophoresis gel. Manual searches for already annotated proteins exhibiting such PTMs were also performed within proteome databases of *E. granulosus* s.l. and other platyhelminthes. In addition, key enzymes involved in PTMs modifications were searched for within *E. granulosus* s.l. proteome. Finally, the presence of selected PTMs was further confirmed by a high-resolution proteomic approach (nanoLC-MS/MS). A set of 22 different PTMs most likely to be present in the parasite was suggested, 9 of them with high confidence as they were identified in the same m/z fragment by both proteomic techniques (acetylation, deamidation, deamidation followed by methylation, mono- and di-hydroxylation, mono- and di-methylation, S-nitrosylation and phosphorylation). Interestingly, 5 PTMs were herein identified for the first time in *E. granulosus* s.l. proteins. Our results expand the scarcely studied topic of PTMs in platyhelminthes.

The Role of Tissue Inhibitor of Metalloproteinase-1 and 2 in *Echinococcus granulosus sensu lato*-Induced Human Hepatic Fibrosis.

Hasanzadeh, A., Rafiei, A., Kazemi, M., Beirumvand, M., Bahreini, A., Khanahmad, H.

16-03-2022

Acta Parasitol<https://doi.org/10.1007/s11686-022-00534-4>

The main mechanism underlying hepatic fibrosis is the imbalance between tissue Matrix Metalloproteinases (MMPs) and Tissue Inhibitors of Metalloproteinases (TIMPs). This study aimed to investigate the potential role of TIMP-1 and TIMP-2 in the process of hepatic fibrosis caused by *Echinococcus granulosus sensu lato* (*E. granulosus s.l.*). The expressions levels of TIMP-1 and TIMP-2 mRNAs were evaluated in fibrotic and normal hepatic tissues of 30 patients with Cystic Echinococcus (CE) using qRT-PCR. Moreover, their serum levels of TIMP-1 were assessed before CE cyst removal and 6 months after surgery using ELISA. The qRT-PCR results showed that the expression levels of TIMP-1 and TIMP-2 mRNAs were significantly higher in the fibrotic hepatic tissue compared to the normal liver tissue, in a way that the TIMP-1 and TIMP-2 mRNA expression levels were 19.07 and 6.58 folds higher in the fibrotic tissue compared to the normal liver tissue. Among these TIMPs, TIMP-1 exhibited the higher area under the curve (AUC) value for predicting liver fibrosis. However, we could not find a significant difference in the serum levels of TIMP-1 before and after the cyst removal procedure ($p=0.48$). For the first time, our study showed that the significant overexpression of both TIMP mRNAs in the fibrotic liver tissue of the CE patients may be due to the increased expression of MMPs in the peri-cystic tissue. However, we could not find a significant difference in the pre- and post-operative TIMP-1 levels, which may be due to recurrence or heterogeneity in the cyst type. Therefore, performing further studies with a larger sample size of the CE patients is recommended.

Surveillance of berries sold on the Norwegian market for parasite contamination using molecular methods.

Temesgen, T., Stigum, V., Robertson, L.

12-01-2022

Food Microbiol<https://pubmed.ncbi.nlm.nih.gov/35287809>

The risk of foodborne parasite infection linked to the consumption of contaminated fresh produce has long been known. However, despite epidemiological links between the outbreaks and contaminated berries, few studies have assessed the magnitude of parasite contamination on fresh produce sold in Europe. The present study was aimed to address the knowledge gap on parasite contamination of berries sold in Norway. Samples of blueberries, strawberries, and raspberries were analysed by multiplex qPCR for detection of *Echinococcus multilocularis*, *Toxoplasma gondii*, and *Cyclospora cayetanensis*. In addition, a simplex qPCR method was employed for detecting contamination of the berries with *Cryptosporidium* spp. A total of 820 samples of berries, each of around 30 g (274 samples of blueberries, 276 samples of raspberries, and 270 samples of strawberries), were analysed. We found an overall occurrence of 2.9%, 6.6%,

and 8.3% for *T. gondii*, *C. cayetanensis*, and *Cryptosporidium* spp., respectively, whereas *E. multilocularis* was not detected from any of the samples investigated. Strawberries and raspberries were most often contaminated with *Cryptosporidium* spp., whereas blueberries were contaminated mostly with *C. cayetanensis*. Detection of parasite contaminants on fresh berries indicates the need for a system to ensure the parasitological safety of fresh berries.

Design of highly sensitive nano-biosensor for diagnosis of hydatid cyst based on gold nanoparticles.

Jafari, F., Maghsood, A., Fallah, M., Jalilvand, A., Matini, M., Amini, B.

26-02-2022

Photodiagnosis Photodyn Ther<https://pubmed.ncbi.nlm.nih.gov/35231618>

Cystic echinococcosis, a zoonotic parasitic infection, is a major public health and economic concern, with worldwide distribution. The development of sensitive diagnostic methods for hydatid disease is important. We designed a highly sensitive nano-biosensor for the diagnosis of hydatid cyst based on gold nanoparticles (AuNPs). AuNPs were synthesized. *Echinococcus granulosus* antigen was coated on the ELISA microwells. Then, the *E. granulosus* IgG antibody was added to the microwells. After incubation and washing, the Ag-Ab complex was incubated with a human IgG HRP-conjugated antibody. Then, the synthesized AuNPs and tetramethylbenzidine (TMB), as a chromogenic substrate of HRP, were added to the reaction. Finally, the absorption rate was measured by spectrophotometry. The results showed that the enzyme peroxide and TMB change the color of the reaction from red to yellow by oxidizing AuNPs. The sensitivity and specificity of the designed method were investigated. The linear equation and regeneration of nanobiosensor designed for red color $Y = 0.0312X + 0.649$, $R^2 = 9962$ and for yellow color $Y = 0.013X + 0.398$, $R^2 = 9851$ were determined. The limit of detection of the designed nanobiosensor was $0.001 \mu\text{g mL}^{-1}$. The results confirmed that the designed nanobiosensor was completely specific for the detection of *E. granulosus* antibody.

In vitro Scolicidal Efficacy of 5-Fluorouracil and Radiation Against Protoscoleces of Echinococcus granulosus Sensu Lato.

Lu, P., Li, J., Mao, R., Qi, H., Yang, L., Zhou, Q., Tian, M., Zhang, W., Bao, Y.

03-02-2022

Acta Parasitol<https://doi.org/10.1007/s11686-022-00518-4>

Cystic echinococcosis (CE) caused by *Echinococcus granulosus sensu lato* (*s.l.*) is a globally distributed zoonosis. CE treatment is difficult, but radiation and 5-fluorouracil (5-FU) can be effective. However, the combination of radiation and 5-FU has not been reported. This study evaluated the effect of

combination of 5-FU and radiation on *E. granulosus* s.l. protoscolices (PSCs). In this study, PSCs were collected from the liver of diseased sheep, and some were exposed to a single dose of 20 Gy 6-MV X-ray combined with (5 µg/mL or 10 µg/mL) 5-FU in vitro. Methylene blue staining was used to detect the viability of the PSCs. Transcription of EgHSP70 and Egp38 was measured by quantitative real-time PCR (qRT-PCR). A single dose of radiation killed 18% of the PSCs, and 5-FU showed weak parasitocidal efficacy on the first day of treatment. After 14 d, 5 µg and 10 µg/mL of 5-FU killed 40.20% and 50.02% of the PSCs, whereas 20 Gy of radiation killed 31.44%. The combination of 5-FU (10 µg/mL) with 20 Gy of radiation showed 77.55% killing efficacy. qRT-PCR showed that 5-FU inhibited Egp38 expression, whereas radiation increased its expression. EgHSP70 was highly expressed 14 days after radiation treatment. The data indicate that 5-FU has parasitocidal efficacy against the PSCs of *E. granulosus* s.l. The lethal efficacy of PSCs caused by a single dose of radiation exposure is related to the upregulated expression level of Egp38 and EgHSP70. The killing effect of 5-FU (10 µg/mL) with 20Gy of radiation was significantly better than that of single treatment group. This study provided a basis for the potential role of 5-FU combined with radiation in the treatment of CE.

Modelling diagnostics for *Echinococcus granulosus* surveillance in sheep using Latent Class Analysis: Argentina as a case study.

Sykes, A., Larrieu, E., Poggio, T., Céspedes, M., Mujica, G., Basáñez, M., Prada, J.

04-12-2021

One Health

<https://doi.org/10.1016/j.onehlt.2021.100359>

Echinococcus granulosus sensu lato is a globally prevalent zoonotic parasitic cestode leading to cystic echinococcosis (CE) in both humans and sheep with both medical and financial impacts, whose reduction requires the application of a One Health approach to its control. Regarding the animal health component of this approach, lack of accurate and practical diagnostics in livestock impedes the assessment of disease burden and the implementation and evaluation of control strategies. We use of a Bayesian Latent Class Analysis (LCA) model to estimate ovine CE prevalence in sheep samples from the Río Negro province of Argentina accounting for uncertainty in the diagnostics. We use model outputs to evaluate the performance of a novel recombinant B8/2 antigen B subunit (rEgAgB8/2) indirect enzyme-linked immunosorbent assay (ELISA) for detecting *E. granulosus* in sheep. Necropsy (as a partial gold standard), western blot (WB) and ELISA diagnostic data were collected from 79 sheep within two Río Negro slaughterhouses, and used to estimate individual infection status (assigned as a latent variable within the model). Using the model outputs, the performance of the novel ELISA at both individual and flock levels was evaluated, respectively, using a receiver operating characteristic (ROC) curve, and simulating a range of sample sizes and prevalence levels within hypothetical flocks. The estimated (mean) prevalence of ovine CE was 27.5% (95%Bayesian credible

interval (95%BCI): 13.8%-58.9%) within the sample population. At the individual level, the ELISA had a mean sensitivity and specificity of 55% (95%BCI: 46%-68%) and 68% (95%BCI: 63%-92%), respectively, at an optimal optical density (OD) threshold of 0.378. At the flock level, the ELISA had an 80% probability of correctly classifying infection at an optimal cut-off threshold of 0.496. These results suggest that the novel ELISA could play a useful role as a flock-level diagnostic for CE surveillance in the region, supplementing surveillance activities in the human population and thus strengthening a One Health approach. Importantly, selection of ELISA cut-off threshold values must be tailored according to the epidemiological situation.

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

Stage-specific miRNAs regulate gene expression associated with growth, development and parasite-host interaction during the intra-mammalian migration of the zoonotic helminth parasite *Fasciola hepatica*.

Ricafrente, A., Cwiklinski, K., Nguyen, H., Dalton, J., Tran, N., Donnelly, S.

04-06-2022

BMC Genomics

<https://doi.org/10.1186/s12864-022-08644-z>

MiRNAs are small non-coding RNAs that post-transcriptionally regulate gene expression in organisms ranging from viruses to mammals. There is great relevance in understanding how miRNAs regulate genes involved in the growth, development, and maturation of the many parasitic worms (helminths) that together afflict more than 2 billion people. Here, we describe the miRNAs expressed by each of the predominant intra-mammalian development stages of *Fasciola hepatica*, a foodborne flatworm that infects a wide range of mammals worldwide, most importantly humans and their livestock. A total of 124 miRNAs were profiled, 72 of which had been previously reported and three of which were conserved miRNA sequences described here for the first time. The remaining 49 miRNAs were novel sequences of which, 31 were conserved with *F. gigantica* and the remaining 18 were specific to *F. hepatica*. The newly excysted juveniles express 22 unique miRNAs while the immature liver and mature bile duct stages each express 16 unique miRNAs. We discovered several sequence variant miRNAs (IsomiRs) as well as miRNA clusters that exhibit strict temporal expression paralleling parasite development. Target analysis revealed the close association between miRNA expression and stage-specific changes in the transcriptome; for example, we identified specific miRNAs that

target parasite proteases known to be essential for intestinal wall penetration (cathepsin L3). Moreover, we demonstrate that miRNAs fine-tune the expression of genes involved in the metabolic pathways that allow the parasites to move from an aerobic external environment to the anaerobic environment of the host. These results provide novel insight into the regulation of helminth parasite development and identifies new genes and miRNAs for therapeutic development to limit the virulence and pathogenesis caused by *F. hepatica*.

Epidemiology of *Fasciola* spp. in the intermediate host in China: A potential risk for fasciolosis transmission.

Pan, M., Bai, S., Ji, T., Fan, Y., Liu, D., Yang, Y., Tao, J., Huang, S.
09-03-2022

Acta Trop

<https://pubmed.ncbi.nlm.nih.gov/35278366>

Fasciolosis is a zoonotic disease as 600 million animals have been infected, and 180 million people are at risk of the infection in the world. Snail as the intermediate host of *Fasciola* is an essential and important factor in the transmission of fasciolosis, while its potential risk for transmission has not been studied. In this study, 3561 snails collected from large-scale regions of China were examined by nest-PCR method. A total of 345 snails were positive for *Fasciola* spp., with an overall prevalence of 9.7%. Prevalence in central and southern China, characterized by a subtropical monsoon climate, was relatively low (8.0%), while a high infection rate (36.9%) was found on the plateau area (altitude > 500 m). In combination with previous findings, the study showed a highly positive correlation between snails and animal infection in central and eastern China, thus indicating that infected snails could be an indispensable risk factor for fasciolosis transmission. Epidemiological surveillance of snails will help assess the risk of fasciolosis in humans or ruminants, which promotes future prevention of this zoonotic disease.

Molecular analyses confirm the coexistence of *Fasciola gigantica* and parthenogenetic *Fasciola* in the Philippines.

Itagaki, T., Jin, S., Takashima, S., Ohari, Y., Angeles, J.
18-02-2022

Parasitol Int

<https://pubmed.ncbi.nlm.nih.gov/35183771>

Fasciola flukes collected from domestic buffalos and cattle in the Philippines were confirmed as *Fasciola gigantica* and parthenogenetic *Fasciola* based on DNA analyses of nuclear *pepck* and *pold* genes, and the mitochondrial ND1 gene. This study is the first to elucidate that *F. gigantica* and parthenogenetic *Fasciola* coexist in the Philippines with prevalences of 90.6% and 9.4%, respectively. The *F. gigantica* population showed a high genetic diversity with 25 ND1 haplotypes, suggesting that *F. gigantica* has existed in the Philippines for a long time. In contrast, parthenogenetic *Fasciola* flukes showed a single ND1 haplotype (*Fsp*-ND1-P1),

which was identical to the founder haplotype, *Fg*-C2 of parthenogenetic *Fasciola* in China. These results indicate that parthenogenetic *Fasciola* in the Philippines is a recently introduced population from a neighboring continent.

Identification of new polymorphic positions in rDNA sequences of the "intermediate" *Fasciola* forms.

Zeng, M., Wang, X., Lan, Z., Guo, X., Jiang, Y., Wu, T., Chang, Q., Wang, C.

05-02-2022

Parasitol Int

<https://pubmed.ncbi.nlm.nih.gov/35131471>

Fascioliasis is a foodborne zoonotic disease generally caused by the parasitic flukes *Fasciola gigantica* and *Fasciola hepatica* in class Trematoda. An "intermediate" *Fasciola* forms between *F. gigantica* and *F. hepatica* has been shown to exist. However, the relationships among *F. gigantica*, *F. hepatica*, and "intermediate" *Fasciola* forms remain unclear. In this study, we found five new polymorphic positions in 18S and 28S rDNAs sequences of "intermediate" *Fasciola* forms. According to the high-throughput sequencing results, all known 16 polymorphic positions of "intermediate" *Fasciola* forms show a clear and consistent tendency for *F. gigantica* or *F. hepatica*, and the percentages of the most frequently occurring bases were different in specimens. In the three ITS sequence fragments, hybrid-type base combinations of the polymorphic positions were detected, and the percentages of the most frequent base combinations were different in specimens too. In addition, interestingly, the newly detected ITS-802 position was not a traditional polymorphic position in "intermediate" *Fasciola* forms, and the bases in ITS-802 position are not same as the allele bases of *F. gigantica* or *F. hepatica*. Our results will be helpful to investigations into the molecular taxonomy, population genetics, and ecology of *F. gigantica*, *F. hepatica*, and "intermediate" *Fasciola* forms.

Metabolome alterations in *Clonorchis sinensis* after treatment with tribendimidine and praziquantel in vivo.

Yufen, W., Xinru, L., Jian, X., Huolele, ., Zhihua, J., Yu, C., Mingyong, L., Haobing, Z.

25-01-2022

Acta Trop

<https://pubmed.ncbi.nlm.nih.gov/35090859>

Tribendimidine (TBD) is a broad-spectrum anthelmintic drug that is also significantly effective in treating clonorchiasis. In this study, the altered metabolomes of *Clonorchis sinensis* (*C. sinensis*) in rats after TBD administration were quantified by using ultrahigh-performance liquid chromatography-tandem mass spectrometry (UHPLC-MS/MS) and gas chromatography-mass spectrometry (GC-MS) to explore the possible active sites of TBD against clonorchiasis through altered metabolites and metabolic pathway analysis, and the results are expected to provide a target for the future design of anti-*Clonorchis*

sinensis drugs. The worm burden reduction rate and scanning electron microscopy demonstrated that praziquantel (PZQ, positive control drug) and TBD had significant effects on *C. sinensis* in rats after treatment at a single dose of 200 mg/kg for 24 h. For the MS-based metabolomic analysis, a total of 173 standard metabolites (126 amino acids, 10 phospholipids and 37 fatty acids) were utilized as a reference metabolite database for metabolome identification. In total, 32 amino acids, 71 phospholipids and 27 fatty acids were detected in the *C. sinensis* of each group. Among these metabolites, 10 amino acids were significantly decreased in both drug-treated groups. Four lysophosphatidyl cholines (LPCs), six lysophosphatidyl ethanolamines (LPEs) and one phosphatidyl inositol (PI) were significantly increased after treatment with TBD. There were no significant changes in fatty acids among the control group and the two drug-treated groups. The results indicated that TBD administration caused a decrease in amino acids involved in the metabolic pathways of energy consumption and an increase in lysophospholipids, which are the hydrolysis products of phospholipase2 (PLA2) in the phospholipid metabolic pathways. The increased lysophospholipid content can destroy the cell membrane, increase membrane permeability, and even cause exposure to internal antigens that can be attacked by host antibodies. Perhaps the destroyed membrane, the exposed internal antigens and the consumed energy are the cause of the damage and death of *C. sinensis* after TBD administration. This is an interesting problem that can be examined in future research.

FILARIOSE LYMPHATIQUE

Towards elimination of Lymphatic Filariasis in Kenya: improving advocacy, communication and social mobilization activities for mass drug administration, a qualitative study.

Kibe, L., Kimani, B., Okoyo, C., Omondi, W., Sultani, H., Njomo, D.

06-06-2022

Trop Dis Travel Med Vaccines

<https://doi.org/10.1186/s40794-022-00172-8>

Introduction: The Kenya Breaking Transmission Strategy for Neglected Tropical Diseases (NTD) from 2019 to 2023 intensifies advocacy, coordination, and partnerships. The purpose of this study was to explore views and experiences of stakeholders and health workers on ways of improving the Advocacy, Communication and Social Mobilization (ACSM) activities of Mass Drug Administration (MDA) for Lymphatic Filariasis (LF) programs through participatory approaches in Kilifi County, Kenya. **Methods:** Two wards were purposely selected in the Kaloleni sub-county, Kilifi County, where there was an average treatment coverage of 56% in 2015, 50.5% in 2016. Qualitative data collection methods were employed,

which included participatory meetings with county stakeholders to understand their views, experiences, and suggestions on how ACSM strategies can be improved in MDA for LF. Twelve In-Depth Interviews (IDIs) were conducted (six with opinion leaders and six with Community Health Extension Workers (CHEWs) and two semi-structured interviews (SSIs) were held with county and sub-county coordinators involved in MDA administration. The aim was to better to understand their perceptions of the NTD program about ACSM, challenges to ACSM strategies, and ways to improve the strategies for ACSM in MDA for LF. The Data was organized and classified into codes and themes using QSR NVIVO version 12. **Results:** The study observed the low participation of stakeholders in the ACSM activities of MDA for LF and identified potential areas for stakeholders' involvement to strengthen the activities. Challenges hindering effective implementation of ACSM activities include late delivery of Information, Educational and Communication (IEC) and few IEC materials, insufficient funding, inadequate time allocated to reach the assigned households with messages, messaging, and packaging of information for dissemination due to the vastness of the area. The stakeholders recommended innovative strategies and techniques to improve ACSM activities. **Discussion and conclusion:** The results of this study show key challenges to ACSM implementation of MDA for LF. Implementers need to pay attention to these challenges to enhance the effectiveness of MDA per the Kenya NTD Breaking Transmission Strategy. ACSM efforts in MDA for LF control and elimination should be linked with overarching efforts to mainstream partnerships and coordination in control and elimination.

The Prospective Effects of Climate Change on Neglected Tropical Diseases in the Eastern Mediterranean Region: a Review.

Revue de littérature

Al-Delaimy, A.

14-03-2022

Curr Environ Health Rep

<https://doi.org/10.1007/s40572-022-00339-7>

An increase in the annual daily temperature is documented and predicted to occur in the coming decades. Climate change has a direct effect and adverse impact on human health, as well as on multiple ecosystems and their species. The purpose of this paper is to review the effect of climate change on neglected tropical diseases including leishmaniasis, schistosomiasis, and lymphatic filariasis in the Eastern Mediterranean Region (EMR). A list of engine web searches was done; 280 full-text records were assessed for eligibility. Only 48 original records were included within the final selection for the review study. Most research results show an alteration of neglected diseases related to climate change influencing specifically the Eastern Mediterranean Region, in addition to the expectation of more effects at the level of vectors and reservoir whether its vector transmission route or its egg hatching and replication or even the survival of adult

worms in the coming years. At the same time, not all articles related to the region interpret the direct or indirect effect of climate variations on these specific diseases. Although few studies were found describing some of climate change effects on neglected tropical diseases in the region, still, the region lacks research funding, technical, and mathematical model expertise regarding the direct effect of climate change on the ecosystems of these neglected tropical diseases.

Integrated serological surveillance of acute febrile illness in the context of a lymphatic filariasis survey in Timor-Leste: a pilot study using dried blood spots.

Arkell, P., Angelina, J., do Carmo Vieira, A., Wapling, J., Marr, I., Monteiro, M., Matthews, A., Amaral, S., da Conceicao, V., Kim, S., Bailey, D., Yan, J., Fancourt's, N., Vaz Nery, S., Francis, J.

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Trans R Soc Trop Med Hyg

<https://doi.org/10.1093/trstmh/trab164>

Acute febrile illnesses (AFIs), including dengue, scrub typhus and leptospirosis, cause significant morbidity and mortality in Southeast Asia. Serological surveillance can be used to investigate the force and distribution of infections. Dried blood spot (DBS) samples are an attractive alternative to serum because they are easier to collect and transport and require less cold storage. We conducted a pilot study to determine the feasibility of integrating serological surveillance for dengue, scrub typhus and leptospirosis into a population-representative lymphatic filariasis seroprevalence survey in Timor-Leste using DBSs. A total of 272 DBSs were collected from healthy community participants. DBSs were analysed at the National Health Laboratory using commercially available enzyme-linked immunosorbent assays. To validate assays for DBSs, 20 anonymised serum samples of unknown serostatus were used to create dried serum spots (DSSs). These were analysed with optical densities compared with those of serum. Where low variance was observed (dengue assay) the published kit cut-offs for serum were applied to the analysis of DBSs. For the other assays (scrub typhus and leptospirosis), index values (IVs) were calculated and cut-offs were determined to be at 2 standard deviations (SDs) above the mean. Of the 272 samples analysed, 19 (7.0% [95% confidence interval {CI} 4.3 to 10.7]) were positive for dengue immunoglobulin G (IgG), 11 (4.0% [95% CI 2.1 to 7.1]) were positive for scrub typhus IgG and 16 (5.9% [95% CI 3.4 to 9.4%]) were positive for leptospira IgG. While dengue seroprevalence was lower than in nearby countries, results represent the first evidence of scrub typhus and leptospirosis transmission in Timor-Leste. Integrated programmes of serological surveillance could greatly improve our understanding of infectious disease epidemiology in remote areas and incur minimal additional fieldwork costs. However, when planning such studies, the choice of assays, their validation for DBSs and the laboratory infrastructure and technical expertise at the proposed location of analysis must be considered.

MYCETOME

Bedside Diagnosis for Disseminated Deep Dermatophytosis: a Case Series Study.

Xia, X., Shen, H., Zhi, H., Zhong, Y., Sang, B., Lv, W., Li, Q., Liu, Z.
20-04-2022

Mycopathologia

<https://doi.org/10.1007/s11046-022-00633-w>

Deep cutaneous fungal infections including deep dermatophytosis are responsible for significant morbidity and mortality, especially in immunocompromised patients. Variable and longer turnaround time on tissue culture results delay diagnosis. We sought to seek the fast bedside diagnosis for disseminated deep dermatophytosis by direct microscopy using a blunt scalpel or needle aspiration before biopsy. This is a 6-year retrospective review of patients with a diagnosis of disseminated deep dermatophytosis seen at a single tertiary care institution. *Trichophyton rubrum* was isolated in four patients, and *T. mentagrophyte* complex in one patient. All the dermatophyte isolates can grow at 37 °C. Microscopy of purulence sampling from intact nodules demonstrated abundant septate hyphae, and also isolation from purulence was concordance with skin tissue culture. Ultrasound-guided sampling from non-eroded can yield purulence, and direct microscopy of purulence may facilitate rapid diagnosis of deep dermatophytosis and serve to prevent disease progression and dissemination.

Dermoscopic features of actinomycetoma: a case series.

Guerrero-Putz, M., Gómez-García, L., Regalado-Ceballos, A., Pérez-Romero, A., Moreno, D., Villarreal-Martinez, A., Chavez-Alvarez, S., Ocampo-Candiani, J., Cuellar-Barboza, A.

17-02-2022

Clin Exp Dermatol

<https://doi.org/10.1111/ced.15108>

Dermoscopy of mycetoma has white structures as the predominant feature, while white scale and yellowish structures were also consistent in our findings with available literature.

ONCHOCERCOSE

SCHISTOSOMIASE

Itraconazole, a cytochrome P450 inhibitor, enhanced the efficacy of praziquantel against *Schistosoma mansoni* infection and alleviated liver injury in mice.

Sabra, A., Salem, M., William, S., Hammam, O., El-Lakkany, N.
03-06-2022

Exp Parasitol

<https://pubmed.ncbi.nlm.nih.gov/35667394>

Treatment of schistosomiasis is heavily reliant on the single antischistosomal drug praziquantel (PZQ). The use of synergistic drug-drug interactions is one possible solution, which could be used to mitigate PZQ's poor and variable bioavailability. Itraconazole (ITZ), a triazole antifungal agent, is a potent CYP3A inhibitor that can cause significant drug-drug interactions when used with CYP3A substrates. This study investigates the effect of ITZ as adjuvant therapy with PZQ on worm load, egg deposition and maturation, and the consequent histopathology and biochemical abnormalities in the liver during the immature and mature stages of *Schistosoma mansoni* (*S. mansoni*) infection. *S. mansoni*-infected mice were divided into five groups of eight-ten mice each: (I) infected untreated, (II) infected and treated with PZQ 3 weeks PI, (III) infected and treated with both ITZ and PZQ 3 weeks PI, (IV) infected and treated with PZQ 7 weeks PI, and (V) infected and treated with both ITZ and PZQ 7 weeks PI. All mice were killed by rapid decapitation 9 weeks PI. Data revealed that ITZ in combination with PZQ at both immature and mature stages improved the parasitological criteria of cure, and greatly reduced inflammation, granuloma and fibrotic tissue formation, and apoptosis versus PZQ alone. Furthermore, it showed the greatest impact on improving liver injury and oxidative stress markers. Notably, the effect was considerably stronger at the mature stage of *S. mansoni* infection. These findings support the notion that ITZ increased PZQ's antischistosomal activity by inhibiting CYP450 expression, potentially reducing PZQ metabolism and increasing systemic exposure.

Excessive immunosuppression by regulatory T cells antagonizes T cell response to schistosome infection in PD-1-deficient mice.

Lu, L., Li, T., Feng, X., Liu, Z., Liu, Y., Chao, T., Gu, Y., Huang, R., Zhang, F., He, L., Zhou, B., Kong, E., Liu, Z., Wang, X., Chen, Z., Wang, H., Malissen, M., Malissen, B., Zhang, L., Liang, Y.
06-06-2022

PLoS Pathog

<https://doi.org/10.1371/journal.ppat.1010596>

Schistosomiasis is caused by parasitic flatworms known as schistosomes and affects over 200 million people worldwide. Prevention of T cell exhaustion by blockade of PD-1 results in clinical benefits to cancer patients and clearance of viral infections, however it remains largely unknown whether loss of PD-1 could prevent or cure schistosomiasis in susceptible mice. In this study, we found that *S. japonicum* infection dramatically induced PD-1 expression in T cells of the liver where the parasites chronically inhabit and elicit deadly inflammation. Even in mice infected by non-egg-producing unisex parasites, we still observed potent induction of PD-1 in liver T cells of C57BL/6 mice following *S. japonicum* infection. To determine the function of PD-1 in schistosomiasis, we

generated PD-1-deficient mice by CRISPR/Cas9 and found that loss of PD-1 markedly increased T cell count in the liver and spleen of infected mice. IL-4 secreting Th2 cells were significantly decreased in the infected PD-1-deficient mice whereas IFN- γ secreting CD4+ and CD8+ T cells were markedly increased. Surprisingly, such beneficial changes of T cell response did not result in eradication of parasites or in lowering the pathogen burden. In further experiments, we found that loss of PD-1 resulted in both beneficial T cell responses and amplification of regulatory T cells that prevented PD-1-deficient T cells from unleashing anti-parasite activity. Moreover, such PD-1-deficient Tregs exert excessive immunosuppression and express larger amounts of adenosine receptors CD39 and CD73 that are crucial for Treg-mediated immunosuppression. Our experimental results have elucidated the function of PD-1 in schistosomiasis and provide novel insights into prevention and treatment of schistosomiasis on the basis of modulating host adaptive immunity.

Fluconazole as *Schistosoma mansoni* cytochrome P450 inhibitor: In vivo murine experimental study.

Elzoheiry, M., Elmehankar, M., Aboukamar, W., El-Gamal, R., Sheta, H., Zenezan, D., Nabih, N., Elhenawy, A.

02-06-2022

Exp Parasitol

<https://pubmed.ncbi.nlm.nih.gov/35660528>

Schistosomiasis is a chronic disease caused by blood flukes of the *Schistosoma* spp. New approaches against this morbid infection are needed. In this study, we investigated fluconazole (FLZ) as an inhibitor of *Schistosoma mansoni* cytochrome P450 (*S. mansoni* CYP450) enzyme at different life cycle stages. We compared FLZ (10 mg/kg for two days) effects when administered early 5 days post-infection (dpi) (Early I) and 21 dpi (Early II) versus late administration 60 dpi on *S. mansoni* CYP450 gene expression. These different FLZ treatment regimens were evaluated in experimentally infected mice with *S. mansoni*. This study showed that administration of FLZ, whether early or late during schistosomal infection, resulted in significant inhibition of *S. mansoni* CYP450 expression in the adult stage ($P < 0.001$). Early exposure to FLZ during the first week of infection significantly decreased the number of schistosomes that reached the adult stage compared to the infected control group and resulted in significant inhibition of *S. mansoni* CYP450 expression ($P < 0.001$) in the adult stage. In the Early I group, the fewest number of eggs per liver tissue gram was recorded. Our data suggested that FLZ is a *S. mansoni* CYP450 gene expression inhibitor with greater effect on schistosome stages.

Tumour-like breast lesions due to ectopic schistosomiasis in a European traveller.

Palaprat, O., Nika, E., Delouche, A., Quenard, F., Chevalier, M., Maubon, D., Pelloux, H., Robert, M.

02-06-2022

J Travel Med

<https://pubmed.ncbi.nlm.nih.gov/35652615>

Schistosomiasis is a neglected tropical disease classically responsible for intestinal or urogenital forms. We report the incidental diagnosis of ectopic mammary schistosomiasis involving *Schistosoma haematobium* following a breast cancer screening mammogram in a European patient with a distant history of travel.

Contribution of researchers in Arab countries to scientific publications on neglected tropical diseases (1971 - 2020).

Sweileh, W.

01-06-2022

Trop Dis Travel Med Vaccines

<https://doi.org/10.1186/s40794-022-00173-7>

The neglected tropical diseases (NTDs) are endemic in several Arab countries. The purpose of the current study was to assess the contribution of researchers in Arab countries to the knowledge base on NTDs using bibliometric indicators. Keywords related to all 20 NTDs were obtained from previously published bibliometric studies and were combined with the names of Arab countries listed as country affiliation. The search strategy was implemented in the Scopus database and bibliometric indicators were generated for the study period from 1971 to 2020. RESULTS: The search strategy generated 6542 documents; representing less than 4% of the global research in the field. Scientific research on NTDs from researchers in Arab countries (a) has experienced slow growth; (b) generated a relatively inadequate number of publications over the study period; (c) was disseminated mainly through journals in the field of parasitology or tropical medicine; (d) was contributed by researchers from the 22 Arab countries, but mainly by researchers from Egypt, Saudi Arabia, and Sudan; (e) has fragmented author networks with weak collaboration between active authors in the field; (f) was characterized by strong cross-country research collaboration with researchers in the US and the UK; (g) has focused on three main diseases, specifically, schistosomiasis, leishmaniasis, and onchocerciasis, and (h) showed less emphasis on soil-transmitted helminthiasis infections despite high prevalence. Arab countries cannot achieve the 2030 global agenda without control and elimination of prevalent NTDs. Researchers in Arab countries need to establish strong research networks to exchange expertise on all NTDs.

Host-dependent impairment of parasite development and reproduction in the acanthocephalan model.

Schmidt, H., Mauer, K., Hankeln, T., Herlyn, H.

31-05-2022

Cell Biosci

<https://doi.org/10.1186/s13578-022-00818-2>

A central question in parasitology is why parasites mature and reproduce in some host species but not in others. Yet, a better understanding of the inability of parasites to complete their

life cycles in less suitable hosts may hold clues for their control. To shed light on the molecular basis of parasite (non-)maturation, we analyzed transcriptomes of thorny-headed worms (Acanthocephala: Pomphorhynchus laevis), and compared developmentally arrested worms excised from European eel (*Anguilla anguilla*) to developmentally unrestricted worms from barbel (*Barbus barbus*). Based on 20 RNA-Seq datasets, we demonstrate that transcriptomic profiles are more similar between *P. laevis* males and females from eel than between their counterparts from barbel. Impairment of sexual phenotype development was reflected in gene ontology enrichment analyses of genes having differential transcript abundances. Genes having reproduction- and energy-related annotations were found to be affected by parasitizing either eel or barbel. According to this, the molecular machinery of male and female acanthocephalans from the eel is less tailored to reproduction and more to coping with the less suitable environment provided by this host. The pattern was reversed in their counterparts from the definitive host, barbel. Comparative analysis of transcriptomes of developmentally arrested and reproducing parasites elucidates the challenges parasites encounter in hosts which are unsuitable for maturation and reproduction. By studying a gonochoric species, we were also able to highlight sex-specific traits. In fact, transcriptomic evidence for energy shortage in female acanthocephalans associates with their larger body size. Thus, energy metabolism and glycolysis should be promising targets for the treatment of acanthocephaliasis. Although inherently enabling a higher resolution in heterosexuals, the comparison of parasites from definitive hosts and less suitable hosts, in which the parasites merely survive, should be applicable to hermaphroditic helminths. This may open new perspectives in the control of other helminth pathogens of humans and livestock.

Experimental infection with *Schistosoma mansoni* isolated from the wild rodent *Holochilus sciureus* shows a low parasite burden but induces high schistosomiasis severity in BALB/c mice.

Miranda, G., Rodrigues, J., Rezende, M., Resende, S., Camelo, G., Silva, J., Maggi, L., Rodrigues, V., Oliveira, V., Negrão-Corrêa, D.

01-06-2022

Parasitology

<https://doi.org/10.1017/S0031182022000774>

Immunotoxic, neurotoxic, histopathological and immunohistopathological alterations of *Nerium oleander* and *Tecoma stans* methanolic extract on *Biomphalaria alexandrina* snails.

Ibrahim, A., Ahmed, A., Hammam, O., Abdel-Ghaffar, F.

13-03-2022

Acta Trop

<https://pubmed.ncbi.nlm.nih.gov/35296391>

Schistosomiasis is a severe illness that caused socioeconomic

problems. The present study aimed to investigate the molluscicidal activities of the methanolic extract of Nerium oleander and Tecoma stans on *B. alexandrina* snails. The present results showed that *N. oleander* had the higher molluscicidal effect (LC₅₀: 138.6 mg/l) than *T. stans* methanolic extract (LC₅₀: 256.0 mg/l). These concentrations had no mortality effects on *Daphnia magna* during the first 12 h of the exposure, while, they had a cercaricidal activity. Exposure of *B. alexandrina* snails to the sub lethal concentrations (LC₁₀ and LC₂₅) of the methanolic extract of either *N. oleander* or *T. stans* caused a concentration- dependent significant decrease in their mean total number of hemocyte and hyalinocytes percent, while, both the round small and the granulocytes were increased than the control group. Exposure of *B. alexandrina* snails to LC₂₅ of the methanolic extract of *N. oleander* or *T. stans*, caused morphological alterations in the hemocytes that were studied by both light and electron microscopy. The sub lethal concentration (LC₂₅) significantly decreased the acetyl cholinesterase activities, acid and alkaline phosphatase levels and the protein content. Histopathological changes occurred in the digestive and the hermaphrodite glands of exposed *B. alexandrina* snails to LC₂₅ of the methanolic extracts. These alterations were confirmed by Immunohistochemistry for PCNA and Cyclin D1 expressions. Conclusively, these plants could be used to decrease the spread of schistosomiasis as they are cheap and environmentally safe to replace the synthetic molluscicides for snail control.

The Prospective Effects of Climate Change on Neglected Tropical Diseases in the Eastern Mediterranean Region: a Review.

Revue de littérature

Al-Delaimy, A.

14-03-2022

Curr Environ Health Rep

<https://doi.org/10.1007/s40572-022-00339-7>

An increase in the annual daily temperature is documented and predicted to occur in the coming decades. Climate change has a direct effect and adverse impact on human health, as well as on multiple ecosystems and their species. The purpose of this paper is to review the effect of climate change on neglected tropical diseases including leishmaniasis, schistosomiasis, and lymphatic filariasis in the Eastern Mediterranean Region (EMR). A list of engine web searches was done; 280 full-text records were assessed for eligibility. Only 48 original records were included within the final selection for the review study. Most research results show an alteration of neglected diseases related to climate change influencing specifically the Eastern Mediterranean Region, in addition to the expectation of more effects at the level of vectors and reservoir whether its vector transmission route or its egg hatching and replication or even the survival of adult worms in the coming years. At the same time, not all articles related to the region interpret the direct or indirect effect of climate variations on these specific diseases. Although few studies were found describing some of climate change effects

on neglected tropical diseases in the region, still, the region lacks research funding, technical, and mathematical model expertise regarding the direct effect of climate change on the ecosystems of these neglected tropical diseases.

Heterorhabditis bacteriophora (Rhabditida: Heterorhabditidae), isolate HP88, induces reproductive and physiological alterations in Biomphalaria glabrata (Gastropoda: Planorbidae): an alternative for biological control of schistosomiasis.

Santos Amaral, L., Tunholi-Alves, V., Castro, L., Tunholi, V., Gaudêncio, F., Monteiro, C., Couto-Chambarelli, M., Pinheiro, J., Freire-Martins, I.

10-03-2022

Acta Trop

<https://pubmed.ncbi.nlm.nih.gov/35283103>

Heterorhabditis bacteriophora is an entomopathogenic nematode (EPN) that is mutually associated with *Photorhabdus luminescens*, utilized globally for biological control of numerous organisms. Freshwater snails of the species *Biomphalaria glabrata* have been incriminated as the main intermediate hosts of *Schistosoma mansoni* in Brazil, but virtually nothing is known about the susceptibility of these gastropod to EPNs. Information in this respect is relevant for control of these intermediate hosts, and thus of the helminthiasis they transmit. This paper for the first time reports the susceptibility of *B. glabrata* to infective juveniles of *H. bacteriophora* (isolate HP88) under laboratory conditions. For that purpose, six groups were formed: three Control groups (not exposed) and three Treated groups, in which the snails were exposed to 300 juveniles infecting the nematode over three weeks. The entire experiment was conducted in triplicate, using a total of 270 snails. Significant physiological alterations in *B. glabrata* were observed in response to the infection by *H. bacteriophora* HP88, characterized by decreased levels of hemolymphatic glucose as well as reduced contents of glycogen stored in the host's digestive gland. In parallel, the hemolymphatic activity of lactate dehydrogenase increased in the infected snails, indicating that the infection induces breakdown of carbohydrate homeostasis in *B. glabrata*. Additionally, all the reproductive parameters analyzed were reduced as a consequence of the infection. The results indicate the occurrence of the phenomenon of parasitic castration in the *B. glabrata*/*H. bacteriophora* HP88 interface, probably due to the depletion of galactogen in the parasitized organism. Although the infection did not cause lethality in the population of infected snails, *H. bacteriophora* HP88 compromised the reproductive performance of *B. glabrata*, suggesting its applicability in programs for biological control of this planorbid.

Molluscicidal and cercaricidal activities of the essential oil of *Dysphania ambrosioides* (L.) Mosyakin & Clemants: Implications for the control of schistosomiasis.

Pereira, L., Ribeiro, E., Brito, M., Araruna, F., Araruna, F., Leite, J., Silveira, D., de Oliveira, T., Cantanhede, S., Firmo, W., Monteiro, O., Maia, J., da Franca Rodrigues, K., Coutinho, D.
09-03-2022

Acta Trop

<https://pubmed.ncbi.nlm.nih.gov/35278368>

Schistosomiasis is one of the most important tropical diseases. A fundamental strategy to control its spread is the use of natural products against its vectors, which are snails of the genus *Biomphalaria*. The present study evaluated the chemical composition, the molluscicidal and cercaricidal effects, and the ecotoxicity of the essential oil from the aerial parts of *Dysphania ambrosioides* (L.) Mosyakin & Clemants (DAEO). The essential oil was obtained by hydrodistillation and analyzed by gas chromatography-mass spectrometry (GC-MS). Molluscicidal and cercaricidal activities were determined by the immersion method. Environmental toxicity was assessed from bioassays using *Artemia salina* larvae and *Danio rerio* fish. DAEO presented a 0.8% yield. The GC-MS analysis revealed the predominance of hydrocarbon monoterpenes in the oil. A total of 32 constituents was identified, with α -terpinene (50.69%) being the major compound, followed by p-cymene (13.27%) and ascaridole (10.26%). DAEO was active against adult *Biomphalaria glabrata* snails and demonstrated lethal effect against *Schistosoma mansoni* cercariae, with LC_{50} values of 25.2 (22.7-27.8) and 62.4 (61.8-62.9) $\mu\text{g/mL}$, respectively. Regarding toxicity to non-target aquatic organisms, the oil showed LC_{50} values of 86.9 (84.7-87.6) and 18.6 $\mu\text{g/mL}$ (15.5-22.8) for *A. salina* and *D. rerio*, respectively. DAEO proved to be a promising natural product for the control of schistosomiasis, acting on both the vectors and the etiological agent of the disease. However, the use of the oil is safer in transmission sites where there are no non-target organisms, as it has showed toxicity to *D. rerio* fish.

Novel Hepatic Schistosomula Antigens as Promising Targets for Immunodiagnosis and Immunoprotection of Schistosomiasis japonica.

Hou, N., Piao, X., Jiang, N., Liu, S., Cai, P., Liu, B., McManus, D., Chen, Q.

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J Infect Dis

<https://doi.org/10.1093/infdis/jiac077>

Antigens of migrating schistosomula are promising candidates as schistosomiasis vaccine targets, since immune attack on hepatic schistosomula would interrupt the parasites life cycle and reduce egg burden on the host. In this study, we report a collection of *Schistosoma japonicum* schistosomula proteins (SjScPs) that are highly expressed in hepatic schistosomula. The expression characteristics, antigenicity and immune protection of these proteins were studied by western blot, ELISA, immunofluorescence and challenge assays. We found that several of these SjScPs were highly antigenic and could effectively stimulate humoral immune responses in both human and other mammalian hosts. In particular, SjScP25, SjScP37, SjScP41, SjScP80, and SjScP88 showed high potential as biomarkers for schistosomiasis immunodiagnosis.

Furthermore, we demonstrated that immunization with several of the recombinant SjScPs were able to protect mice from *S japonicum* challenge infection, with SjScP25 generating the most protective results. Our work represents a group of novel schistosome immunogens, which may be promising schistosomiasis japonica diagnosis and vaccine candidates.

Neglected Tropical Diseases in Lebanon.

Alam, W., Mobayed, T., Younis, N., Zarif, R., Bizri, N., Tamim, H., Musharrafieh, U., Bizri, A.

03-02-2022

Acta Parasitol

<https://doi.org/10.1007/s11686-021-00510-4>

Neglected tropical diseases (NTDs) are highly endemic and distributed within the Middle East and North Africa (MENA) region, affecting an estimated 65 million people. Lebanon suffers from several NTDs as they are either endemic in the country or imported via expats residing in endemic regions, refugees, and foreign labor force. The Syrian crisis and the displacement of refugees to Lebanon have made the country the largest host of refugees per capita right after the Syrian crisis in 2011, peaking in the year of 2013. Additionally, foreign labor in Lebanon come from different countries in Africa and Asia that are endemic with certain NTDs. The Lebanese diaspora is approximately twice the number of those residing in the country and is distributed throughout the continents carrying the risk of importing new NTDs. A descriptive study about the prevalence of NTDs in Lebanon, their distribution, and factors contributing to spread was performed. The Lebanese Ministry of Public Health (LMPH) database regarding reportable transmissible diseases was reviewed for reportable NTDs between 2002 and 2020 in relation to age, gender, prevalence, and geographical distribution. The medical literature was searched using several engines looking for all reports about NTDs in Lebanon, those relevant to regions hosting Lebanese diaspora, and countries where the refugees and migrant workers came from. Only leishmaniasis, leprosy, echinococcosis, schistosomiasis, and rabies are mandatorily reportable NTDs by the LMPH. Additionally, case reports about fasciolosis, ascariidiosis, and Dengue were reported from Lebanon. The presence of the Syrian refugees in the country affected the prevalence of leishmaniasis and rabies. The most prevalent NTD in Lebanon is cutaneous leishmaniasis. The Lebanese diaspora reside mainly in South America, Africa, and in some Arab states known to be endemic with certain NTDs. Little information is known about NTDs in Lebanon. The country is at an increased risk of experiencing several new NTDs due to refugee influx, foreign labor, economic crisis, and ever-growing number of Lebanese seeking work opportunities abroad. More information is needed to assess the true burden of NTDs in Lebanon and the future steps to contain and mitigate their effects.

Dandelion (*Taraxacum officinale*) Improves the Therapeutic Efficiency of Praziquantel in Experimental Schistosomiasis.

Atwa, M., Abd-Elrazek, A., Salem, N.

24-01-2022

Acta Parasitol

<https://doi.org/10.1007/s11686-021-00513-1>

Although praziquantel (PZQ) has a wide use as an anti-schistosome agent, many of its imperfections and side effects have been reported in many studies. The current study aims to evaluate the curative effect of a natural dandelion extract (*Taraxacum officinale*) on schistosomiasis either alone or in combination with PZQ based on parasitological, immunological, histopathological and molecular investigations. Mice were experimentally infected with *Schistosoma mansoni* cercariae and then divided into four groups, *Schistosoma* spp.-infected untreated group (IC group), *Schistosoma* spp.-infected group of mice treated with dandelion (I-Dn group), *Schistosoma* spp.-infected group of mice treated with PZQ (I-PZQ group), and *Schistosoma* spp.-infected group of mice treated with both PZQ and dandelion (I-PZQ+Dn group). Treatment started 45 days' post-infection. Besides, non-infected, non-treated mice served as the negative healthy control group (HC group). The present results indicated that dandelion administration significantly reduced the worm burden, ova number, and the number and diameter of hepatic granulomas as compared to the untreated infected group. The results also showed that the levels of IL-6 and TNF- α were significantly decreased in the combined treatment group (I-PZQ+Dn) as compared to the I-PZQ group. Administration of dandelion-only remarkably reduced AST and ALT activities associated with schistosomiasis. Moreover, hepatic DNA damage assessed by comet assay was significantly inhibited in the combined treated group compared to the infected untreated and PZQ treated groups. The results concluded that combined treatment of PZQ and dandelion extract improved immune response, decreased the number and diameter of granulomas, and inhibited DNA damage, indicating a reduction in liver fibrosis associated with schistosomiasis. The present study focused on the potential effect of dandelion as an adjunct medication for therapeutic properties of PZQ.

R-praziquantel integrated population pharmacokinetics in preschool- and school-aged African children infected with *Schistosoma mansoni* and *S. haematobium* and Lao adults infected with *Opisthorchis viverrini*.

Falcoz, C., Guzy, S., Kovač, J., Meister, I., Coulibaly, J., Sayasone, S., Wesche, D., Lin, Y., Keiser, J.

13-01-2022

J Pharmacokinetic Pharmacodyn

<https://doi.org/10.1007/s10928-021-09791-8>

Racemic praziquantel (PZQ) is the standard treatment for schistosomiasis and liver fluke infections (opisthorchiasis and clonorchiasis). The development of an optimal pediatric

formulation and dose selection would benefit from a population pharmacokinetic (popPK) model. A popPK model was developed for R-PZQ, the active enantiomer of PZQ, in 664 subjects, 493 African children (2-15 years) infected with *Schistosoma mansoni* and *S. haematobium*, and 171 Lao adults (15-78 years) infected with *Opisthorchis viverrini*. Racemate tablets were administered as single doses of 20, 40 and 60 mg/kg in children and 30, 40 and 50 mg/kg in 129 adults, and as 3 \times 25 mg/kg apart in 42 adults. Samples collected by the dried-blood-spot technique were assayed by LC-MS/MS. A two-compartment disposition model, with allometric scaling and dual first-order and transit absorption, was developed using Phoenix™ software. Inversely parallel functions of age described the apparent oral bioavailability (BA) and clearance maturation in children and ageing in adults. BA decreased slightly in children with dose increase, and by 35% in adults with multiple dosing. Crushing tablets for preschool-aged children increased the first-order absorption rate by 64%. The mean transit absorption time was 70% higher in children. A popPK model for R-PZQ integrated African children over 2 years of age with schistosomiasis and Lao adults with opisthorchiasis, and should be useful to support dose optimization in children. In vitro hepatic and intestinal metabolism data would help refining and validating the model in younger children as well as in target ethnic pediatric and adult groups.

A comparison of modelling the spatio-temporal pattern of disease: a case study of schistosomiasis japonica in Anhui Province, China.

Su, Q., Bergquist, R., Ke, Y., Dai, J., He, Z., Gao, F., Zhang, Z., Hu, Y.

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Trans R Soc Trop Med Hyg

<https://doi.org/10.1093/trstmh/trab174>

The construction of spatio-temporal models can be either descriptive or dynamic. In this study we aim to evaluate the differences in model fitting between a descriptive model and a dynamic model of the transmission for intestinal schistosomiasis caused by *Schistosoma japonicum* in Guichi, Anhui Province, China. The parasitological data at the village level from 1991 to 2014 were obtained by cross-sectional surveys. We used the fixed rank kriging (FRK) model, a descriptive model, and the integro-differential equation (IDE) model, a dynamic model, to explore the space-time changes of schistosomiasis japonica. In both models, the average daily precipitation and the normalized difference vegetation index are significantly positively associated with schistosomiasis japonica prevalence, while the distance to water bodies, the hours of daylight and the land surface temperature at daytime were significantly negatively associated. The overall root mean square prediction error of the IDE and FRK models was 0.0035 and 0.0054, respectively, and the correlation reflected by Pearson's correlation coefficient between the predicted and observed values for the IDE model (0.71; $p < 0.01$) was larger than that for the FRK model (0.53; $p = 0.02$). The IDE model fits better in capturing the geographic variation of schistosomiasis

japonica. Dynamic spatio-temporal models have the advantage of quantifying the process of disease transmission and may provide more accurate predictions.

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

Assessing the role of eosinophil-mediated immune response markers in detecting hookworm infection: A case-control study in Kintampo, Ghana.

Sakyi, S., Amoani, B., Opoku, S., Dzata, L., Aniagyei, W., Senu, E., Dankwa, K., Wilson, M.

03-06-2022

Health Sci Rep

<https://doi.org/10.1002/hsr2.674>

Human hookworm disease caused by *Ancylostoma duodenale* and *Necator americanus* is a serious public health problem. Hookworm infection activates eosinophil-mediated tissue inflammatory responses, involving the production of the eosinophil-specific chemokine (eotaxin), recruitment of eosinophils, secretion of the cationic protein, and production of antiparasite immunoglobulin E (IgE). We investigated eosinophil-mediated immune response as markers (CCL11, eosinophil cationic protein [ECP], and IgE) for detecting hookworm infection. This case-control study was carried out in hookworm endemic areas within the Kintampo North Municipality. Forty hookworm-positive subjects and 36 apparently healthy individuals were recruited as cases and controls, respectively. Stool samples were collected for hookworm detection by the Kato-Katz technique and speciation by polymerase chain reaction. Approximately, 5ml of intravenous blood was used to obtain plasma for the immunological assays. Of eosinophil-mediated immune response markers studied, ECP and CCL11 were significantly higher among hookworm patients compared to controls. Increasing CCL11 ($\beta=-0.81$, $p=0.015$) was associated with a significant decrease hookworm intensity. However, increasing eosinophil count ($\beta=0.62$, $p=0.027$) was associated with significant increase in hookworm intensity. In receiver operator characteristics analysis, ECP could significantly detect hookworm infection with a very high area under the curve (AUC) (AUC=0.97, $p<0.0001$). At a cutoff of 39.05, ECP was the best eosinophil-mediated immune response marker for detecting hookworm infection with a sensitivity of 97.2%, specificity of 87.8%, a positive predictive value of 89.7%, and a negative predictive value of 96.6%. ECP best predicts eosinophil-mediated immune response for detecting hookworm infection, while CCL11 and eosinophil count better predict the intensity of hookworm. Moreover, the ECP level is a good indicator of hookworm infection and intensity and may require additional investigations to augment current hookworm diagnostic techniques.

Helminth infections and allergic diseases: Systematic review and meta-analysis of the global literature.

Arrais, M., Maricoto, T., Nwaru, B., Cooper, P., Gama, J., Brito, M., Taborda-Barata, L.

28-12-2021

J Allergy Clin Immunol

<https://pubmed.ncbi.nlm.nih.gov/34968529>

There is considerable research interest in the role of helminth infections in the development of allergic diseases. However, findings from previous studies are mixed. Existing systematic reviews of these studies are outdated. We performed a systematic review of the global literature on the association between helminth infections and development and clinical outcomes of allergic diseases. We searched Cochrane Library, MEDLINE, EMBASE, ISI Web of Science, PubMed, Global Index Medicus, Scielo, KoreaMed, Google Scholar, and Lilacs for studies published up to January 2020. We included observational epidemiological studies (cohort, case-control, and cross-sectional studies) of children and adults reporting associations between helminth infections and asthma, allergic rhinitis, eczema, and atopy. We performed random-effects meta-analysis to summarize the effect estimates. We included 80 studies with 99,967 participants. In the meta-analyses, we did not observe an overall association between helminth infections and allergic diseases. There was, however, evidence that *Ascaris lumbricoides* infections were associated with an increased risk of bronchial hyperreactivity in children (risk ratio, 1.41; 95% CI, 1.17-1.70; $I^2 = 50$; P for $I^2 = .09$), and were associated with an increased risk of atopy among helminth-infected adults (risk ratio, 1.37; 95% CI, 1.18-1.61; $I^2 = 52$; P for $I^2 = .02$). We found no study that addressed the association between helminth infection and clinical outcomes of allergic diseases. The overall strength of the underlying evidence was low to moderate. Helminth infections may increase the risk of bronchial hyperreactivity in children and atopy in adults. Well-designed longitudinal cohorts may help clarify potential causal associations between chronic helminth infections and allergic diseases.

GALE

Diagnosis and Clinical Characteristics of Scabies in a Tertiary Care Hospital During the SARS-CoV-2 Pandemic: A Descriptive Study.

Aguado Vázquez, Á., Gegúndez Hernández, H., Melgosa Ramos, F., Díaz Corpas, T.

02-06-2022

Actas Dermosifiliogr

<https://pubmed.ncbi.nlm.nih.gov/35659613>

Health status assessment of a population of asylum seekers in Northern Italy.

Manfredi, L., Sciannameo, V., Destefanis, C., Prisecaru, M., Cossu, G., Gnani, R., Macciotta, A., Catalano, A., Pepe, R., Sacerdote, C., Ricceri, F.

03-06-2022

Global Health

<https://doi.org/10.1186/s12992-022-00846-0>

Since 2011 Italy has faced an extraordinary increase in migrants arrivals, mainly from the Mediterranean route, one of the world's most dangerous journeys. The purpose of the present article is to provide a comprehensive picture of the migrants' health status in the "T. Fenoglio" centre, Settimo Torinese (Turin, Italy). A retrospective cross-sectional study was conducted using data collected from June 2016 to May 2018 on adult migrants (over 18 years old) from Africa, Middle East and South East Asia (Bangladesh, Cambodia, India, Nepal). Data was collected through the migrants' medical records. Descriptive statistics were performed on socio-demographic variables. The diagnosed diseases were anonymously registered and classified according to the International Classification of Primary Care (ICPC-2). Conditional Inference Trees were used to perform a descriptive analysis of the sample and to detect the covariates with the strongest association with the variables Disease on arrival, Disease after arrival, ICPC on arrival and ICPC after arrival. Analyzed observations were 9 857. 81.8% were men, median age was 23 (Interquartile range: 20.0-27.4). 70.3% of the sample came from Sub-Saharan Africa. 2 365 individuals (24%) arrived at the centre with at least one disease. On arrival, skin (27.71%), respiratory (14.46%), digestive (14.73%) and generic diseases (20.88%) were the most frequent. During the stay respiratory diseases were the most common (25.70%). The highest probability of arriving with a disease occurred in 2018 and during the period September-November 2016, in particular for people from the Horn of Africa. During this period and also in the first half of 2017, skin diseases were the most reported. In seasons with lower prevalence of diseases on arrival the most common disease code was generic for both men and women (usually fever or trauma). This study provides information on the diverse diseases that affect the asylum seekers population. In our sample, the Horn of Africa was the most troubled area of arrival, with severe conditions frequently reported regarding skin diseases, in particular scabies. 2018 was the most critical year, especially for migrants from the Horn of Africa and Sub-Saharan Africa. During the stay at the camp, the prevalence of respiratory diseases increased. However, skin diseases remained the main issue for people from the Horn of Africa. Overall, the most reported diseases in the sample were dermatological, respiratory, digestive and generic diseases, both on arrival and during the stay. A better understanding of the health status of asylum seekers is an important factor to determine a more efficient reception and integration process and a better allocation of economic resources in the context of migrants' health care.

Occurrence of sarcoptic mange in free-ranging vicuñas (*Vicugna vicugna*) of the Andean high plateau region of Argentina.

Sosa, F., Bertoni, E., Micheloud, J., Vallejo, D., Olmos, L., Florin-Christensen, M., Romero, S.

09-04-2022

Parasitol Res

<https://doi.org/10.1007/s00436-022-07506-7>

Free-ranging vicuñas (*Vicugna vicugna*) are handled in some areas of the Andean high plateau region following an ancestral practice known as chaku, which consists in their transient capture and shearing of their fiber for commercialization. In this study, 807 vicuñas captured during 12 chaku events that took place in 2019 in the province of Jujuy, Argentina, were examined for typical mange skin lesions. Twenty-eight of the examined vicuñas presented alopecia with erythema, exudation, hyperkeratosis, and/or bleeding scarred lesions, mostly in the chest, rear and front legs, and inguinal zone. Most of the cases (82%) appeared in Laguna Cucho at 4900 masl, where 23% of the animals presented these skin reactions. Microscopic evaluation of skin scrapings revealed the presence of a great number of 0.1- to 0.4-mm-long mites of different life cycle stages, morphologically compatible with the species *Sarcoptes scabiei*. This etiological agent was confirmed by PCR amplification and sequencing of a cox-1 species-specific segment. Histopathological examination of skin biopsies showed extensive infiltration of the dermis with lymphocytes, neutrophils and eosinophils, hyperplasia at different stages, epidermis degeneration, and hyperkeratosis. This is the first characterization of sarcoptic mange in free-ranging vicuñas by clinical examination, mite morphology, histopathological studies, and molecular confirmation in the region. Mange hampers the welfare of vicuñas and the economy of the local communities that organize chaku events since infested vicuñas cannot be sheared. Its long-term effects are unknown but it might affect the fitness and survival of this iconic South American camelid.

Unexpected consequences of SARS-CoV-2 pandemic: scabies infestation.

Griffin, L., Pender, E., Laing, M., Markham, T.

06-04-2022

Clin Exp Dermatol

<https://doi.org/10.1111/ced.15151>

The use of dermoscopy to support the diagnosis of sarcoptic mange in two dogs.

Legnani, S., Buckley, L.

20-02-2022

Vet Dermatol

<https://doi.org/10.1111/vde.13059>

Two unrelated adult dogs presenting with chronic pruritic dermatitis were diagnosed with sarcoptic mange through the in vivo dermoscopic visualisation of *Sarcoptes scabiei* mites. The species of mite was confirmed via microscopy of

superficial skin scrapings taken from lesional skin. Dermoscopy offers rapid point-of-care, noninvasive screening for dogs with sarcoptic mange.

Serial dermoscopic monitoring of subungual scabies mites in an infant with crusted scabies.

Jiang, Y., Zhan, A., Qiu, F., Fan, Y.

15-02-2022

J Eur Acad Dermatol Venereol

<https://doi.org/10.1111/jdv.17994>

Direct microscopy in the dermatology clinic: enhancing the management of skin infections and infestations.

Revue de littérature

Chandler, D.

03-04-2022

Clin Exp Dermatol

<https://doi.org/10.1111/ced.15118>

Direct microscopy is a valuable skill in the management of skin infections and infestations, yet it is underutilized in dermatology clinics. This review details its use in identifying fungal skin infections and scabies infestations, outlining the steps involved in sample collection, preparation and interpretation.

Prevalence of Scabies in the Covid-19 Pandemic Period and Determination of Risk Factors for Scabies: a Hospital-Based Cross-Sectional Study in Northeast Turkey.

Karaca Ural, Z., Çatak, B., Ağaoğlu, E.

02-02-2022

Acta Parasitol

<https://doi.org/10.1007/s11686-022-00524-6>

There is an increase in the incidence of scabies in Turkey, which started before the Covid-19 pandemic, and this situation is considered as an epidemic. With this study, we aimed to reveal the prevalence of scabies during the pandemic period and the risk factors that are effective in the transmission of scabies. Our study was performed as a cross-sectional study in 376 patients who applied to our dermatology outpatient clinic between 1st and 30th April 2021. Sociodemographic and socioeconomic characteristics, living space, health behavior, and health care utilization of the patients were questioned. The prevalence of scabies was determined as 10.9%. Features such as sex, area of residence, age, formal education status, employment status, total income, number of shower, number of people per room, water source, and heating method, which were found to be significant as a result of the double test, were included in the logistic regression analysis. Scabies was found 2.728 times (CI 1.325-5.557) more in those who live in rural areas than those who live in urban areas, 2.714 times (CI 1.365-5.451) more in men than women, 2.707 times (CI 1.256-5.833) more in

nonworking than working, 2.354 times (CI 1.057-5.243) more in those with less than 9 showers per month than those with 9 or more showers per month. During the Covid-19 pandemic period, the prevalence of scabies in Turkey is increasing and it is becoming a serious health problem. Our study emphasizes this increase and determines the risk factors for transmission.

MORSURES DE SERPENT

Acute ischemic stroke: a rare complication of hump-nosed pit viper (*Hypnale spp.*) bite: a case report.

Namal Rathnayaka, R., Nishanthi Ranathunga, P., Kularatne, S., Jayasinghe, S.

04-06-2022

J Med Case Rep

<https://doi.org/10.1186/s13256-022-03442-3>

Hump-nosed pit viper is a medically important deadly venomous snake in Sri Lanka and is the commonest cause of venomous snakebites in the country. It frequently causes local effects and systemic manifestations such as acute kidney injury and coagulopathy that occur in less than 10% of all bites. This also includes some atypical presentations such as thrombotic microangiopathy and myocardial infarction. Currently, no antivenom is available for hump-nosed pit viper bites in Sri Lanka, and patients are managed with supportive treatment. This case illustrates an acute ischemic stroke following a hump-nosed viper bite, which is the second case in the literature. A 71-year-old a Sinhalese male patient presented with left-sided hemiparesis with mouth deviation on day 2 of hump-nosed viper (*Hypnale spp.*) bite on the right foot. Non-contrast computed tomography of brain showed right ischemic stroke in internal capsule. He was given antiplatelets and statins and continued supportive treatment including limb physiotherapy and speech therapy. He recovered completely and was discharged on day 4 with clinic follow-up. Physicians should be aware that ischemic cerebral infarcts may occur following hump-nosed pit viper bites.

Coagulopathy following *Crotalinae* snakebites in northeast Florida.

Maharaj, S., Seegobin, K., Chang, S.

10-01-2022

Blood Coagul Fibrinolysis

<https://doi.org/10.1097/MBC.0000000000001123>

Effects of *Crotalinae* envenomation vary by geographical areas and research into coagulopathy and effects of antivenom are needed to optimize management. This was a single-center retrospective review with testing on presentation and 4h after; antivenom administration was noted and data analyzed overall and comparing envenomations. One hundred and nineteen snakebites evaluated with 59 identified as *Crotalinae*

and half receiving antivenom. PT/aPTT was elevated in 20% of water moccasin/copperhead and 21% of rattlesnake bites. DIC-like syndrome occurred in 8% water moccasin/copperhead and 6% rattlesnake bites. Antivenom did not seem to correct PT or aPTT at 4 h follow-up in most cases. Thrombotic microangiopathy was not seen. Coagulopathy was prevalent affecting one in five patients in this cohort and does seem to persist at short interval follow-up, even in those receiving antivenom. We support guidelines recommending clinical monitoring and serial coagulation profiles in such cases. Blood Coagul Fibrinolysis 30:000 - 000 Copyright © 2022 Wolters Kluwer Health, Inc. All rights reserved.

Brief Information on Nonvenomous Snakebites in Brazil.

Citeli, N., Monteiro, W., Bernarde, P.

07-04-2022

Wilderness Environ Med

<https://pubmed.ncbi.nlm.nih.gov/35400570>

Venomous animals in a changing world.

Martinez, P., Gutiérrez, J., Olalla-Tárraga, M., Amado, T.

05-04-2022

Glob Chang Biol

<https://doi.org/10.1111/gcb.16175>

The climatic changes of the next decades will modify human and livestock interactions with venomous animals; Some venomous species will disappear in the coming decades; Other venomous species will shift their distributions or increase their geographic ranges invading new countries that may not have specific antivenoms.

"At the hospital they do not treat venom from snakebites": A qualitative assessment of health seeking perspectives and experiences among snakebite victims in Rwanda.

Schurer, J., Dam, A., Mutuyimana, M., Runanira, D.,

Nduwayezu, R., Amuguni, J.

24-02-2022

Toxicon X

<https://doi.org/10.1016/j.toxcx.2022.100100>

Snakebite envenomation (SBE) is a serious medical condition with human, animal, and environmental factors driving occurrence. In Rwanda, the number of SBE cases reported by the medical system is far lower than regional estimates for SBE incidence, suggesting that victims might be seeking care outside of formal medical structures. Our goals were to describe circumstances surrounding snakebite and to explore experiences of snakebite victims in accessing treatment. For this qualitative study, our team recruited individuals bitten by snakes between 2013 and 2018, who sought care either from traditional healers (N = 40) or hospitals (N = 65). In-depth interviews based on a semi-structured interview guide were

conducted by telephone in Kinyarwanda. Inductive thematic analysis was conducted by two team members. Our respondents reported similar environmental circumstances surrounding their snake encounters; namely, farm fields, roads, and their homes, as well as inadequate lighting. Unsafe First Aid practices, including burning/sucking/cutting the skin and tourniquet, were often performed immediately after bites. Respondents reported various reasons for seeking traditional or hospital care, such as perceived cost, distance, transportation, and especially, community beliefs and treatment outcomes of other victims. Respondents described envenomation of livestock as well as the sale of livestock to pay SBE-related medical expenses. Improving trust and use of formal medical services will require enhanced hospital delivery of high quality medical services for SBE through improved stocking of appropriate anti-venom and reduced delays during intake. Communities might also benefit from education campaigns that discourage unsafe First Aid practices and address the common misperception that physicians are not trained to treat SBE.

Assessment of the availability of snakebite antivenom in health facilities in Ndola District, Zambia: a cross-sectional study.

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Despite snakebite antivenom being included on the WHO list of essential medicines, many parts of the world, especially Africa, lack effective and safe antivenoms. A descriptive, field-based, cross-sectional study was undertaken from August to November 2020 in 40 out of 71 health facilities in Ndola district. Interviews and physical inspection were conducted at each facility. The study revealed that only three (8%) of all the private health facilities had antivenom available at the time of the assessment. Factors significantly associated with antivenom supply included lack of central country supply (90%), lack of demand of the antivenom (55%) and no budget allocation for the antivenom (95%). Despite the high number of notified snakebites within Ndola district, there remains poor availability of snakebite antivenom within the district.