



Réseau MTN Francophone

Veille scientifique Maladies tropicales négligées

Semaine 20

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DENGUE, CHIKUNGUNYA ET MALADIE A VIRUS ZIKA

Performance Evaluation of a Dengue IgG Rapid Diagnostic Test Designed to Determine Dengue Serostatus as Part of Prevaccination Screening.

Liberal, V., Forrat, R., Zhang, C., Pan, C., Bonaparte, M., Yin, W., Zheng, L., Viscardi, V., Wu, Y., Ataman-Önal, Y., Savarino, S., Chen, C.

23-05-2022

Microbiol Spectr

<https://doi.org/10.1128/spectrum.00711-21>

The World Health Organization has recommended prevaccination screening for prior dengue infection as the preferred approach prior to vaccination with the dengue vaccine CYD-TDV. These screening tests need to be highly specific and sensitive, and deliverable at the point-of-care. We evaluate here the sensitivity and specificity of the newly developed *OnSite* Dengue IgG rapid diagnostic test (RDT). A retrospective double-blind study of the sensitivity and specificity of the *OnSite* Dengue IgG RDT was performed using a sample panel consisting of archived serum specimens collected during CYD-TDV clinical trials in Latin American and Asia, with the reference serostatus for each sample determined by an algorithm using measured dengue PRNT₉₀, PRNT₅₀, and NS1 IgG ELISA. An additional panel of dengue seronegative samples positive for other flaviviruses and infections was used to assess cross-reactivity. Samples were included from 579 participants; 346 in the specificity panel and 233 in the sensitivity panel. The *OnSite* dengue IgG RDT exhibited a specificity of 98.0% (95% CI = 95.9 to 99.2) and sensitivity of 95.3% (95% CI = 91.7 to 97.6). The sensitivity for samples exhibiting a multitypic immune profile (PRNT₉₀-positive to >1 dengue serotype) was 98.8% while for monotypic immune samples (PRNT₉₀-positive to a single dengue serotype) it was 88.1%. The *OnSite* dengue IgG RDT showed minimal to no cross-reactivity to related flaviviruses. These findings support the use of the *OnSite* dengue IgG RDT to determine dengue serostatus in CYD-TDV prevaccination screening. **IMPORTANCE** Dengue remains a significant public health issue, with over 5.2 million cases reported to the World Health Organization (WHO) in 2019. The tetravalent dengue vaccine (CYD-TDV) is currently licensed for use in those aged ≥9 years; however, vaccinees with no previous exposure to dengue experience an increased risk of hospitalized and severe dengue upon subsequent heterotypic infection. Consequently, WHO recommends screening for prior dengue infection before vaccination. Screening tests for previous infection need to be highly specific and sensitive, and deliverable at the point-of-care. High sensitivity ensures that the largest number of individuals with previous infection can be identified and vaccinated, while high specificity prevents the inadvertent vaccination of those without previous infection. This study of the *OnSite* Dengue IgG Rapid Test, which was explicitly developed to meet this need, found that it had both high specificity (98.0% [95% CI = 95.9 to 99.2]) and sensitivity (95.3% [95% CI = 91.7 to 97.6]).

Gold, Bonds, and Epidemics: A safe haven study.

Choudhury, T., Kinateder, H., Neupane, B.

16-05-2022

Financ Res Lett

<https://doi.org/10.1016/j.frl.2022.102978>

The COVID-19 pandemic raised the question whether gold and sovereign bonds are a safe haven during epidemics. We study the effectiveness as safe haven during the epidemics caused by SARS, Ebola, Zika, Swine Flu, and COVID-19. To this end, this study employs a DCC-GARCH model to analyze the conditional correlations between daily returns of S&P 500 and MSCI Emerging Markets Index with gold and the major sovereign bonds. Our results show that gold is a weak safe haven for stock market investors during the epidemics, and U.S. treasuries are the safest option, followed by Japanese sovereign bonds.

Effectiveness of environmental interventions to reduce entomological indices of dengue, Zika, and chikungunya vector.

Revue de littérature

Tortosa-La Osa, S., Martín-Ruiz, E., Galán-Relaño, Á., de Labry-Lima, A.

19-05-2022

Acta Trop

<https://pubmed.ncbi.nlm.nih.gov/35598649>

Vector-borne diseases are a major public health problem. Among them, dengue, Zika and chikungunya illnesses are increasing their incidence and geographical expansion. Since vector control is the main measure to prevent these diseases, this systematic review aims to determine the effectiveness of environmental interventions for the prevention of the transmission of these three diseases, as well as for the reduction of their burden. Experimental studies of environmental management interventions aimed at vector control were included. The outcome variables of interest were disease burden indicators and entomological indicators. Of the 923 references initially retrieved, after discarding those that were duplicated or didn't comply with the inclusion criteria, a total of 7 articles were included. All included studies carried out environmental manipulation interventions and only 1 carried out an environmental modification intervention. Regarding the outcome variables, all used entomological indicators (larval or pupae indices). Of those, pupae indices are better indicators of vector abundance. In 4 out of the 6 studies, there was a statistically significant reduction of the pupae indices related to the elimination of small containers, manipulation of large tanks and cleaning outdoor spaces. These interventions are easy to implement and involve little resources, which acquires special importance regarding areas with limited resources. Although it is assumed that a reduction of mosquitoes would lead to a reduction or the risk of transmission, a little evidence proving this has been published. It would be advisable that, in addition to entomological indicators, epidemiological, environmental and sociodemographic factors would be taken into consideration,

bearing in mind that mosquito density is one of the many factors that influence the transmission of these viruses. None of the papers included used disease indicators, not allowing to demonstrate if environmental interventions contribute to reduce disease burden.

Zika in the MIDST of the COVID-19 Pandemic.

Tangsathapornpong, A., Thisyakorn, U.

20-05-2022

Asia Pac J Public Health

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

Suppression of TGF- β /Smad2 signaling by GW788388 enhances DENV-2 clearance in macrophages.

Gs, T., Aa, A., Lr, T., D, C., Oc, M., Rs, A., Mc, W., Em, d.

20-05-2022

J Med Virol

<https://doi.org/10.1002/jmv.27879>

Dengue fever, caused by the dengue virus (DENV-1, -2, -3 and -4), affects millions of people in the tropical and subtropical regions worldwide. Severe dengue is correlated with high viraemia and cytokine storm, such as high levels of transforming growth factor- β 1 (TGF- β 1) in the patient's serum. Here, the TGF- β 1 signaling was investigated in the context of in vitro viral clearance. Macrophages were infected with DENV-2 at MOI 5 and treated with the TGF- β receptor 1 and 2 inhibitor, GW788388. TGF- β 1 expression, signal transduction and viral load were evaluated 48 h after DENV-2 infection by ELISA, immunofluorescence, and RT-qPCR assays. Total TGF- β 1 level was reduced in 15% after DENV-2 infection, but the secretion of its biologically active form increased 3-fold during infection, which was followed by the phosphorylation of Smad2 protein. Phosphorylation of Smad2 was reduced by treatment with GW788388 and it was correlated with reduced cytokine production. Importantly, treatment led to a dose-dependent reduction in viral load, ranging from 6.6×10^5 RNA copies/mL in untreated cultures to 2.3×10^3 RNA copies /mL in cultures treated with 2 ng/mL of GW788388. The anti-TGF- β 1 antibody treatment also induced a significant reduction in viral load to 1.6×10^3 RNA copies /mL. On the other hand, the addition of recombinant TGF- β 1 in infected cultures promoted an increase in viral load to 7.0×10^6 RNA copies /mL. These results support that TGF- β 1 plays a significant role in DENV-2 replication into macrophages and suggest that targeting TGF- β 1 may represent an alternative therapeutic strategy to be explored in dengue infection. This article is protected by copyright. All rights reserved.

Ultrasound-assisted nanoemulsion of *Trachyspermum ammi* essential oil and its constituent thymol on toxicity and biochemical aspect of *Aedes aegypti*.

Subaharan, K., Senthamarai Selvan, P., Subramanya, T., Senthooraja, R., Manjunath, S., Das, T., Pragadheesh, V.,

Bakthavatsalam, N., Mohan, M., Senthil-Nathan, S., Uragayala, S., Samuel, P., Govindarajan, R., Eswaramoorthy, M.
21-05-2022

Environ Sci Pollut Res Int

<https://doi.org/10.1007/s11356-022-20870-2>

Aedes aegypti is the main vector of yellow fever, chikungunya, Zika, and dengue worldwide and is managed by using chemical insecticides. Though effective, their indiscriminate use brings in associated problems on safety to non-target and the environment. This supports the use of plant-based essential oil (EO) formulations as they are safe to use with limited effect on non-target organisms. Quick volatility and degradation of EO are a hurdle in its use; the present study attempts to develop nanoemulsions (NE) of *Trachyspermum ammi* EO and its constituent thymol using Tween 80 as surfactant by ultrasonication method. The NE of EO had droplet size ranging from 65 ± 0.7 to 83 ± 0.09 nm and a poly dispersity index (PDI) value of 0.18 ± 0.003 to 0.20 ± 0.07 from 1 to 60 days of storage. The NE of thymol showed a droplet size ranging from 167 ± 1 to 230 ± 1 nm and PDI value of 0.30 ± 0.03 to 0.40 ± 0.008 from 1 to 60 days of storage. The droplet shape of both NEs appeared spherical under a transmission electron microscope (TEM). The larvicidal effect of NEs of EO and thymol was better than BEs (Bulk emulsion) of EO and thymol against *Ae. aegypti*. Among the NEs, thymol (LC₅₀ 34.89 ppm) had better larvicidal action than EO (LC₅₀ 46.73 ppm). Exposure to NEs of EO and thymol causes the shrinkage of the larval cuticle and inhibited the acetylcholinesterase (AChE) activity in *Ae. aegypti*. Our findings show the enhanced effect of NEs over BEs which facilitate its use as an alternative control measure for *Ae. aegypti*.

Economic burden of dengue fever in China: A retrospective research study.

Xu, M., Chang, N., Tu, T., Sun, J., Jiang, J., Xia, Y., Tang, W., Ji, H., Zhao, X., Zhu, J., Qi, L., Liu, X., Liu, Q.

20-05-2022

PLoS Negl Trop Dis

<https://doi.org/10.1371/journal.pntd.0010360>

Background: Dengue fever has been a significant public health challenge in China. This will be particularly important in the context of global warming, frequent international travels, and urbanization with increasing city size and population movement. In order to design relevant prevention and control strategies and allocate health resources reasonably, this study evaluated the economic burden of dengue fever in China in 2019. **Methods:** The economic burden of dengue fever patients was calculated from both family and the organisation perspectives. A survey was conducted among 1,027 dengue fever patients in Zhejiang, Chongqing, and Yunnan Provinces. Treatment expenses, lost working days, and insurance reimbursement expenses information were collected to estimate the total economic burden of dengue fever patients in 2019. The expenditures related to dengue fever prevention and control from government, Center for Disease Control and Prevention (CDC), communities and subdistrict offices of 30

counties (or districts) in Zhejiang Province and Chongqing City were also collected. **Results:** The direct, indirect and total economic burden for dengue fever patients in 2019 in the three Provinces were about 36,927,380.00 Chinese Yuan (CNY), 10,579,572.00 CNY and 46,805,064.00 CNY, respectively. The costs for prevention and control of dengue fever for the counties (or districts) without cases, counties (or districts) with imported cases, and counties (or districts) with local cases are 205,800.00 CNY, 731,180.00 CNY and 6,934,378.00 CNY, respectively. The total investment of dengue fever prevention and control in the 30 counties in China in 2019 was approximately 3,166,660,240.00 CNY. **Conclusion:** The economic burden of dengue fever patients is relatively high, and medical insurance coverage should be increased to lighten patients' direct medical economic burden. At the same time, the results suggests that China should increase funding for primary health service institutions to prevent dengue fever transmission.

Detection of pyrethroid resistance mutations and intron variants in the voltage-gated sodium channel of *Aedes (Stegomyia) aegypti* and *Aedes (Stegomyia) albopictus* mosquitoes from Lao People's Democratic Republic.

Marcombe, S., Shimell, K., Savage, R., Howlett, E., Luangamath, P., Nilaxay, S., Vungkyly, V., Baby, A., King, M., Clarke, J., Jeffries, C., Jojo, J., Lacey, E., Bhatti, F., Mabika, D., Dela Cruz, A., Fisher, C., Mbadu, M., Despiniadis, I., Brey, P., Thammavong, P., Jones, A.

20-05-2022

Med Vet Entomol

<https://doi.org/10.1111/mve.12580>

In Lao People's Democratic Republic, *Aedes aegypti* (Linnaeus 1762) and *Aedes albopictus* (Skuse 1894) mosquitoes (Diptera: Culicidae) are vectors of arboviral diseases such as dengue. As the treatment for these diseases is limited, control of the vectors with the use of pyrethroid insecticides is still essential. However, mutations in the voltage-gated sodium channel (vgsc) gene giving rise to pyrethroid resistance are threatening vector control programs. Here, we analysed both *Ae. aegypti* and *Ae. albopictus* mosquitoes, which were collected in different districts of Laos (Kaysone Phomvihane, Vangvieng, Saysettha and Xaythany), for vgsc mutations commonly found throughout Asia (S989P, V1016G and F1534C). Sequences of the vgsc gene showed that the F1534C mutation was prevalent in both *Aedes* species. S989P and V1016G mutations were detected in *Ae. aegypti* from each site and were always found together. In addition, the mutation T1520I was seen in *Ae. albopictus* mosquitoes from Saysettha district as well as in all *Ae. aegypti* samples. Thus, mutations in the vgsc gene of *Ae. aegypti* are prevalent in the four districts studied indicating growing insecticide resistance throughout Laos. Constant monitoring programmes and alternative strategies for controlling *Aedes* should be utilized in order to prolong the effectiveness of pyrethroids thereby maximizing vector control.

Natural products as Zika antivirals.

Revue de littérature

Fong, Y., Chu, J.

20-05-2022

Med Res Rev

<https://doi.org/10.1002/med.21891>

Zika virus (ZIKV) is an arbovirus belonging to the flavivirus genus and is transmitted in *Aedes* mosquito vectors. Since its discovery in humans in 1952 in Uganda, ZIKV has been responsible for many outbreaks in South America, Africa, and Asia. Patients infected with ZIKV are usually asymptomatic; mild symptoms include fever, joint and muscle pain, and fatigue. However, severe infections may have neurological implications, such as Guillain-Barré syndrome and fetal microcephaly. To date, there are no existing approved therapeutic drugs or vaccines against ZIKV infections; treatments mainly target the symptoms of infection. Preventive measures against mosquito breeding are the main strategy for limiting the spread of the virus. Antiviral drug research for the treatment of ZIKV infection has been rapidly developing, with many drug candidates emerging from drug repurposing studies, and compound screening. In particular, several studies have demonstrated the potential of natural products as antivirals for ZIKV infection. Hence, this paper will review recent advances in natural products in ZIKV antiviral drug discovery.

Transcriptome analysis of *Aedes albopictus* midguts infected by dengue virus identifies a gene network module highly associated with temperature.

Liu, Z., Xu, Y., Li, Y., Xu, S., Li, Y., Xiao, L., Chen, X., He, C., Zheng, K.

19-05-2022

Parasit Vectors

<https://doi.org/10.1186/s13071-022-05282-y>

Background: Dengue is prevalent worldwide and is transmitted by *Aedes* mosquitoes. Temperature is a strong driver of dengue transmission. However, little is known about the underlying mechanisms. **Methods:** *Aedes albopictus* mosquitoes exposed or not exposed to dengue virus serotype 2 (DENV-2) were reared at 23 °C, 28 °C and 32 °C, and midguts and residual tissues were evaluated at 7 days after infection. RNA sequencing of midgut pools from the control group, midgut breakthrough group and midgut nonbreakthrough group at different temperatures was performed. The transcriptomic profiles were analyzed using the R package, followed by weighted gene correlation network analysis (WGCNA) and Kyoto Encyclopedia of Genes and Genomes (KEGG) analysis to identify the important molecular mechanisms regulated by temperature. **Results:** The midgut infection rate and midgut breakthrough rate at 28 °C and 32 °C were significantly higher than those at 23 °C, which indicates that high temperature facilitates DENV-2 breakthrough in the *Ae. albopictus* midgut. Transcriptome sequencing was performed to investigate the antiviral

mechanism in the midgut. The midgut gene expression datasets clustered with respect to temperature, blood-feeding and midgut breakthrough. Over 1500 differentially expressed genes were identified by pairwise comparisons of midguts at different temperatures. To assess key molecules regulated by temperature, we used WGCNA, which identified 28 modules of coexpressed genes; the ME3 module correlated with temperature. KEGG analysis indicated that RNA degradation, Toll and immunodeficiency factor signaling and other pathways are regulated by temperature. **Conclusions:** Temperature affects the infection and breakthrough of *Ae. albopictus* midguts invaded by DENV-2, and *Ae. albopictus* midgut transcriptomes change with temperature. The candidate genes and key pathways regulated by temperature provide targets for the prevention and control of dengue.

Cross-reactive antibodies facilitate innate sensing of dengue and Zika viruses.

Aisenberg, L., Rousseau, K., Cascino, K., Massaccesi, G., Aisenberg, W., Luo, W., Muthumani, K., Weiner, D., Whitehead, S., Chattergoon, M., Durbin, A., Cox, A.
19-05-2022

JCI Insight

<https://doi.org/10.1172/jci.insight.151782>

The *Aedes aegypti* mosquito transmits both dengue (DENV) and Zika (ZIKV) viruses. Individuals in endemic areas are at risk for infection with both viruses as well as repeated DENV infection. In the presence of anti-DENV antibodies, outcomes of secondary DENV infection range from mild to life-threatening. Further, the role of cross-reactive antibodies on the course of ZIKV infection remains unclear. We assessed the ability of cross-reactive DENV monoclonal antibodies or polyclonal immunoglobulin isolated after DENV vaccination to upregulate type I interferon (IFN) production by plasmacytoid dendritic cells (pDCs) in response to both heterotypic DENV- and ZIKV- infected cells. We found a range in the ability of antibodies to increase pDC IFN production and a positive correlation between IFN production and the ability of an antibody to bind to the infected cell surface. Engagement of Fc receptors on the pDC and Fab binding of an epitope on infected cells was required to mediate increased IFN production by providing specificity to and promoting pDC sensing of DENV or ZIKV. This represents a mechanism independent of neutralization by which pre-existing cross-reactive DENV antibodies could protect a subset of individuals from severe outcomes during secondary heterotypic DENV or ZIKV infection.

Characterization of m⁶ A modifications in the contemporary Zika virus genome and host cellular transcripts.

Liu, Y., Li, K., Xu, Y., Zhu, Z., Zhao, H., Li, X., Ye, Q., Yi, C., Qin, C.
19-05-2022

J Med Virol

<https://doi.org/10.1002/jmv.27869>

Zika virus (ZIKV) suddenly evolved from a neglected arthropod-borne flavivirus into a pandemic pathogen during 2015-2016. A panel of amino acid mutations have been shown to be responsible for the enhanced neurovirulence and transmissibility of ZIKV. Recent studies have demonstrated that ZIKV genomic RNA is modified by host N⁶-methyladenosine (m⁶ A) machinery during viral replication in host cells, and the m⁶ A profiles vary among different isolates and different host cells. In the present study, using a contemporary Asian ZIKV strain isolated in 2019 (SZ1901) as a model, we profiled m⁶ A modifications on both the viral genome RNA and cellular transcripts from the ZIKV-infected human hepatocarcinoma cell line Huh7. Methylated RNA immunoprecipitation sequencing (MeRIP-seq) identified a unique m⁶ A map in the genome of ZIKV strain SZ1901 that is different from all previous isolates. Meanwhile, ZIKV infection induced m⁶ A upregulation in the CDS regions but downregulation in the 3' UTR of host RNA transcripts. The m⁶ A peak intensity in the majority of host genes was downregulated, include including ISG-related genes. Overall, our study describes unique viral and host m⁶ A profiles in contemporary ZIKV-infected Huh7 cells, highlighting the complexity and importance of m⁶ A modification during viral infection. This article is protected by copyright. All rights reserved.

Association between nutritional status and dengue severity in Thai children and adolescents.

Te, H., Sriburin, P., Rattanamahaphoom, J., Sittikul, P., Hattasingh, W., Chatchen, S., Sirinam, S., Limkittikul, K.
19-05-2022

PLoS Negl Trop Dis

<https://doi.org/10.1371/journal.pntd.0010398>

Most cases of dengue virus infection are mild, but severe cases can be fatal. Therefore, identification of factors associated with dengue severity is essential to improve patient outcomes and reduce mortality. The objective of this study was to assess associations between nutritional status and dengue severity among Thai children and adolescents. This retrospective cross-sectional study was based on the medical records of 355 patients with dengue treated at the Hospital for Tropical Disease (Bangkok, Thailand) from 2017 to 2019. Subjects were Thai children aged less than 18 years with dengue virus infection confirmed by positive NS1 antigen or IgM. The 1997 and 2009 World Health Organization (WHO) dengue classifications were used to define disease severity and body mass index for age while the WHO growth chart was used to classify nutritional status. The proportions of patients with dengue fever who were underweight, normal weight, and overweight were 8.8%, 61.5%, and 29.7%, respectively. The proportions of patients with dengue haemorrhagic fever (DHF) who were underweight, normal weight, and overweight were 10.2%, 66.1%, and 23.7%, respectively. The proportions of patients with non-severe dengue who were underweight, normal weight, and overweight were 8.6%, 60.9%, and 30.5%, respectively; the same proportions of patients with severe dengue were 10.5%, 67.1%, and 22.4%, respectively. Higher

proportions of patients with severe plasma leakage (DHF grade III and IV) were overweight compared with those with mild plasma leakage (DHF grade I and II) (45.5% vs. 18.8%). No difference in nutritional status was observed in patients with different dengue severity.

Anti-Dengue Activity of ZnO Nanoparticles of Crude Fucoidan from Brown Seaweed *S.marginatum*.

Kothai, R., Arul, B., Anbazhagan, V.

19-05-2022

Appl Biochem Biotechnol

<https://doi.org/10.1007/s12010-022-03966-w>

Dengue fever is a rapidly spreading infection that affects people all over the tropics and subtropics, posing a significant public health threat. The brown seaweed *Stoechospermum marginatum* was found all over the world, from South Africa (Indian Ocean) to Australia (Pacific Ocean), among other places. In India, it is only available along the coast of the Bay of Bengal, which is a small region. Various metal oxides were proved to be successful in the formation of nanoparticles and zinc is one among them. In this present study, an attempt was made to study the anti-dengue activity of green synthesized zinc oxide nanoparticles of crude fucoidan isolated from brown seaweed *S. marginatum*. The fucoidan was isolated from the seaweed by acid extraction method and then characterized by UV, HPLC, and Fourier Transform Infra-Red (FT-IR) Spectroscopy. Then it was biosynthesized into ZnO nanoparticles and characterized by SEM-EDAX analysis. The results showed the formation of fucoidans and SEM studies showed the crystalline nature of the synthesized nanoparticles. The size of nanoparticles was in the range of 80-126 nm. The synthesized nanoparticles were tested with the C6/36 cell line and it was shown 99.09% of anti-dengue activity against the tested cell line. As an antiviral agent, the ZnO nanoparticles of fucoidans have been shown to be an excellent lead molecule for the treatment of dengue fever.

Climate Change and Cascading Risks from Infectious Disease.

Revue de littérature

Semenza, J., Rocklöv, J., Ebi, K.

19-05-2022

Infect Dis Ther

<https://doi.org/10.1007/s40121-022-00647-3>

Climate change is adversely affecting the burden of infectious disease throughout the world, which is a health security threat. Climate-sensitive infectious disease includes vector-borne diseases such as malaria, whose transmission potential is expected to increase because of enhanced climatic suitability for the mosquito vector in Asia, sub-Saharan Africa, and South America. Climatic suitability for the mosquitoes that can carry dengue, Zika, and chikungunya is also likely to increase, facilitating further increases in the geographic range and longer transmission seasons, and raising concern for expansion of these diseases into temperate zones, particularly

under higher greenhouse gas emission scenarios. Early spring temperatures in 2018 seem to have contributed to the early onset and extensive West Nile virus outbreak in Europe, a pathogen expected to expand further beyond its current distribution, due to a warming climate. As for tick-borne diseases, climate change is projected to continue to contribute to the spread of Lyme disease and tick-borne encephalitis, particularly in North America and Europe. Schistosomiasis is a water-borne disease and public health concern in Africa, Latin America, the Middle East, and Southeast Asia; climate change is anticipated to change its distribution, with both expansions and contractions expected. Other water-borne diseases that cause diarrheal diseases have declined significantly over the last decades owing to socioeconomic development and public health measures but changes in climate can reverse some of these positive developments. Weather and climate events, population movement, land use changes, urbanization, global trade, and other drivers can catalyze a succession of secondary events that can lead to a range of health impacts, including infectious disease outbreaks. These cascading risk pathways of causally connected events can result in large-scale outbreaks and affect society at large. We review climatic and other cascading drivers of infectious disease with projections under different climate change scenarios. Supplementary file1 (MP4 328467 KB).

Distance to public transit predicts spatial distribution of dengue virus incidence in Medellín, Colombia.

Shragai, T., Pérez-Pérez, J., Del Pilar Quimbayo-Forero, M., Rojo, R., Harrington, L., Rúa-Uribe, G.

18-05-2022

Sci Rep

<https://doi.org/10.1038/s41598-022-12115-6>

Dengue is a growing global threat in some of the world's most rapidly growing landscapes. Research shows that urbanization and human movement affect the spatial dynamics and magnitude of dengue outbreaks; however, precise effects of urban growth on dengue are not well understood because of a lack of sufficiently fine-scaled data. We analyzed nine years of address-level dengue case data in Medellín, Colombia during a period of public transit expansion. We correlate changes in the spread and magnitude of localized outbreaks to changes in accessibility and usage of public transit. Locations closer to and with a greater utilization of public transit had greater dengue incidence. This relationship was modulated by socioeconomic status; lower socioeconomic status locations experienced stronger effects of public transit accessibility and usage on dengue incidence. Public transit is a vital urban resource, particularly among low socioeconomic populations. These results highlight the importance of public health services concurrent with urban growth.

Machine Learning Based Forecast of Dengue Fever in Brazilian Cities using Epidemiological and Meteorological Variables.

Roster, K., Connaughton, C., Rodrigues, F.

18-05-2022

Am J Epidemiol

<https://pubmed.ncbi.nlm.nih.gov/35584963>

Dengue is a serious public health concern in Brazil and globally. In the absence of a universal vaccine or specific treatments, prevention relies on vector control and disease surveillance. Accurate and early forecasts can help reduce the spread of the disease. In this study, we develop a model to predict monthly dengue cases in Brazilian cities one month ahead from 2007-2019. We compare different machine learning algorithms and feature selection methods using epidemiological and meteorological variables. We find that different models work best in different cities, and a random forests model trained on monthly dengue cases performs best overall. It produces lower errors than a seasonal naïve baseline model, gradient boosting regression, feed-forward neural network, and support vector regression. For each city, we compute the mean absolute error between predictions and true monthly dengue cases on the test set. For the median city, the error is 12.2 cases. This error is reduced to 11.9 when selecting the optimal combination of algorithm and input features for each city individually. Machine learning and especially decision tree ensemble models may contribute to dengue surveillance in Brazil, as they produce low out-of-sample prediction errors for a geographically diverse set of cities.

Description of the mitogenome and phylogeny of *Aedes* spp. (Diptera: Culicidae) from the Amazon region.

da Silva E Silva, L., da Silva, F., Medeiros, D., Cruz, A., da Silva, S., Aragão, A., Dias, D., Sena do Nascimento, B., Júnior, J., Vieira, D., Monteiro, H., Neto, J.

16-05-2022

Acta Trop

<https://pubmed.ncbi.nlm.nih.gov/35584780>

The genus *Aedes* (Diptera: Culicidae) includes species of great epidemiological relevance, particularly involved in transmission cycles of leading arboviruses in the Brazilian Amazon region, such as the Zika virus (ZIKV), Dengue virus (DENV), Yellow fever virus (YFV), and Chikungunya virus (CHIKV). We report here the first putatively complete sequencing of the mitochondrial genomes of Brazilian populations of the species *Aedes albopictus*, *Aedes scapularis* and *Aedes serratus*. The sequences obtained showed an average length of 14,947 bp, comprising 37 functional subunits, typical in animal mitochondria (13 PCGs, 22 tRNA, and 2 rRNA). The phylogeny reconstructed by Maximum likelihood method, based on the concatenated sequences of all 13 PCGs produced at least two non-directly related groupings, composed of representatives of the subgenus *Ochlerotatus* and *Stegomyia* of the genus *Aedes*. The data and

information produced here may be useful for future taxonomic and evolutionary studies of the genus *Aedes*, as well as the Culicidae family.

A cytotoxic-skewed immune set point predicts low neutralizing antibody levels after Zika virus infection.

McCarthy, E., Odorizzi, P., Lutz, E., Smullin, C., Tenvooren, I., Stone, M., Simmons, G., Hunt, P., Feeney, M., Norris, P., Busch, M., Spitzer, M., Rutishauser, R.

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Cell Rep

<https://pubmed.ncbi.nlm.nih.gov/35584677>

Although generating high neutralizing antibody levels is a key component of protective immunity after acute viral infection or vaccination, little is known about why some individuals generate high versus low neutralizing antibody titers. Here, we leverage the high-dimensional single-cell profiling capacity of mass cytometry to characterize the longitudinal cellular immune response to Zika virus (ZIKV) infection in viremic blood donors in Puerto Rico. During acute ZIKV infection, we identify widely coordinated responses across innate and adaptive immune cell lineages. High frequencies of multiple activated cell types during acute infection are associated with high titers of ZIKV neutralizing antibodies 6 months post-infection, while stable immune features suggesting a cytotoxic-skewed immune set point are associated with low titers. Our study offers insight into the coordination of immune responses and identifies candidate cellular biomarkers that may offer predictive value in vaccine efficacy trials aimed at inducing high levels of antiviral neutralizing antibodies.

Molecular and genomic investigation of an urban outbreak of dengue virus serotype 2 in Angola, 2017-2019.

Neto, Z., Martinez, P., Hill, S., Jandondo, D., Thézé, J., Mirandela, M., Aguiar, R., Xavier, J., Dos Santos Sebastião, C., Cândido, A., Vaz, F., Castro, G., Paixão, J., Loman, N., Lemey, P., Pybus, O., Vasconcelos, J., Faria, N., de Moraes, J.

18-05-2022

PLoS Negl Trop Dis

<https://doi.org/10.1371/journal.pntd.0010255>

Background: Transmission patterns and genetic diversity of dengue virus (DENV) circulating in Africa remains poorly understood. Circulation of the DENV serotype 1 (DENV1) in Angola was detected in 2013, while DENV serotype 2 (DENV2) was detected for the first time in 2018. Here, we report results from molecular and genomic investigations conducted at the Ministry of Health national reference laboratory (INIS) in Angola on suspected dengue cases detected between January 2017 and February 2019. **Methods:** A total of 401 serum samples from dengue suspected cases were collected in 13 of the 18 provinces in Angola. Of those, 351 samples had complete data for demographic and epidemiological analysis, including age, gender, province, type of residence, clinical

symptoms, as well as dates of onset of symptoms and sample collection. RNA was extracted from samples and tested for DENV-RNA by two distinct real time RT-PCR protocols. On-site whole genome nanopore sequencing was performed for PCR+ cases. Bayesian coalescent models were used to estimate date and origin of outbreak emergence, as well as population growth rates. **Results:** Molecular diagnosis shows that 66 out of 351 (19%) suspected cases were DENV-RNA positive across 5 provinces in Angola. DENV PCR+ cases were diagnosed more frequently in urban sites compared to rural sites. Of the DENV positive samples, most were collected within 6 days of symptom onset. 93% of infections were confirmed by serotype-specific RT-PCR as DENV2 and 1 case (1.4%) was confirmed as DENV1. Six CHIKV RT-PCR positive cases were also detected during the study period, including 1 co-infection with DENV1. Most cases (87%) were detected in Luanda during the rainy season between April and October. Symptoms associated with severe dengue were observed in 11 patients, including 2 with a fatal outcome. On-site nanopore genome sequencing followed by genetic analysis revealed an introduction of DENV2 Cosmopolitan genotype (also known as DENV2-II genotype) possibly from India in or around October 2015, at least 1.5 years before its detection in the country. Coalescent models suggest relatively moderately rapid epidemic growth rates and doubling times, and a moderate expansion of DENV2 in Angola during the studied period. **Conclusion:** This study describes genomic, epidemiological and demographic characteristic of predominately urban transmission of DENV2 in Angola. We also find co-circulation of DENV2 with DENV1 and CHIKV and report several RT-PCR confirmed severe dengue cases in the country. Increasing dengue awareness in healthcare professional, expanding the monitorization of arboviral epidemics across the country, identifying most common mosquito breeding sites in urban settings, implementing innovative vector control interventions and dengue vaccination campaigns could help to reduce vector presence and DENV transmission in Angola.

Forming and updating vaccination beliefs: does the continued effect of misinformation depend on what we think we know?

Pluviano, S., Watt, C., Pompéia, S., Ekuni, R., Della Sala, S.

18-05-2022

Cogn Process

<https://doi.org/10.1007/s10339-022-01093-2>

People may cling to false facts even in the face of updated and correct information. The present study confronted misconceptions about the measles, mumps and rubella vaccine and a novel, fictitious Zika vaccine. Two experiments are reported, examining misconceptions as motivated by a poor risk understanding (Experiment 1, N=130) or the exposure to conspiracy theories (Experiment 2, N=130). Each experiment featured a Misinformation condition, wherein participants were presented with fictitious stories containing some misinformation (Experiment 1) and rumours focused on conspiracy theories (Experiment 2) that were later retracted

by public health experts and a No misinformation condition, containing no reference to misinformation and rumours. Across experiments, participants were more hesitant towards vaccines when exposed to stories including vaccine misinformation. Notwithstanding, our results suggest a positive impact of a trusted source communicating the scientific consensus about vaccines. Zika virus represents a particular case showing how missing information can easily evolve into misinformation. Implications for effective dissemination of information are discussed.

Acute haemorrhagic encephalomyelitis following dengue infection.

Vasireddy, A., Mehta, A., Seshadri, S., Madhyastha, S.

17-05-2022

BMJ Case Rep

<https://pubmed.ncbi.nlm.nih.gov/35580949>

Assessing the role of multiple mechanisms increasing the age of dengue cases in Thailand.

Huang, A., Takahashi, S., Salje, H., Wang, L., Garcia-Carreras, B., Anderson, K., Endy, T., Thomas, S., Rothman, A., Klungthong, C., Jones, A., Fernandez, S., Iamsirithaworn, S., Doung-Ngern, P., Rodriguez-Barraquer, I., Cummings, D.

09-05-2022

Proc Natl Acad Sci U S A

<https://doi.org/10.1073/pnas.2115790119>

SignificanceThe age of reported dengue hemorrhagic fever (DHF) cases, the severe form of dengue infections, has been increasing in Thailand for four decades. Factors underlying this shift remain poorly understood, challenging public health planning. Here, we found aging of the population and its effect on the hazard of transmission to be the dominant contributors, with temporal changes in surveillance practices playing a lesser role. With ongoing population aging, we expect a continuing shift of DHF toward older individuals, heightening the chance of clinical complications with comorbidities. With most other highly endemic countries facing similar shifts in age structure, the pattern is expected to appear elsewhere. Awareness is needed to improve diagnosis and treatment.

Resurfaced ZIKV EDIII nanoparticle immunogens elicit neutralizing and protective responses in vivo.

Georgiev, G., Malonis, R., Wirchnianski, A., Wessel, A., Jung, H., Cahill, S., Nyakatura, E., Vergnolle, O., Dowd, K., Cowburn, D., Pierson, T., Diamond, M., Lai, J.

28-02-2022

Cell Chem Biol

<https://pubmed.ncbi.nlm.nih.gov/35231399>

Zika virus (ZIKV) is a flavivirus that can cause severe disease, but there are no approved treatments or vaccines. A complication for flavivirus vaccine development is the potential of immunogens to enhance infection via antibody-

dependent enhancement (ADE), a process mediated by poorly neutralizing and cross-reactive antibodies. Thus, there is a great need to develop immunogens that minimize the potential to elicit enhancing antibodies. Here we utilized structure-based protein engineering to develop "resurfaced" (rs) ZIKV immunogens based on E glycoprotein domain III (ZDIII), in which epitopes bound by variably neutralizing antibodies were masked by combinatorial mutagenesis. We identified one resurfaced ZDIII immunogen (rsZDIII-2.39) that elicited a protective but immune-focused response. Compared to wild type ZDIII, immunization with resurfaced rsZDIII-2.39 protein nanoparticles produced fewer numbers of ZIKV EDIII antigen-reactive B cells and elicited serum that had a lower magnitude of induced ADE against dengue virus serotype 1 (DENV1). Our findings enhance our understanding of the structural and functional determinants of antibody protection against ZIKV.

RAGE

Recurrence of Herpetic Keratitis after COVID-19 Vaccination: A Report of Two Cases.

Fard, A., Desilets, J., Patel, S.
19-05-2022

Case Rep Ophthalmol Med

<https://doi.org/10.1155/2022/7094893>

Background: Recurrence of herpetic keratitis following vaccination has been documented following vaccination with the Zostavax, trivalent flu, hepatitis A, and rabies vaccines. The USFDA and WHO have acknowledged that the novel COVID-19 vaccines similarly have a risk of reactive immunologic-based inflammation, namely, myositis, pericarditis, and Guillain-Barré syndrome. *Case Presentation.* We present two patients with latent herpetic keratitis who experienced reactivation of keratitis within weeks of COVID-19 vaccination despite prolonged periods of prior latency. A 52-year-old healthy male with no herpes simplex virus (HSV) keratitis recurrences in two years developed visual decline and patchy stromal haze within 24-48 hours of receiving the second Pfizer-BioNTech (COVID-19 BNT162b2) vaccine. A 67-year-old female with chronic neurotrophic keratitis developed her most severe exacerbation of herpes zoster keratitis in over 10 years occurring 2-3 weeks after her first Moderna (mRNA-1273) vaccine, which was later complicated by bacterial superinfection. **Conclusions:** The COVID-19 vaccines work by generating both adaptive humoral and cellular immune responses in humans, including elevation of anti-spike neutralizing antibody titers, antigen-specific CD4+ and CD8+ T-cell responses, and increased levels of proinflammatory cytokines such as interferon gamma (IFN γ). The general activation of the T-cell-mediated immune response and proinflammatory cytokines such as IFN γ may underlie the role of the COVID vaccines in reactivation of herpetic stromal keratitis and the clinical findings in our reported cases.

Elimination of human rabies in Goa, India through an integrated One Health approach.

Gibson, A., Yale, G., Corfmat, J., Appupillai, M., Gigante, C., Lopes, M., Betodkar, U., Costa, N., Fernandes, K., Mathapati, P., Suryawanshi, P., Otter, N., Thomas, G., Ohal, P., Airikkala-Otter, I., Lohr, F., Rupprecht, C., King, A., Sutton, D., Deuzeman, I., Li, Y., Wallace, R., Mani, R., Gongal, G., Handel, I., Bronsvort, M., Naik, V., Desai, S., Mazeri, S., Gamble, L., Mellanby, R.
19-05-2022

Nat Commun

<https://doi.org/10.1038/s41467-022-30371-y>

Dog-mediated rabies kills tens of thousands of people each year in India, representing one third of the estimated global rabies burden. Whilst the World Health Organization (WHO), World Organization for Animal Health (OIE) and the Food and Agriculture Organization of the United Nations (FAO) have set a target for global dog-mediated human rabies elimination by 2030, examples of large-scale dog vaccination programs demonstrating elimination remain limited in Africa and Asia. We describe the development of a data-driven rabies elimination program from 2013 to 2019 in Goa State, India, culminating in human rabies elimination and a 92% reduction in monthly canine rabies cases. Smartphone technology enabled systematic spatial direction of remote teams to vaccinate over 95,000 dogs at 70% vaccination coverage, and rabies education teams to reach 150,000 children annually. An estimated 2249 disability-adjusted life years (DALYs) were averted over the program period at 526 USD per DALY, making the intervention 'very cost-effective' by WHO definitions. This One Health program demonstrates that human rabies elimination is achievable at the state level in India.

Rabies in a Dog Imported from Azerbaijan - Pennsylvania, 2021.

Whitehill, F., Bonaparte, S., Hartloge, C., Greenberg, L., Satheshkumar, P., Orziari, L., Niezgod, M., Yager, P., Pieracci, E., McCullough, J., Evenson, A., Brown, C., Schnitzler, H., Lipton, B., Signs, K., Stobierski, M., Austin, C., Slager, S., Ernst, M., Kerins, J., Simeone, A., Singh, A., Hale, S., Stanek, D., Shehee, P., Slavinski, S., McDermott, D., Zinna, P., Campagna, R., Wallace, R.

20-05-2022

MMWR Morb Mortal Wkly Rep

<https://doi.org/10.15585/mmwr.mm7120a3>

On June 16, 2021, rabies virus infection was confirmed in a dog included in a shipment of rescue animals imported into the United States from Azerbaijan. A multistate investigation was conducted to prevent secondary rabies cases, avoid reintroduction of a dog-maintained rabies virus variant (DMRVV), identify persons who might have been exposed and would be recommended to receive rabies postexposure prophylaxis, and investigate the cause of importation control failures. Results of a prospective serologic monitoring (PSM) protocol suggested that seven of 32 (22%) animals from the same shipment as the dog with confirmed rabies virus infection and who had available titer results after rabies vaccine booster had not been adequately vaccinated against

rabies before importation. A requirement for rabies vaccination certificates alone will not adequately identify improper vaccination practices or fraudulent paperwork and are insufficient as a stand-alone rabies importation prevention measure. Serologic titers before importation would mitigate the risk for importing DMRVV.

Hotspots in a cold land-reported cases of rabies in wildlife and livestock in Mongolia from 2012-2018.

Matulis, G., Altantogtokh, D., Lantos, P., Jones, J., Wofford, R., Janko, M., Tsogbadrakh, N., Bayar, T., Ganzorig, S., Boldbaatar, B., Poole-Smith, B., Hertz, J., Fiorenzano, J., von Fricken, M.
18-05-2022

Zoonoses Public Health

<https://doi.org/10.1111/zph.12954>

The epidemiological profile of rabies virus within Mongolia remains poorly characterized despite 21,302 domestic animal cases being reported between 1970-2005. This lack of knowledge is particularly concerning given that roughly 26% of the population lives a pastoral herding lifestyle and livestock production contributes up to 18% of Mongolia's total gross domestic product (GDP). The gaps in knowledge of the rabies disease ecology within Mongolia combined with the lack of routine vaccination of domestic animals and wildlife poses a significant threat to the more than 60 million heads of livestock within Mongolia. Animal rabies case data from the General Authority for Veterinary Services and National Center for Zoonotic Diseases were used in this study. Each data point included year of report, an animal descriptor, geographic coordinates and the aimag (province) of origin. A total of 2,359 animal rabies cases were reported between 2012-2018. Cattle were the most commonly reported animal overall (861 cases), followed by goats (268), sheep (251) and dogs (221) within the domestic animal category. Red foxes were responsible for most reported wildlife cases (317) followed by wolves (151). Most rabid animals were reported in the Khuvsgul, Uvurkhangai and Govi-Altai aimags, and a positive correlation was found between livestock numbers per soum and the number of rabies cases reported. Rabies poses a significant threat to the Mongolian economy and the health of human and animal populations within Mongolia. The close association of the nomadic pastoralists with both domestic animals and wildlife represents a significant threat for disease emergence and necessitates studies that describe the ecology of rabies, which may threaten these populations.

Recombinant adeno-associated virus serotype 9 AAV-RABVG expressing a Rabies Virus G protein confers long-lasting immune responses in mice and non-human primates.

Shi, C., Tian, L., Zheng, W., Zhu, Y., Sun, P., Liu, L., Liu, W., Song, Y., Xia, X., Xue, X., Zheng, X.
17-05-2022

Emerg Microbes Infect

<https://doi.org/10.1080/22221751.2022.2078226>

Three or four intramuscular doses of the inactivated human rabies virus vaccines are needed for pre- or post- exposure prophylaxis in humans. This procedure has made a great contribution to prevent human rabies deaths, which bring huge economic burdens in developing countries. Herein, a recombinant adeno-associated virus serotype 9, AAV9-RABVG, harboring a RABV G gene, was generated to serve as a single dose rabies vaccine candidate. The RABV G protein was stably expressed in the 293T cells infected with AAV9-RABVG. A single dose of 2×10^{11} v.p. of AAV9-RABVG induced robust and long term positive seroconversions in BALB/c mice with a 100% survival from a lethal RABV challenge. In *Cynomolgus* Macaques vaccinated with a single dose of 1×10^{13} v.p. of AAV9-RABVG, the titers of rabies VNAs increased remarkably from 2 weeks after immunity, and maintained over 31.525 IU/ml at 52 weeks. More DCs were activated significantly for efficient antigen presentations of RABV G protein, and more B cells were activated to responsible for antibody responses. Significantly more RABV G specific IFN- γ -secreting CD4+ and CD8+ T cells, and IL-4-secreting CD4+ T cells were activated, and significantly higher levels of IL-2, IFN- γ , IL-4 and IL-10 were secreted to aid immune responses. Overall, the AAV9-RABVG was a single dose rabies vaccine candidate with great promising by inducing robust, long term humoral responses and both Th1 and Th2 cell-mediated immune responses in mice and non-human primates.

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

<https://doi.org/10.1021/acs.analchem.2c00954>

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.

Rabies Anterograde Monosynaptic Tracing Allows Identification of Postsynaptic Circuits Receiving Distinct Somatosensory Input.

Pimpinella, S., Sauve, I., Dietrich, S., Zampieri, N.

16-03-2022

Neuroscience

<https://pubmed.ncbi.nlm.nih.gov/35306143>

Somatosensory neurons detect vital information about the environment and internal status of the body, such as temperature, touch, itch, and proprioception. The circuit mechanisms controlling the coding of somatosensory information and the generation of appropriate behavioral responses are not clear yet. In order to address this issue, it is important to define the precise connectivity patterns between primary sensory afferents dedicated to the detection of different stimuli and recipient neurons in the central nervous system. In this study we describe and validate a rabies tracing approach for mapping mouse spinal circuits receiving sensory input from distinct, genetically defined, modalities. We analyzed the anatomical organization of spinal circuits involved in coding of thermal and mechanical stimuli and showed that somatosensory information from distinct modalities is relayed to partially overlapping ensembles of interneurons displaying stereotyped laminar organization, thus highlighting the importance of positional features and population coding for the processing and integration of somatosensory information.

TRACHOME

WHO Program May Eliminate Active Trachoma's Blindness Risk by 2030.

Larkin, H.

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JAMA

<https://doi.org/10.1001/jama.2022.7383>

ULCERE DE BURULI

What the snake leaves in its wake: Functional limitations and disabilities among snakebite victims in Ghanaian communities.

Aglanu, L., Amuasi, J., Schut, B., Steinhorst, J., Beyuo, A., Dari, C., Agbogbaley, M., Blankson, E., Punguyire, D., Lalloo, D., Blessmann, J., Abass, K., Harrison, R., Stienstra, Y.

23-05-2022

PLoS Negl Trop Dis

<https://doi.org/10.1371/journal.pntd.0010322>

Background: The estimated five million snakebites per year are an important health problem that mainly affect rural poor populations. The global goal is to halve both mortality and morbidity from this neglected tropical disease by 2030. Data on snakebite morbidity are sparse and mainly obtained from hospital records. **Methods:** This community-based study was conducted among 379 rural residents with or without a history of snakebite in the Ashanti and Upper West regions of Ghana. All participants in the snakebite group were bitten at least six months before the day of survey. The World Health Organisation Disability Assessment Schedule 2.0 (WHODAS 2.0) and the Buruli Ulcer Functional Limitation Score were used to obtain patient-reported measure of functioning and disability. Long-term consequences were evaluated based on the severity of the symptoms at the time of the snakebite.

Findings: The median (IQR) time since the snakebite was 8.0 (3.5-16.5) years. The relative risk of disability was 1.54 (95% CI, 1.17-2.03) in the snakebite group compared to the community controls. Among patients with clinical symptoms suggesting envenoming at the time of bite, 35% had mild/moderate disabilities compared to 20% in the control group. The disability domains mainly affected by snakebite envenoming were cognition level, mobility, life activities and participation in society. A combination of the severity of symptoms at the time of the bite, age, gender and region of residence most accurately predicted the odds of having functional limitations and disabilities. **Conclusion:** The burden of snakebite in the community includes long-term disabilities of mild to moderate severity, which need to be considered when designing appropriate public health interventions. Estimating the total burden of snakebite is complicated by geographic differences in types of snakes and their clinical manifestations.

PIAN

LEPRE

Dapsone is an anticatalysis for Alzheimer's disease exacerbation.

Lee, J., Kanwar, B., Lee, C., Sergi, C., Coleman, M.

20-04-2022

iScience

<https://doi.org/10.1016/j.isci.2022.104274>

Brain inflammation generally accelerates neurodegeneration. Alzheimer's disease (AD) triggers an innate immune response by activating a cytosolic DNA sensor cyclic-GMP-AMP synthase (cGAS)/stimulator of interferon genes (STING) signaling pathway. Our study investigated patients with leprosy and AD. They were treated with dapsone (4,4'-diaminodiphenyl sulfone, DDS) as a neuroinflammation competitor and cGAS/STING pathway inhibitor. Four groups were defined: Treatment (T) 1: DDS prescribed AD diagnosed, T 2: DDS prescribed AD undiagnosed, T 3 DDS unprescribed AD diagnosed, and T 4: DDS unprescribed AD undiagnosed. Dapsone effects on AD can be clearly distinguished according to dapsone presence or absence. T1:T3 proved that the incidence of AD was significantly reduced by dapsone. T2:T3 proved that the prevalence of AD was significantly high without dapsone. T1:T4 proved that the prevalence decreased when taking dapsone. Our study demonstrates that dapsone can prevent AD exacerbation and may represent a preventive therapeutic option for exacerbated AD.

TRYPANOSOMES (TRYPANOSOMIASE ET MALADIE DE CHAGAS)

Physiologic Targets and Modes of Action for CBL0137, a Lead for Human African Trypanosomiasis Drug Development.

Sanz-Rodriguez, C., Hoffman, B., Guyett, P., Purmal, A., Singh, B., Pollastri, M., Mensa-Wilmot, K.

23-05-2022

Mol Pharmacol

<https://pubmed.ncbi.nlm.nih.gov/35605992>

CBL0137 is a lead drug for human African trypanosomiasis, caused by *Trypanosoma brucei*. Herein, we use a four-step strategy to (a) identify physiologic targets and (b) determine modes of molecular action of CBL0137 in the trypanosome. First, we identified fourteen CBL0137-binding proteins using affinity chromatography. Second, we developed hypotheses of molecular modes of action, using predicted functions of CBL0137-binding proteins as guides. Third, we documented effects of CBL0137 on molecular pathways in the trypanosome. Fourth, we identified physiologic targets of the drug, by knocking down genes encoding CBL0137-binding proteins and comparing their molecular effects to those obtained when trypanosomes were treated with CBL0137.

CBL0137-binding proteins included glycolysis enzymes (aldolase, glyceraldehyde-3-phosphate dehydrogenase, phosphofructokinase, phosphoglycerate kinase), and DNA-binding proteins (UMSBP2, RPA1, RPA2). In chemical biology studies CBL0137 did not reduce ATP level in the trypanosome, ruling out glycolysis enzymes as crucial targets for the drug. Thus, many CBL0137-binding proteins are not physiological targets of the drug. Instead, CBL0137 inhibited (i) nucleus mitosis, (ii) nuclear DNA replication, and (iii) polypeptide synthesis as the first carbazole inhibitor of eukaryote translation. RNAi against RPA1 inhibited both DNA synthesis and mitosis, whereas RPA2 knockdown inhibited mitosis, consistent with both proteins being physiologic targets of CBL0137. Principles used here to distinguish drug-binding proteins from physiological targets of CBL0137 can be deployed with different drugs in other biological systems. **Significance Statement** To distinguish drug-binding proteins from physiologic targets in the African trypanosome we devised and executed a multi-disciplinary approach involving biochemical, genetic, cell, and chemical biology experiments. The strategy we employed can be used for drugs in other biological systems.

Evaluation of Selective Deltamethrin Application with Household and Community Awareness for the Control of Chagas Disease in Southern Ecuador.

Grijalva, M., Moncayo, A., Yumiseva, C., Ocaña-Mayorga, S., Baus, E., Villacís, A.

23-05-2022

J Med Entomol

<https://pubmed.ncbi.nlm.nih.gov/35604412>

Chagas disease is endemic in ~70% of Ecuador. *Rhodnius ecuadoriensis* and *Triatoma carrioni* (Hemiptera: Reduviidae) are the primary vectors of Chagas disease in Southern Ecuador. This study tested the effectiveness of selective deltamethrin application of Domiciliary Units (DUs) infested with triatomines, coupled with community education activities and a community-based surveillance system. Ten communities were selected in Loja Province, 466 DUs were examined, of these, 5.6% were infested with *R. ecuadoriensis* (Density [D] = 4 triatomines/DUs searched, Crowding [CR] = 71 triatomines/infested house, Colonization Index [CI] = 77% infested DUs with nymphs) and 8% with *T. carrioni* (D = 0.6, CR = 7, CI = 64%). Infested DUs were sprayed with deltamethrin. Subsequent visits were conducted at 6 and 12 mo after spraying. At each time point, new entomological searches were carried out in all DUs. All entomological indexes dropped significantly for the primary vector species one year after the initial intervention (*R. ecuadoriensis*: I = 2%, D = 0.1, CR = 7, CI = 100%; *T. carrioni*: I = 1.6%, D = 0.1, CR = 5.5, CI = 50%). Fifteen min educational talks were conducted in every DUs and workshops for schoolchildren were organized. Community-based surveillance system was established. However, there is a high risk of DUs reinfestation, possibly from sylvatic habitats (especially of *R. ecuadoriensis*) and reinforcing educational and surveillance activities are necessary.

A note on the the discovery of Chagas' disease.

de Avila-Pires, F.

16-05-2022

Mem Inst Oswaldo Cruz

<https://pubmed.ncbi.nlm.nih.gov/35584512>

Chagas disease and its historicity.

Gomes, A.

16-05-2022

Mem Inst Oswaldo Cruz

<https://pubmed.ncbi.nlm.nih.gov/35584511>

Chagas disease challenge - New techniques for diagnosis and treatment address to control in endemic areas.

Marins, J.

16-05-2022

Mem Inst Oswaldo Cruz

<https://pubmed.ncbi.nlm.nih.gov/35584510>

The challenges for targeting Chagas disease for elimination as a public health problem.

Werneck, G.

16-05-2022

Mem Inst Oswaldo Cruz

<https://pubmed.ncbi.nlm.nih.gov/35584509>

Emerging and reemerging forms of Trypanosoma cruzi transmission.

Revue de littérature

Shikanai Yasuda, M.

16-05-2022

Mem Inst Oswaldo Cruz

<https://pubmed.ncbi.nlm.nih.gov/35584508>

This review aims to update and discuss the main challenges in controlling emergent and reemergent forms of Trypanosoma cruzi transmission through organ transplantation, blood products and vertical transmission in endemic and non-endemic areas as well as emergent forms of transmission in endemic countries through contaminated food, currently representing the major cause of acute illness in several countries. As a neglected tropical disease potentially controllable with a major impact on morbimortality and socioeconomic aspects, Chagas disease (CD) was approved at the WHO global plan to interrupt four transmission routes by 2030 (vector/blood transfusion/organ transplant/congenital). Implementation of universal or target screening for CD are highly recommended in blood banks of non-endemic regions; in organ transplants donors in endemic/non-endemic areas as well as in women at risk from endemic areas (reproductive age women/pregnant women-respective babies). Moreover, main challenges for surveillance are the application of molecular methods for identification of infected babies, donor

transmitted infection and of live parasites in the food. In addition, the systematic recording of acute/non-acute cases and transmission sources is crucial to establish databases for control and surveillance purposes. Remarkably, antiparasitic treatment of infected reproductive age women and infected babies is essential for the elimination of congenital CD by 2030.

The history of Chagas disease: reflections on science in action.

Kropf, S., Lima, N.

16-05-2022

Mem Inst Oswaldo Cruz

<https://pubmed.ncbi.nlm.nih.gov/35584507>

Approaching from the perspective of the history and social studies of science, the article analyses some aspects of the early history of Chagas disease, from its discovery through initial research. It is our goal to show that historians of science can explore this topic as a way not only of remembering and narrating past events but also of examining the processes through which science is produced. To this end, we present five basic precepts that have guided historical and sociological studies of "science in action": science as a collective endeavor, as a social activity, as a set of practices, as a process that involves controversies, and as a formative process. By examining the topic in the light of these five points, we demonstrate how the history of this successful research tradition can lead us to broader reflections about the complex dynamics interweaving science and society.

African Animal Trypanosomiasis: A Systematic Review on Prevalence, Risk Factors and Drug Resistance in Sub-Saharan Africa.

Okello, I., Mafie, E., Eastwood, G., Nzalawahe, J., Mboera, L.

17-05-2022

J Med Entomol

<https://pubmed.ncbi.nlm.nih.gov/35579072>

African animal trypanosomiasis (AAT) a parasitic disease of livestock in sub-Saharan Africa causing tremendous losses. Sub-Saharan continental estimation of mean prevalence in both large and small domestic animals, risk factors, tsetse and non-tsetse prevalence and drug resistance is lacking. A review and meta-analysis was done to better comprehend changes in AAT prevalence and drug resistance. Publish/Perish software was used to search and extract peer-reviewed articles in Google scholar, PubMed and CrossRef. In addition, ResearchGate and African Journals Online (AJOL) were used. Screening and selection of articles from 2000-2021 was performed according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). Articles 304 were retrieved; on domestic animals 192, tsetse and non-tsetse vectors 44, risk factors 49 and trypanocidal drug resistance 30. Prevalence varied by, host animals in different countries, diagnostic methods and species of Trypanosoma. Cattle had the highest prevalence with Ethiopia and Nigeria leading, T. congolense

(11.80-13.40%) and *T. vivax* (10.50-18.80%) being detected most. This was followed by camels and pigs. Common diagnostic method used was buffy coat microscopy. However; polymerase chain reaction (PCR), CATT and ELISA had higher detection rates. *G. pallidipes* caused most infections in Eastern regions while *G. palpalis* followed by *G. mortisans* in Western Africa. Eastern Africa reported more non-tsetse biting flies with *Stomoxys* leading. Common risk factors were, body conditions, breed type, age, sex and seasons. Ethiopia and Nigeria had the highest trypanocidal resistance 30.00-35.00% and highest AAT prevalence. Isometamidium and diminazene showed more resistance with *T. congolense* being most resistant species 11.00-83.00%.

LEISHMANIOSE

Diversity of cave Phlebotomines (Diptera: Psychodidae) from a Colombian cave.

Velazquez, M., Stuckert, A., Vivero, R., Matute, D.

20-05-2022

Acta Trop

<https://pubmed.ncbi.nlm.nih.gov/35605671>

Sandflies are vector species of *Leishmania*, among many other pathogens, with a global distribution and a variety of ecological niches. Previous samplings have found that karstic formations (i.e., caves, grottos, and folds formed by the erosion of limestone) serve as a natural habitat to sandfly species. The majority of samplings of cave sandfly diversity have occurred in Brazil and to date none have studied the species composition in a cave in the Northern Andes. We collected sandflies in the Cave "Los Guácharos", in the state of Antioquia, Colombia. The sampling was carried out during two consecutive nights in September 2019. CDC-type light traps were installed inside the cavern and in other surrounding karst systems (caves, rock-breaks, and folds). In total, we identified 17 species of sandfly from the cave and surrounding karst systems, including a new record for Colombia (*Bichromomyia olmeca*), and provide the first karstic reports for four other species (*Lutzomyia gomezi*, *Lutzomyia hartmanni*, *Pintomyia ovallesi*, and *Psychodopygus panamensis*). We then used the results of our survey and published literature to test two hypotheses. First, that sandfly diversity in Neotropical caves is richest nearer to the equator, and second that there is a phylogenetic signal of karstic habitat use in sandflies. Counter to our predictions, we found no evidence that diversity follows a latitudinal gradient. Further, we find no evidence of a phylogenetic signal of karstic habitat use, instead finding that the use of caves likely evolved multiple times across several genera. Our results highlight the importance of a wide sampling to understand the natural habitat of sandflies and other disease vectors.

Genetic diversity and population structure of *Leishmania (Viannia) braziliensis* in the Peruvian jungle.

De Los Santos, M., Ramírez, I., Rodríguez, J., Beerli, P., Valdivia, H.

23-05-2022

PLoS Negl Trop Dis

<https://doi.org/10.1371/journal.pntd.0010374>

Background: Human cutaneous leishmaniasis caused by *Leishmania (Viannia) braziliensis* is highly prevalent in the Peruvian jungle, where it affects military forces deployed to fight against drug trafficking and civilian people that migrate from the highland to the lowland jungle for economic activities such as mining, agriculture, construction, and chestnut harvest. We explored the genetic diversity and population structure of 124 *L. (V.) braziliensis* isolates collected from the highland (Junín, Cusco, and Ayacucho) and lowland Peruvian jungle (Loreto, Ucayali, and Madre de Dios). All samples were genotyped using Multilocus Microsatellite Typing (MLMT) of ten highly polymorphic markers. **Principal findings:** High polymorphism and genetic diversity were found in Peruvian isolates of *L. (V.) braziliensis*. Most markers are not in Hardy-Weinberg equilibrium; this deviation is most likely caused by local inbreeding, as shown by the positive FIS values. Linkage Disequilibrium in subpopulations was not strong, suggesting the reproduction was not strictly clonal. Likewise, for the first time, two genetic clusters of this parasite were determined, distributed in both areas of the Peruvian jungle, which suggested a possible recent colonization event of the highland jungle from the lowland jungle. **Conclusions:** *L. (V.) braziliensis* exhibits considerable genetic diversity with two different clusters in the Peruvian jungle. Migration analysis suggested a colonization event between geographical areas of distribution. Although no human migration was observed at the time of sampling, earlier displacement of humans, reservoirs, or vectors could have been responsible for the parasite spread in both regions.

Mucocutaneous Leishmaniasis due to *Leishmania infantum* Infection.

Linse, K., Bogdan, C., Haenssle, H., Toberer, F.

23-05-2022

Acta Derm Venereol

<https://doi.org/10.2340/actadv.v102.2321>

Retrospective Results of Hacettepe University Faculty of Medicine Parasitology Laboratory Between 2014-2019.

İnal, N., Ünalın Altıntop, T., Ergüven, S., Akyön Yılmaz, Y.

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Türkiye Parazitoloj Derg

<https://doi.org/10.4274/tpd.galenos.2022.84429>

Objective: Parasitic infections emerge as a significant health problem, especially in underdeveloped and developing countries. Epidemiological data play an important role in taking effective measures against parasitic diseases. **Methods:**

Clinical samples (stool, blood, bone marrow and tissue samples, etc.) that were sent to Hacettepe University Hospitals Parasitology Laboratory between 2014 and 2019 were analyzed retrospectively. **Results:** The positivity rates of the parasites detected in this study are as follows; *Blastocystis* sp. (71.6%), *Dientamoeba fragilis* (13.3%), *Giardia lamblia* (4.7%), *Echinococcus* spp. (1.9%), *Enterobius vermicularis* (1.8%) and *Taenia* spp. (0.3%). In this study, four of the patients were found to be positive for *Leishmania* spp. and two patients for *Plasmodium falciparum* and four patients for *Plasmodium* spp. *E. histolytica*/*E. dispar* cysts and/or trophozoites examined by Trichrome staining in our study were not detected within six years. **Conclusion:** According to this data and in the light of the results obtained from different regions of our country, it will be possible to properly direct the necessary strategies for the diagnosis, treatment of parasitic infections and the implementation of preventive measures.

Investigation of *in vitro* Efficacy of Miltefosine on Chronic Cutaneous Leishmaniasis

Tunali, V., Harman, M., Çavuş, İ., Zorbozan, O., Özbilgin, A., Turgay, N.

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Turkiye Parazitol Derg

<https://doi.org/10.4274/tpd.galenos.2022.85856>

Objective: Leishmaniasis is the second deadliest parasitic disease in the World Health Organisation's list of neglected diseases, following malaria. Cutaneous leishmaniasis (CL) is the most common form of the disease and it is one of the few communicable diseases with increasing incidence rates owing to factors like armed conflicts and climate change. CL can be divided into two major groups: Acute CL (ACL) and chronic CL (CCL). The aim of this study was to compare the *in vitro* efficacy of miltefosine and pentavalent antimony compounds in the CCL patient samples. **Methods:** Five isolates previously isolated from 5 CCL patients were included in this study. Genotyping is performed using internal transcribed spacer 1 (ITS 1) gene region real-time PCR. *In vitro* drug efficacy tests were applied to determine their activity against meglumine antimoniate (MA) and miltefosine. Serial dilutions (512, 256, 128, 64, 32, 16, 8 and 4 µg/mL) prepared from MA and miltefosine were prepared in 96-well flat-bottom cell culture plates and incubated at 24 °C for 48 hours. The efficacy of the drug on *Leishmania* spp. promastigotes after 24 and 48 hours was evaluated by hemocytometer slide and XTT cell viability test. **Results:** All of the samples were genotyped as *L. tropica*. Evaluation of 24 and 48 hours showed, 128 µg/mL and 256 µg/mL and 32 µg/mL and 64 µg/mL concentrations of miltefosine and MA were enough to kill all the promastigotes respectively. The results of the hemocytometer slide and XTT were consistent. **Conclusion:** There are no studies investigating the *in vitro* efficacy of miltefosine with the CCL patient group. To overcome the treatment challenges experienced in this special patient group, more studies are needed. According to our results, it is concluded that miltefosine is efficient for the treatment of CCL and further clinical studies with miltefosine will reveal valuable data.

The *in vitro* anti-*Leishmania* Effect of *Zingiber officinale* Extract on Promastigotes and Amastigotes of *Leishmania major* and *Leishmania tropica*

Saki, J., Biranvand, E., Arjmand, R.

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Turkiye Parazitol Derg

<https://doi.org/10.4274/tpd.galenos.2021.53825>

Objective: Recently, the use of pentavalent antimony compounds for *Leishmaniasis* treatment has been associated with disease recurrence, drug resistance, and severe side effects. Therefore, there is a need to develop alternative treatment strategies. This study investigates the *in vitro* effects of *Zingiber officinale* on promastigotes and amastigotes of *Leishmania major* and *Leishmania tropica*. **Methods:** Promastigotes and amastigotes of *Leishmania major* and *Leishmania tropica* were cultured and mass-produced in an RPMI1640 medium enriched with other necessary compounds. The MTT colorimetric method and calculating the IC50 value were used to evaluate the anti-leishmania activity of hydroalcoholic extract of *Zingiber officinale*. **Results:** The hydroalcoholic extract of *Zingiber officinale* inhibited the growth of *Leishmania major* and *Leishmania tropica* promastigotes in 24, 48, and 72 hours after *in vitro* incubation. The IC50 of hydroalcoholic extract of *Zingiber officinale* was 56 µg/mL for *Leishmania major* and 275 µg/mL for *Leishmania tropica* promastigotes after 72 hours. The IC50 of hydroalcoholic extract of *Zingiber officinale* was 75 µg/mL for *Leishmania major* and 325 µg/mL for *Leishmania tropica* amastigotes after 72 hours. **Conclusion:** The results showed that hydroalcoholic extract of *Zingiber officinale* has cytotoxicity properties, and *Leishmania tropica* has a higher resistance to hydroalcoholic extract of *Zingiber officinale* than *Leishmania major*. Further research is recommended.

Increasing the Sensitivity of *Leishmania* RNA Virus 2 (LRV2) Detection with a Modification in cDNA Synthesis

Nalçacı, M., Karakuş, M., Özbel, Y., Özbilgin, A., Töz, S.

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Turkiye Parazitol Derg

<https://doi.org/10.4274/tpd.galenos.2022.30074>

Objective: *Leishmania* RNA virus was detected the first time in the New World *Leishmania* species. Recent studies were also showed the presence of *Leishmania* RNA virus 2 (LRV2) in Old World *Leishmania* species including Turkish *L. major* and *L. tropica* isolates. This study aimed to increase the sensitivity of qPCR with a modification in the denaturation step of cDNA preparation protocol. **Methods:** In this study, LRV2+ three *L. major*, two *L. tropica* strains and *L. major* control strain (MHOM/SU/73/5-ASKH) were included. Total RNA isolation was done using different numbers of *Leishmania* promastigotes (10^8 , 10^5 and 10^3). Before cDNA synthesis, samples were denatured at 95 °C for 2 min, as a modification of the kit procedure. qPCR was undertaken using 0.5 mM primers (LRV F-HR/LRV R-HR) diluted in SYBR Green Master mix. **Results:** We observed lower Ct values in amplicons with

the modified version than with the classical kit protocol for cDNA synthesis, in all of the strains used in the study. The addition of pre-denaturation step at 95 °C showed lower Ct values meaning the sensitivity increased. Different parasite dilutions showed similar results. **Conclusion:** It is important to increase the sensitivity especially with the aim for detecting LRV in clinical samples obtained from patients probably have less number of parasites. The presence and burden of the virus can help to understand the relationship between the clinical findings and the pathogenicity of the parasite which may lead to changes in the course of treatment.

Sustainability of the rice-crayfish co-culture aquaculture model: microbiome profiles based on multi-kingdom analyses.

Zhu, X., Ji, L., Cheng, M., Wei, H., Wang, Z., Ning, K.
22-05-2022

Environ Microbiome

<https://doi.org/10.1186/s40793-022-00422-4>

While the rice-crayfish culture (RCFP) model, an important aquaculture model in Asia, is generally considered a sustainable model, its sustainability in terms of microbial community profiles has not been evaluated. In this study, multi-kingdom analyses of microbiome profiles (i.e., bacteria, archaea, viruses, and eukaryotes) were performed using environmental (i.e., water and sediment) and animal gut (i.e., crayfish and crab gut) microbial samples from the RCFP and other aquaculture models, including the crab-crayfish co-culture, crayfish culture, and crab culture models, to evaluate the sustainability of the RCFP systematically. Results showed that RCFP samples are enriched with a distinct set of microbes, including *Shewanella*, *Ferroplasma*, *Leishmania*, and *Siphoviridae*, when compared with other aquaculture models. Additionally, most microbes in the RCFP samples, especially microbes from different kingdoms, were densely and positively connected, which indicates their robustness against environmental stress. Whereas microbes in different aquaculture models demonstrated moderate levels of horizontal gene transfer (HGT) across kingdoms, the RCFP showed relatively lower frequencies of HGT events, especially those involving antibiotic resistance genes. Finally, environmental factors, including pH, oxidation-reduction potential, temperature, and total nitrogen, contributed profoundly to shaping the microbial communities in these aquaculture models. Interestingly, compared with other models, the microbial communities of the RCFP model were less influenced by these environmental factors, which suggests that microbes in the latter have stronger ability to resist environmental stress. The findings collectively reflect the unique multi-kingdom microbial patterns of the RCFP model and suggest that this model is a sustainable model from the perspective of microbiome profiles.

Development of antibodies to the iron-binding proteins transferrin and ferritin in dogs and mice infected with *Leishmania* parasites.

Sassi, A.

18-05-2022

Acta Trop

<https://pubmed.ncbi.nlm.nih.gov/35597263>

Most microorganisms including *Leishmania* parasites compete with the innate immune defenses of the infected hosts to acquire iron, an essential nutrient necessary for their growth and replication. In mammals, iron is predominantly bound to protein carriers such as transferrin and ferritin and the strategies adopted by the infected host to restrict its uptake by pathogens are still not elucidated. We compared herein the development of anti-transferrin and anti-ferritin antibodies in hosts that differs by their susceptibility to *Leishmania* infection. Results showed that *Leishmania infantum* naturally-infected dogs which have developed canine leishmaniasis (CanL) demonstrated higher titers of IgG antibodies anti-leishmanial antigens and anti-iron binding proteins than those infected without clinical signs. In the experimental mouse model, C57BL/6 mice resisted *L. major* infection, developed lower titers of *Leishmania*-specific IgG antibodies than BALB/c susceptible mice but demonstrated also the production of anti-transferrin and anti-ferritin IgG antibodies. Overall, results are in favor that mechanisms, other than the polyclonal activation of B cells associated-hypergammaglobulinemia, a characteristic of susceptible animals, are likely involved and require a replicating parasite for the limitation of iron uptake.

Epigenetic paradigms/exemplars of the macrophage: inflammasome axis in Leishmaniasis.

Revue de littérature

Aljedaie, M.

20-05-2022

Mol Cell Biochem

<https://doi.org/10.1007/s11010-022-04460-x>

The infectious paradigms have recently led to the recognition interplay of complex phenomenon underpinning disease diagnosis and prognosis. Evidently, parasitic infection studies are depicting converging trends of the epigenetic, environmental, and microbiome contributions, assisting pathogen-directed modulations of host biological system. The molecular details of epigenetic variations and memory, along with the multi-omics data at the interface of the host-pathogen level becomes strong indicator of immune cell plasticity, differentiation, and pathogen survival. Despite being one of the most important aspects of the disease's etiopathology, the epigenetic regulation of host-pathogen interactions and evolutionary epigenetics have received little attention thus far. Recent evidence has focused on the growing need to link epigenetic and microbiome modulations on parasite phenotypic plasticity and pathogen-induced host phenotypic plasticity for designing futuristic therapeutic regimes. Leishmaniasis is a neglected tropical illness with varying degrees of disease severity that is linked to a trans-species and epigenetic heredity process, including the pathogen-induced host and strain-specific modulations. The review configures research findings aligning to the epigenetic

epidemiology niche, involving co-evolutionary epigenetic inheritance and plasticity disease models. The epigenetic exemplars focus on the host-pathogen interactome expanse at the macrophage-inflammasome axis.

Molecular and Biochemical Detection of Insecticide Resistance in the Leishmania Vector, Phlebotomus papatasi (Diptera: Psychodidae) to Dichlorodiphenyltrichloroethane and Pyrethroids, in Central Iran.

Shirani-Bidabadi, L., Oshaghi, M., Enayati, A., Akhavan, A., Zahraei-Ramazani, A., Yaghoobi-Ershadi, M., Rassi, Y., Aghaei-Afshar, A., Koosha, M., Arandian, M., Ghanei, M., Ghassemi, M., Vatandoost, H.

20-05-2022

J Med Entomol

<https://pubmed.ncbi.nlm.nih.gov/35595289>

The aim of the present study was to explore resistance markers and possible biochemical resistance mechanisms in the Phlebotomine sand fly *Phlebotomus papatasi* in Esfahan Province, central Iran. Homogenous resistant strains of sand flies were obtained by exposing *P. papatasi* collected from Esfahan to a single diagnostic dose of DDT. The adults from the colony were tested with papers impregnated with four pyrethroid insecticides: Permethrin 0.75%, Deltamethrin 0.05%, Cyfluthrin 0.15%, and Lambda-cyhalothrin 0.05% to determine levels of cross-resistance. To discover the presence of mutations, a 440 base pair fragment of the voltage gated sodium channel (VGSC) gene was amplified and sequenced in both directions for the susceptible and resistant colonies. We also assayed the amount of four enzymes that play a key role in insecticide detoxification in the resistant colonies. A resistance ratio (RR) of 2.52 folds was achieved during the selection of resistant strains. Sequence analysis revealed no knockdown resistance (*kdr*) mutations in the VGSC gene. Enzyme activity ratio of the resistant candidate and susceptible colonies were calculated for α -esterases (3.78), β -esterases (3.72), mixed function oxidases (MFO) (3.21), and glutathione-S-transferases (GST) (1.59). No cross-resistance to the four pyrethroids insecticides was observed in the DDT resistant colony. The absence of *kdr* mutations in the VGSC gene suggests that alterations in esterase and MFO enzymes are responsible for the resistant of *P. papatasi* to DDT in central Iran. This information could have significant predictive utility in managing insecticide resistant in this *Leishmania* vector.

Mapping linear B-cell epitopes of the Tryparedoxin Peroxidase and its implications in the serological diagnosis of tegumentary leishmaniasis.

Medeiros, R., Carvalho, A., Ferraz, I., Medeiros, F., Cruz, L., Rocha, M., Coelho, E., Gonçalves, D., Mendes, T., Duarte, M., Menezes-Souza, D.

17-05-2022

Acta Trop

<https://pubmed.ncbi.nlm.nih.gov/35595092>

Diagnosis of tegumentary leishmaniasis (TL) is essential to avoid permanent damage and severe functional sequelae and there is an urgent need to discover new antigens. The present study aimed to comprehensively evaluate the potential use of the Tryparedoxin Peroxidase (TryP) as an antigen for serological tests. The proposal integrates data from immunoproteomics with immunoinformatics, in addition to a precise analysis of protein levels in the evolutionary stages of the parasite by flow cytometry. To evaluate the performance in the diagnosis of TL, Enzyme-Linked Immunosorbent Assay (ELISA) assays were performed using the recombinant protein and the respective B-cell epitope, followed by an analysis of the contribution of this peptide in the recognition of the protein by patients, evaluated by serum depletion assays. We showed that the TryP has a linear B-cell epitope with high divergence compared to orthologs from *Trypanosoma cruzi* and *Homo sapiens*. The results also show high expression and positive cells for TryP (TryP⁺) in the infective metacyclic promastigotes (MET) and intracellular (24 and 48 hours) stages. From the depletion assays, it was possible to confirm the contribution of the peptide in the specific recognition of the TryP protein by patients with TL (13.7-15.9%). ELISA using the peptide showed high performance in the diagnosis compared to the recombinant TryP (rTryP), Soluble *Leishmania braziliensis* Antigen (sLba) and Immunofluorescence Assay (IFA) with accuracy of 94.29, 89.29, 65.00 and 37.14%, respectively). We can conclude that the MNEPAPP peptide is a potential antigen for the diagnosis of TL.

Indoor residual spraying for the control of visceral leishmaniasis: A systematic review.

Faber, C., Montenegro Quiñonez, C., Horstick, O., Rahman, K., Runge-Ranzinger, S.

19-05-2022

PLoS Negl Trop Dis

<https://doi.org/10.1371/journal.pntd.0010391>

Indoor Residual Spraying (IRS) is one of the interventions to control the vectors of Visceral Leishmaniasis (VL). Different insecticides are used in affected countries, also in the Regional Initiative for the Elimination of VL in South-East Asia. This systematic review assesses all available studies analysing the effectiveness of IRS on the key vectors of VL. The systematic review followed PRISMA guidelines, with a broad search strategy, applied to seven key databases. Inclusion criteria were studies focusing on 1) Visceral leishmaniasis 2) Indoor Residual Spraying (IRS) or synonyms, and 3) all primary research methods. 21 studies were included, five cluster randomised controlled trials (cRCTs), one randomised controlled trial (RCT), 11 intervention studies, also included were three modelling studies and one survey. 19 out of 21 included studies were published between 2009 and 2020. 18 of the studies were conducted in the context of the Regional Initiative. Effects of IRS on vector populations are positive, confirmed in terms of effectiveness and by the availability of studies. Deltamethrin and alpha-Cypermethrin reduce total sandfly counts, and/or *Phlebotomus argentipes* counts by up

to 95% with an effect of a minimum of one month. Prolonged effects are not regularly seen. DDT has been used in India only: whereas in the 1990s a good effect could be measured, this effect waned over time. Two intervention studies, embedded in larger programmes in 2019 and 2020, replaced DDT with alpha-Cypermethrin throughout the study. Combinations of different interventions are not systematically researched, however showing some promising results, for example for the combination of IRS and Temephos. Constant monitoring of insecticide resistances and quality delivery of IRS are confirmed as key issues for programmes. No human transmission data are available to directly relate an effect of IRS—although modelling studies confirm the effect of IRS on human transmission. Concluding, IRS continues to be an effective intervention for *Phlebotomus argentipes* control. Delivery requires constant monitoring and quality assurance. Further studies need to assess IRS in different geographical areas affected by VL and combinations of interventions.

Retinoic acid increases the cellular cholesterol predominantly in a mTOR-independent manner.

Prakash, S., Kumar Rai, A.

18-05-2022

Immunol Res

<https://doi.org/10.1007/s12026-022-09292-x>

Retinoic acid (RA) plays a role in the mounting immune response and controls several functions of the human body, including cholesterol homeostasis. The synthesis, uptake, and efflux of cellular cholesterol are significantly linked to the mammalian target of rapamycin complex-1 (mTORC1). Activation of mTORC1 promotes the synthesis and uptake of the cholesterol and suppresses its efflux, thus causing accumulation of cellular cholesterol. It is intriguing to know the effect of a high dose of RA on cholesterol accumulation in macrophages (mφ) and whether it is via mTOR activation. It is important to note that the long-term treatment of RA in humans is safe. Therefore, we chose a high dose of RA to observe its effect, which may be implicated in diseases like visceral leishmaniasis, where cholesterol deficiency is established. In the present study, we found the increased expression of RAPTOR, a regulatory component of the mTORC1 complex, in mφ upon treatment with RA. We observed the increased expression of SREBP2, LDLR, and PCSK9 in RA-treated mφ under sufficient cholesterol conditions, which further increased cellular cholesterol levels. Notably, their expressions were decreased when the mTOR pathway was inhibited by rapamycin. However, treatment with rapamycin did not result in the loss of cellular cholesterol in RA-treated mφ. Comparison with rapamycin-treated mφ suggests that RA induces cellular cholesterol levels in a mTORC1-independent manner.

Revisiting the cave-dwelling sand flies (Diptera, Psychodidae, Phlebotominae) from Brazil: Diversity and potential role in the transmission of *Leishmania Ross, 1903* (Kinetoplastida: Trypanosomatidae).

Revue de littérature

Dutra-Rêgo, F., Freire, M., Carvalho, G., Andrade-Filho, J.

18-05-2022

Med Vet Entomol

<https://doi.org/10.1111/mve.12578>

Brazilian caves, one of the many tourist attractions of the country, may act as a shelter for insects, such as sand flies (Diptera: Psychodidae), natural hosts of various microorganisms including parasites of the genus *Leishmania* Ross, 1903. In the last decades, with the increasing global need for sustainable development, ecotourism has emerged as one of the major activities in Brazil. However, the constant monitoring in environmentally protected areas is not often carried out, endangering visitors and professionals, especially due to the occurrence of zoonoses. Several sand fly species have already been recorded in Brazilian caves, drawing attention to the possibility of *Leishmania* transmission at this ecotope. Indeed, this current systematic review summarizes the fauna of cave-dwelling sand flies in Brazil, focusing on their biological behaviour and the occurrence of potential vectors of *Leishmania* parasites.

Synthesis, in vitro Antileishmanial Efficacy and Hit/Lead Identification of Nitrofurantoin-Triazole Hybrids.

Zuma, N., Aucamp, J., Viljoen, M., N'Da, D.

02-05-2022

ChemMedChem

<https://doi.org/10.1002/cmdc.202200023>

Leishmaniasis is a vector-borne neglected parasitic infection affecting thousands of individuals, mostly among populations in low- to moderate-income developing countries. In the absence of protective vaccines, the management of the disease banks solely on chemotherapy. However, the clinical usefulness of current antileishmanial drugs is threatened by their toxicity and the emergence of multidrug-resistant strains of the causative pathogens. This emphasizes the imperative for the development of new and effective antileishmanial agents. In this regard, we synthesized and evaluated in vitro the antileishmanial activity and cytotoxicity profile of a series of nitrofurantoin-triazole hybrids. The nitrofurantoin derivative 1 featuring propargyl moiety was distinctively the most active of all, was nontoxic to human cells and possessed submicromolar cellular activity selectively directed towards the pathogens of the life threatening visceral leishmaniasis. Hence it was identified as potential antileishmanial lead for further investigation into its prospective to act as alternative to therapies.

CYSTICERCOSIS

Urine 1H-NMR Metabolomics to Discriminate Neurocysticercosis Patients from Healthy Controls: An Exploratory Study.

Lopez, J., Leyva, V., Bustos, J., Perez, E., Sanchez, S., Saavedra, H., Gonzales, I., Maruenda, H., Garcia, H., Cysticercosis Working Group in Peru

23-05-2022

Am J Trop Med Hyg

<https://doi.org/10.4269/ajtmh.22-0045>

The diagnosis of neurocysticercosis (NCC) is principally based on neuroimaging (magnetic resonance imaging or computed tomography), instrumentation that is scarcely available in the rural regions where *Taenia solium* transmission, primarily occurs due to poor sanitation conditions. Immunological assays for antigen or antibody detection complement the neuroimaging approach. However, no field-applicable assays to diagnose viable NCC or to guide the referral of cases for neuroimaging or for appropriate management are available. We performed an exploratory study on urine and serum samples using 1H-nuclear magnetic resonance (NMR)-based metabolomics to discriminate NCC patients ($n = 14$) from healthy control subjects ($n = 22$). Metabolic profiles demonstrated a discrimination between the urines of NCC patients and noninfected control subjects with a moderate predictive accuracy ($R_2 = 0.999$, $Q_2 = 0.434$). NMR metabolomics analysis has been proven useful in depicting biomarkers linked to other infectious diseases, various types of cancer, and other disorders. Our results, albeit preliminary, open a door to the development of better methods for detecting NCC through the identification of biomarkers participating in disturbed metabolic pathways.

Analysis of immune response in BALB/c mice immunized with recombinant plasmids pMZ-X3-Ts14-3-3.3 and pMZ-X3-sp-Ts14-3-3.3 of *Taenia solium*.

Zhang, Y., Luo, B., Liu, M., OuYang, R., Fan, X., Jiang, N., Yang, F., Wang, L., Zhou, B.

17-05-2022

Acta Trop

<https://pubmed.ncbi.nlm.nih.gov/35595093>

There is a lack of vaccine against human cysticercosis, thus making a huge population at the risk of infection. In this study, we chose a novel potential antigen molecule *Taenia solium* 14-3-3.3 (Ts14-3-3.3) and optimized it as sp-Ts14-3-3.3 (sp is immunoglobulin H chain V-region precursor, partial) in order to construct recombinant plasmids pMZ-X3-Ts14-3-3.3 and pMZ-X3-sp-Ts14-3-3.3. BALB/c mice were divided into four groups for immunization: pMZ-X3-Ts14-3-3.3, pMZ-X3-sp-Ts14-3-3.3, pMZ-X3 plasmid control group and PBS control group. Compared with two control groups, the proliferation level of splenic lymphocytes increased significantly in pMZ-X3-Ts14-3-3.3 and pMZ-X3-sp-Ts14-3-3.3 groups and reached the

maximum in week 6. And the same case arose as cytokines associated with Th1 response, IFN- γ , and IL-2 while those with Th2 response, IL-4, IL-10 went up and reached the maximum in week 4. The levels of serum specific IgG, IgG1 and IgG2a rose and reached the maximum in week 6, 4 and 6 respectively. Meanwhile, the proportion of CD4⁺/CD8⁺ splenic T lymphocytes increased and reached the peak in week 6. The results indicated that the recombinant plasmids pMZ-X3-Ts14-3-3.3 and pMZ-X3-sp-Ts14-3-3.3 can induce specific cellular and humoral immune responses in BALB/c mice with immunization. Notably, the recombinant plasmid pMZ-X3-sp-Ts14-3-3.3 has a better immune effect, which proves that Ts14-3-3.3 enjoys a higher possibility as a potential antigen molecule to *T. solium* vaccine.

CystiHuman: A model of human neurocysticercosis.

Bonnet, G., Pizzitutti, F., Gonzales-Gustavson, E., Gabriël, S., Pan, W., Garcia, H., Bustos, J., Vilchez, P., O'Neal, S., Cysticercosis Working Group in Peru

19-05-2022

PLoS Comput Biol

<https://doi.org/10.1371/journal.pcbi.1010118>

Introduction: The *Taenia solium* tapeworm is responsible for cysticercosis, a neglected tropical disease presenting as larvae in the body of a host following taenia egg ingestion. Neurocysticercosis (NCC), the name of the disease when it affects the human central nervous system, is a major cause of epilepsy in developing countries, and can also cause intracranial hypertension, hydrocephalus and death. Simulation models can help identify the most cost-effective interventions before their implementation. Modelling NCC should enable the comparison of a broad range of interventions, from treatment of human taeniasis (presence of an adult taenia worm in the human intestine) to NCC mitigation. It also allows a focus on the actual impact of the disease, rather than using proxies as is the case for other models. **Methods:** This agent-based model is the first model that simulates human NCC and associated pathologies. It uses the output of another model, CystiAgent, which simulates the evolution of pig cysticercosis and human taeniasis, adding human and cyst agents, including a model of cyst location and stage, human symptoms, and treatment. CystiHuman also accounts for delays in the appearance of NCC-related symptoms. It comprises three modules detailing cyst development, seizure probability and timing, and intracranial hypertension/hydrocephalus, respectively. It has been implemented in Java MASON and calibrated in three endemic villages in Peru, then applied to another village (Rica Playa) to compare simulation results with field data in that village. **Results and discussion:** Despite limitations in available field data, parameter values found through calibration are plausible and simulated outcomes in Rica Playa are close to actual values for NCC prevalence and the way it increases with age and cases with single lesions. Initial simulations further suggest that short-term interventions followed by a rapid increase in taeniasis prevalence back to original levels may have limited impacts on NCC prevalence.

Cysticidal Therapy for Diffuse Parenchymal and Calcific Neurocysticercosis (1931).

04-04-2022

Neurology

<https://doi.org/10.1212/WNL.000000000200700>

DRACUNCULOSE

ECHINOCOCCOSE

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

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

20-05-2022

Microb Pathog

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

Cystic Echinococcosis (hydatidosis) is caused by the larval stage of *Echinococcus* sp. It is an animal-borne zoonotic parasitic disease with local epidemic and natural foci, which is very common in northwest China. In recent years, a considerable attention has been paid to the epidemic investigation of hydatid disease in humans and sheep, but there are few large-scale epidemic investigation and data analysis of bovine hydatid disease. We systematically reviewed and analyzed the prevalence of bovine hydatid disease (2000-2021) in China for the first time. Several databases including CNKI, Wanfang, VIP Chinese periodical database, Baidu Library, PubMed and ScienceDirect were used to search 57 articles and 72 sets of valid data about bovine hydatid disease in China from 2000 to 2021. We used the random effect model in META package of R software, and PAS for rate conversion. The subgroup analysis and univariate meta regression analysis were used to reveal the factors leading to the heterogeneity of the study. The total prevalence rate of bovine hydatid disease in China from 2000 to 2021 is estimated to be 17.27% (10898/63113). According to the analysis of sampling years, the lowest positive rate since 2016 is 7.54% (1503/19929). The highest prevalence rate of bovine hydatid disease is 53.93% (4340/8048). The infection rate of bovine liver accounted for the highest proportion of the total infections, 45.2% (2040/4507). We also assessed the effects of different geographical and climatic factors on the prevalence of bovine hydatid disease. The results showed that the prevalence rate of hydatid disease was higher in cold and humid areas. Although the infection rate of bovine hydatid disease has declined in recent years, it is still necessary to carry out long-term surveillance and control of hydatid disease, cut off the infection route and reduce the risk of infection in high-risk areas.

One-tube nested MGB Probe Real-time PCR Assay for Detection of *Echinococcus multilocularis* Infection in Plasma Cell Free DNA.

Li, R., Bao, H., Liu, C., Zhao, L., Kang, Y., Ge, R., Fan, H., Tang, F.
20-05-2022

Acta Trop

<https://pubmed.ncbi.nlm.nih.gov/35605672>

Introduction: The main objective of this study was to develop a One-tube nested MGB probe real-time PCR Assay for detecting *Echinococcus multilocularis* infection in human plasma cell free DNA (cfDNA). **Methods:** cfDNA was extracted from 10 E.m.-infected patients using a NucleoSnap DNA Plasma Kit and characterized by genomic sequencing. We designed nested PCR primers and MGB probe for *Echinococcus multilocularis* detection. The specificity, sensitivity and reproducibility of this assay were analyzed, and its validity was confirmed in 13 early stage clinical samples. **Results:** Several *Echinococcus multilocularis* -specific sequences were detected in the cfDNA of E.m.-infected patients, and CBLO020001206.1 was selected as the candidate sequence. We designed the primers and probe for the one tube nested real-time PCR. No cross-reactions with E.g. were observed. The detection limit was as low as 1 copy for *Echinococcus multilocularis*. The coefficients of variation were lower than 5% in intra- and inter-assays. 11 out of 13 patients were positive with nested MGB Probe PCR Assay and 3 patients were positive without outer primer in early stage Alveolar Echinococcosis patients. **Conclusion:** The one-tube nested MGB probe real-time PCR assay is a simple, rapid, and cost-effective method for detection of *Echinococcus multilocularis* infection in patients' Plasma DNA.

Primary Soft Tissue Hydatid Cysts.

Patmano, M., Çetin, D., Gümüş, T., Patmano, G., Yenigül, A.

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Türkiye Parazitol Derg

<https://doi.org/10.4274/tpd.galenos.2021.03511>

Objective: Hydatid cyst disease is a helminthic infection caused by *Echinococcus granulosus*, which is encountered with cysts in many organs, especially the liver and lungs. Soft tissue and intramuscular hydatid cyst are rare even in endemic countries. It is challenging to distinguish subcutaneous and intramuscular hydatid cysts from soft tissue tumors. This study aimed to present the clinical features of primary soft tissue hydatid cyst cases without liver and lung hydatid cyst in the Southeast Anatolian region, where hydatid cyst disease is endemic. **Methods:** Patients admitted to the Şanlıurfa Training and Research Hospital General Surgery and Orthopedics and Traumatology Outpatient Clinic between September 2018 and December 2019 with complaints of pain and/or swelling under the skin and soft tissue were evaluated. After the examinations, the records of the patients who were operated on with a pre-diagnosis of hydatid cyst and whose histopathologic evaluation was reported as a hydatid cyst were reviewed retrospectively. **Results:** Eight patients were included in the study. The mean age of the patients was

39.75±14.80 years. Lesions were located in neck (12.5%), left thoracic posterior area (25%), gluteus (25%), thigh (12.5%), right upper quadrant of abdominal wall (12.5%), and under the right clavicle (12.5%). When imaging methods were examined, ultrasonography was performed in 7 patients (87.5%), chest computed tomography was performed in 1 patient (12.5%), and magnetic resonance imaging was performed in 2 patients (25%). **Conclusion:** Diagnosis of hydatid cyst should be considered in the differential diagnosis of soft tissue tumors in countries of endemic regions for hydatid cyst disease such as Southeastern Anatolia Region, Turkey.

A Retrospective Evaluation of Serological Results of Cystic Echinococcosis Suspected Cases Admitted to Adiyaman Training and Research Hospital Between 2013-2020.

Çelik, T., Alev, C., Akgün, S., Güldoğan, E., Şahin, F.

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Turkiye Parazitol Derg

<https://doi.org/10.4274/tpd.galenos.2022.29591>

Objective: Cystic echinococcosis (CE) is prevalent, especially in animals in Turkey and stands as a significant zoonose. In this study, we aimed to retrospectively evaluate the indirect hemagglutination (IHA) tests results performed on samples of CE suspected patients in microbiology laboratory of our hospital. **Methods:** One thousand six hundred-seven files of patients admitted to hospital between January 2013 and December 2020 were examined for the presence of anti-*E. granulosus* immunoglobulin G antibodies. The patient's socio-demographic characteristics and radiological data were obtained from the hospital automatization system. **Results:** A total of 1.607 file records; 644 (40.1%) males and 963 (59.9%) females, aged between 1-96 years (average 45.26±19.91) were examined. It was found that 244 (15.18%) of the patients were positive, 78 (4.86%) were determined at an intermediary value and 1.285 (79.96%) were negative. According to the IHA method a titer of 1/320 and above were evaluated as positive. Compared to anti-*E. granulosus* IgG antibody titers 164 radiological data; while 28.6% of 21 patients who are evaluated as negative (1/80) and 46.2% of 78 patients who were evaluated as intermediary titer (1/160) had cystic lesion in the radiological findings. **Conclusion:** Based on the data, it is suggested that while interpreting the patient's serum antibody titers, patient's clinical and radiological findings should also be taken into account. If possible, it should be used along with another serological method like ELISA to assist CE patient's diagnosis and treatment.

Retrospective Determination of the Prevalence of Anti-*Echinococcus granulosus* Antibodies in Cystic Echinococcosis Pre-diagnosed Patients at Erciyes University Faculty of Medicine.

Yürük, M., Yaman, O., Sivcan, E., Erdoğan, E.

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Turkiye Parazitol Derg

<https://doi.org/10.4274/tpd.galenos.2022.32032>

Objective: Cystic echinococcosis (CE) is a parasitic disease that has been known for years in helminth diseases and it is important as human and animal health problem in many parts of the world and in our country due to economic losses. In this study, it was aimed to retrospectively evaluate the distribution of anti-*E. granulosus*-IgG antibodies in patients with pre-diagnosis of CE that referred to parasitology laboratory between January 2013-December 2018. **Methods:** Commercial kit was used for indirect hemagglutination (IHA), indirect fluorescent antibody test (IFAT) and Western blot (WB) methods using sera from patient samples was applied according to the kit proposal. In addition, patient materials for CAM, CSF and blood for which polymerase chain reaction (PCR)/QPCR tests were requested were examined. **Results:** Sera of the patients who were tested with at least one of the IHA, IFAT and WB methods or a combination of these methods, and 443 cases out of 2.283 cases were found to be *E. granulosus* seropositive. It was determined that 369 (62.03%) of 443 positive patients were female and 330 (37.97%) were male patients. Among these patients, 87 patients whose IFAT and/or IHA tests were negative were found to have positive results with the WB method. IFAT or IHA test results of 13 patients with negative WB tests were found to be positive. Four patients were identified with both tests positive but WB test results negative. In addition, 36 of 72 patients who underwent PCR/QPCR tests were found to be positive. **Conclusion:** As a result of a six-year retrospective screening, 22% of the cases were found to be positive, and it was concluded that the prevalence of CE is high and the use of a single test may be insufficient in the diagnosis of CE, therefore, test combinations will increase the sensitivity and reliability in reaching the correct diagnosis.

Seropositivity of Anti-*Echinococcus granulosus* in Patients with of Clinical Prediagnosis Cystic Echinococcosis at Kafkas University Health Research and Application Hospital.

Arslan, M., Mor, N., Bedir, H.

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Turkiye Parazitol Derg

<https://doi.org/10.4274/tpd.galenos.2022.00719>

Objective: Cystic echinococcosis (CE) is a common zoonotic disease in the world, which is caused by the larval form of *Echinococcus granulosus* settling in various organs in both animals and humans. It is common in livestock breeding areas and rural areas. This study was conducted to determine anti-*E. granulosus* seropositivity in patients with clinical pre-diagnosis/suspected CE in Kafkas University Health Research and Application Hospital in the Eastern Anatolia region of Turkey. **Methods:** Study material; between January 2018 and December 2020, 498 blood samples were sent to the Parasitology Laboratory from patients with clinical pre-diagnosis of CE, who applied to Kafkas University Health Research and Application Hospital for three years. The obtained serum samples were analyzed by indirect

hemagglutination method. **Results:** Anti-*Echinococcus granulosus* antibodies were detected in 74 (14.9%) of 498 patients with clinical pre-diagnosis of hydatid cyst. Of the positive cases, 53 (71.6%) were observed in women, and 21 (28.4%) in men ($p < 0.05$). Anti-*E. granulosus* antibodies were most commonly detected in the 16-30 age group (32.9%) ($p < 0.05$), and 19.3% in the 16-60 age group. **Conclusion:** Although the study data do not cover the entire Eastern Anatolia region of Turkey, it has been concluded that KE maintains its importance as a public health problem in the region.

Retrospective Results of Hacettepe University Faculty of Medicine Parasitology Laboratory Between 2014-2019.

İnal, N., Ünal Altıntop, T., Ergüven, S., Akyön Yılmaz, Y.

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Turkiye Parazitol Derg

<https://doi.org/10.4274/tpd.galenos.2022.84429>

Objective: Parasitic infections emerge as a significant health problem, especially in underdeveloped and developing countries. Epidemiological data play an important role in taking effective measures against parasitic diseases. **Methods:** Clinical samples (stool, blood, bone marrow and tissue samples, etc.) that were sent to Hacettepe University Hospitals Parasitology Laboratory between 2014 and 2019 were analyzed retrospectively. **Results:** The positivity rates of the parasites detected in this study are as follows; *Blastocystis* sp. (71.6%), *Dientamoeba fragilis* (13.3%), *Giardia lamblia* (4.7%), *Echinococcus* spp. (1.9%), *Enterobius vermicularis* (1.8%) and *Taenia* spp. (0.3%). In this study, four of the patients were found to be positive for *Leishmania* spp. and two patients for *Plasmodium falciparum* and four patients for *Plasmodium* spp. *E. histolytica*/*E. dispar* cysts and/or trophozoites examined by Trichrome staining in our study were not detected within six years. **Conclusion:** According to this data and in the light of the results obtained from different regions of our country, it will be possible to properly direct the necessary strategies for the diagnosis, treatment of parasitic infections and the implementation of preventive measures.

Contrast-enhanced ultrasound (CEUS) in patients with metastasis-like hepatic alveolar echinococcosis: a cohort study.

Schweizer, M., Schmidberger, J., Schlingeloff, P., Kratzer, W.

21-05-2022

J Ultrasound

<https://doi.org/10.1007/s40477-022-00688-x>

Objective: Hepatic alveolar echinococcosis (HAE) of the metastasis-like pattern, according to the *Echinococcus* Ulm classification, is usually discovered as an incidental finding, and the diagnostic differentiation from "true metastases" is difficult. The aim of this study was to investigate whether lesions of the "metastasis-like pattern" in HAE show a typical contrast behavior that can be used for differentiation from

metastasis in malignancies. **Methods:** This prospective clinical study included 11 patients with histologically confirmed HAE of the metastasis-like pattern (7 female and 4 male; mean age, 57.1 years; mean disease duration, 59.5 months), who had been examined by B-scan sonography and CEUS, from the National Echinococcosis Registry Germany. **Results:** On contrast-enhanced sonography, 11/11 reference lesions showed annular rim enhancement in the arterial and portal venous phases. Throughout the entire 4-min study period, none of the reference lesions showed central contrast enhancement-i.e., all exhibited a complete "black hole sign". A small central scar was seen in 81.8% of cases. **Conclusion:** In clinically unremarkable patients with incidentally detected metastasis-like lesions of the liver, contrast-enhanced sonographic detection of rim enhancement without central contrast uptake (black hole sign) should be considered evidence supporting a diagnosis of hepatic alveolar echinococcosis with a rare metastasis-like pattern. This can help to differentiate HAE from metastases, especially in high-endemic areas.

In vitro protoscolicidal effects of lithocholic acid on protoscoleces of *Echinococcus granulosus* and its mechanism.

Xu, Y., Qing, W., Wang, Z., Chen, L., Wang, L., Lv, H., Jiang, Y.

17-05-2022

Exp Parasitol

<https://pubmed.ncbi.nlm.nih.gov/35594934>

Surgery has been found to be the best choice of treatment for hydatidosis. However, leakage of cyst contents during surgery is the foremost reason for recurrence of hydatidosis. In this study, we investigated the in vitro efficacy of lithocholic acid (LCA) against *Echinococcus granulosus* protoscoleces. The protoscoleces were divided into a control group, an albendazole (ABZ) positive control group and LCA intervention groups at concentrations of 0.5, 1, 2, and 3 mmol/L and stained with 0.1% eosin for observation using an inverted microscope; the protoscolicidal ultrastructure was examined with SEM and TEM; the activities of ROS, SOD, and caspase-3 were investigated using an ROS kit, SOD kit, and caspase-3 kit, respectively; the contents of HO-1 and NQO-1 were analyzed by enzyme-linked immunosorbent assay; and the expression level of cytochrome c (Ctyc) was analyzed by western blotting. **Results:** As the concentration of LCA increased, the survival rate of protoscoleces gradually decreased. The microstructure shows that the external shape and internal structure were gradually deformed and collapse. SOD, GSH, HO-1 and NQO-1 decreased more significantly in the 3 mmol/L LCA group. However, ROS levels gradually increased. LCA treatment for 3 days at all concentrations significantly increased caspase-3 activity and expression in a dose-dependent manner. LCA decreased the level of Ctyc protein in vitro. LCA demonstrated a parasiticidal effect on the protoscoleces of *Echinococcus granulosus* in vitro. LCA may induce apoptosis of *E. granulosus* protoscoleces by oxidative stress and mitochondrial pathways.

Global distribution of *Echinococcus granulosus* genotypes in domestic and wild canids: A systematic review and meta-analysis.

Revue de littérature

Shams, M., Khazaei, S., Naserifar, R., Shariatzadeh, S., Anvari, D., Montazeri, F., Pirestani, M., Majidani, H.

20-05-2022

Parasitology

<https://doi.org/10.1017/S0031182022000658>

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

Cost-effectiveness evaluation of different control strategies for *Clonorchis sinensis* infection in a high endemic area of China: A modelling study.

He, Y., Huang, X., Fang, Y., Zeng, Q., Li, L., Luo, L., Lai, Y.

23-05-2022

PLoS Negl Trop Dis

<https://doi.org/10.1371/journal.pntd.0010429>

Clonorchiasis is an important food-borne parasitic disease caused by *Clonorchis sinensis* infection. The evaluation of long-term cost-effectiveness of control strategies is important for disease control and prevention. The present study aimed to assess the cost-effectiveness of the three recommended strategies (i.e., WHO, Chinese and Guangdong strategies) and different combinations of commonly used measures (i.e., preventive chemotherapy, information, education, and communication (IEC) and environmental improvement) on clonorchiasis. The study area, Fusha town in Guangdong Province, was a typical high endemic area in China. The analysis was based on a multi-group transmission model of *C. sinensis* infection. We set the intervention duration for 10 years and post-intervention period for 50 years. The corresponding costs and DALYs were estimated. Strategies with incremental cost-effectiveness ratios (ICERs) less than 1/5 of the willingness-to-pay threshold were identified as highly cost-effective strategies. The optimal control strategy was obtained using the next best comparator method. The ICERs of Guangdong strategy were \$172 (95% CI: \$143-\$230) US for praziquantel and \$106 (95% CI: \$85-\$143) US for albendazole, suggesting the highest cost-effectiveness among the three recommended strategies. For praziquantel, 470 sets of control strategies were identified as highly cost-effective strategies for achieving infection control (prevalence<5%). The optimal strategy consisted of chemotherapy targeted on at-risk population, IEC and environmental improvement, with coverages all being 100%, and with the ICER of \$202 (95% CI: \$168-\$271) US. The results for transmission control

(prevalence<1%) and albendazole were obtained with the same procedures. The findings may help to develop control policies for *C. sinensis* infection in high endemic areas. Moreover, the method adopted is applicable for assessment of optimal strategies in other endemic areas.

Retrospective Analysis of the Distribution of Intestinal Parasites in Patients Admitted to Dicle University Faculty of Medicine Between the Years 2011-2020.

Akpolat, N., Çakır, F., Çiçek, M., Bilden, A.

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Türkiye Parazitol Derg

<https://doi.org/10.4274/tpd.galenos.2022.88598>

Objective: The purpose of this study was to determine and evaluate retrospectively the distribution of intestinal parasites detected in patients who applied to Dicle University Medical Faculty Parasitology Laboratory between 2011-2020.

Methods: Stool samples sent to the parasitology laboratory for parasite examination were examined by the native-Lugol method and the samples sent with cellophane tape were examined microscopically for parasite examination. In addition, modified acid-fast and trichrome staining methods were used to identify protozoan. **Results:** Parasites were detected in 5.99% of 60.501 stool samples sent to the parasitology laboratory. *Blastocystis* spp. (57.62%) was detected with the highest rate among positive samples, followed by 31.93% *Giardia intestinalis*, 3.75% *Entamoeba histolytica/dispar*, 2.37% *Hymenolepis nana*, 1.57% *Fasciola* spp., 0.91% *Taenia saginata*, 0.72% *Enterobius vermicularis*, 0.52% *Cryptosporidium* spp., 0.42% *Cyclospora cayentanensis*, 0.19 *Ascaris lumbricoides* were detected. **Conclusion:** Although the incidence of intestinal parasite infections in our study decreased over a ten-year period, it continues to maintain its importance. Therefore, to reduce the prevalence of intestinal parasites; It is important to safeguarding clean water resources, solve infrastructure problems, and inform the public about sanitation rules.

A novel use of a geometric morphometric technique to distinguish human parasite eggs of twelve different species.

Suwandittakul, N., Mungthin, M., Kuntawong, K., Laojun, S., Pimsuka, S., Chaiphongpachara, T.

17-05-2022

Exp Parasitol

<https://pubmed.ncbi.nlm.nih.gov/35594932>

Copro-microscopic diagnostic methods are the most common approach for screening patients with parasitic infections. However, expertise is required to identify helminthic eggs from fecal specimens. Consequently, new methods are required. Novel technologies have recently been developed for the classification of organisms, including geometric morphometric (GM) approaches. In this study, the outline-based GM approach was used to distinguish the eggs of 12

common human parasite species, including *Ascaris lumbricoides*, *Trichuris trichiura*, *Enterobius vermicularis*, hookworm, *Capillaria philippinensis*, *Opisthorchis* spp., *Fasciola* spp., *Paragonimus* spp., *Schistosoma mekongi*, *Taenia* spp., *Hymenolepis diminuta* and *Hymenolepis nana*. The GM analysis revealed that the size cannot be used as the main variable in the identification of parasite species at the egg stage, producing only 30.18% overall accuracy. However, comparisons of shape based on the Mahalanobis distances between pairs of parasite species showed significant differences in all pairs ($p < 0.05$). The shape analysis produced 84.29% overall accuracy. This is the first time that outline-based GM has been preliminarily confirmed as a valuable approach to support copro-microscopic analysis, in order to effectively screen helminth eggs. However, further studies with a larger set of helminth eggs and artefacts should be carried out to increase confidence in the identification of parasite species in the absence of local experts.

Multiple biochemical indices and metabolomics of *Clonorchis sinensis* provide a novel interpretation of biomarkers.

Qiu, Y., Chang, Q., Gao, J., Bao, M., Luo, H., Song, J., Hong, S., Mao, R., Sun, Y., Chen, Y., Liu, M., Wang, C., Liu, X.
19-05-2022

Parasit Vectors

<https://doi.org/10.1186/s13071-022-05290-y>

Background: Clonorchiasis, an infectious disease caused by the liver fluke *Clonorchis sinensis*, may lead to the development of liver and gallbladder diseases, and even cholangiocarcinoma (CCA). However, the pathogenesis, host-pathogen interaction, and diagnostic markers for clonorchiasis remain unclear.

Methods: Eighteen rabbits were randomly divided into control group ($n=9$) and *C. sinensis*-infected group ($n=9$), and their plasma samples were collected at 7, 14, 28, and 63 days post-infection (dpi). Biochemical indices and metabolites in different infection periods were detected. A non-targeted ultra-performance liquid chromatography-tandem mass spectrometry (UPLC-MS/MS) approach was employed to investigate the metabolic profiles of plasma in rabbits, and related metabolic pathways of differential metabolites and correlation between candidate biochemical indices and differential metabolites were analyzed. Finally, the candidate biomarkers were verified with human samples using a targeted metabolomics method. **Results:** The result of biochemical indices indicated *C. sinensis* infection would affect the liver function biochemical indices, especially alanine aminotransferase, aspartate transaminase (AST), glutamyl transpeptidase (GGT), total bile acid, high-density lipoprotein, and cholinesterase. The metabolomic results showed that 58, 212, 23, and 21 differential metabolites were identified in different phases of the infection. Multivariate statistical analysis of differential metabolites revealed distinct metabolic signatures during different phases of infection, with most of these signatures being observed at 14 dpi, which mainly influences the amino acid metabolisms. For metabolites and biochemical indices, AST, GGT, hypoxanthine, L-pipecolic acid,

and D-glucuronate represented potential noninvasive biomarkers for the diagnosis of *C. sinensis* ($P < 0.05$ and $AUC > 0.8$). Furthermore, GGT and D-glucuronate levels were positively correlated with the infection ($r(28)=0.98$, $P < 0.0001$) and showed excellent diagnostic performance ($AUC=0.972$; 95% confidence interval, 0.921 to 1.000). **Conclusions:** The present results provide new insights into plasma metabolic changes in rabbits during *C. sinensis* infection, and the potential biomarker may be used for developing an effective method to diagnose clonorchiasis in the future.

Detection of Zoonotic Bacteria and *Paragonimus kellicotti* in Red Swamp Crayfish (*Procambarus clarkii*) and The Assessment of Traditional Crayfish Boils.

Palillo, J., Mollenkopf, D., Marsh, A., Wittum, T., James, J., Reichley, S., Ghosh, S., Palillo, M., Malbrue, R.
19-05-2022

J Food Prot

<https://doi.org/10.4315/JFP-22-035>

Studies on red swamp crayfish (*Procambarus clarkii*) outside of the United States confirm a variety of zoonotic pathogens, but in the \$200 million dollar US commercial crayfish industry it is unknown if these same pathogens occur, demonstrating a need to evaluate this consumer commodity. The study objectives were to evaluate specific zoonotic pathogens present on red swamp crayfish (*P. clarkii*) from two United States southeastern states, Alabama and Louisiana, and to determine the effectiveness of traditional food preparation to reduce pathogens. Experiment A evaluated the presence of *Escherichia coli*, *Salmonella*, *Staphylococcus aureus*, and *Vibrio* spp. in crayfish and environmental samples over a two-month collection period (May-June 2021). Crayfish sampling consisted of swabbing the cephalothorax region and submitting 15 samples testing for *E. coli*, *Salmonella*, and *S. aureus*, and an additional 15 samples testing for *Vibrio* spp. detection. Additionally crayfish shipping materials were sampled. In experiment B, 92 crayfish were evaluated for *Paragonimus kellicotti*. Experiment C compared the presence of *Vibrio* spp. between live and boiled crayfish. In experiment A & B, 100% (60/60) of crayfish samples and 81.25% (13/16) of environmental samples returned characteristic growth of *Vibrio* spp.. A total of 5% (3/60) samples returned *E. coli* growth with no statistical difference ($p = 0.5536$) between farms. *Paragonimus kellicotti*, *Salmonella*, and *S. aureus* were not recovered from any samples. In experiment C, 100% (10/10) of the live pre-boiled crayfish samples returned characteristic growth, while 10% (1/10) of samples of crayfish boiled in unseasoned water returned growth for *Vibrio* ($p < 0.0001$). These results confirm that *Vibrio* spp. and *E. coli* may be present on US commercial crayfish and care should be taken when handling any materials that live crayfish come into contact with as they can potentially be contaminated.

FILARIOSE LYMPHATIQUE

Characterization of a novel microfilarial antigen for diagnosis of *Wuchereria bancrofti* infections.

Greene, S., Fischer, K., Choi, Y., Curtis, K., Budge, P., Mitreva, M., King, C., Fischer, P., Weil, G.

23-05-2022

PLoS Negl Trop Dis

<https://doi.org/10.1371/journal.pntd.0010407>

Background: Lymphatic filariasis (LF) is a neglected tropical disease caused by the filarial nematodes *Wuchereria bancrofti*, *Brugia malayi* and *Brugia timori*. The Global Program to Eliminate LF uses mass drug administration (MDA) of anti-filarial drugs that clear microfilariae (Mf) from blood to interrupt transmission by mosquitos. New diagnostic tools are needed to assess the impact of MDA on bancroftian filariasis, because available serologic tests can remain positive after successful treatment. **Methodology/principal findings:** We identified Wb-bhp-1, which encodes a *W. bancrofti* homologue of BmR1, the *B. malayi* protein used in the *Brugia* Rapid antibody test for brugian filariasis. Wb-bhp-1 has a single exon that encodes a 16.3 kD protein (Wb-Bhp-1) with 45% amino acid identity to BmR1. Immunohistology shows that anti-Wb-Bhp-1 antibodies primarily bind to Mf. Plasma from 124 of 224 (55%) microfilaremic individuals had IgG4 antibodies to Wb-Bhp-1 by ELISA. Serologic reactivity to Wb-Bhp-1 varied widely with samples from different regions (sensitivity range 32-92%), with 77% sensitivity for 116 samples collected from microfilaremic individuals outside of sub-Saharan Africa. This variable sensitivity highlights the importance of validating new diagnostic tests for parasitic diseases with samples from different geographical regions. Individuals with higher Mf counts were more likely to have anti-Wb-Bhp-1 antibodies. Cross-reactivity was observed with a minority of plasma samples from people with onchocerciasis (17%) or loiasis (10%). We also identified, cloned and characterized BmR1 homologues from *O. volvulus* and *L. loa* that have 41% and 38% identity to BmR1, respectively. However, antibody assays with these antigens were not sensitive for onchocerciasis or loiasis. **Conclusions:** Wb-Bhp-1 is a novel antigen that is useful for serologic diagnosis of bancroftian filariasis. Additional studies are needed to assess the value of this antigen for monitoring the success of filariasis elimination programs.

Ivermectin as a possible treatment for COVID-19: a review of the 2022 protocols.

Marques, L., Beneti, S., Pinzon, C., Cardoso, F.

20-05-2022

Braz J Biol

<https://pubmed.ncbi.nlm.nih.gov/35584459>

Ivermectin is a safe and effective drug in humans and has been approved for use in numerous parasitic infections for over 50 years. In addition, many studies have already shown its antiviral activity. Ivermectin is generally well tolerated, with

no indication of central nervous system-associated toxicity at doses up to 10 times the highest FDA-approved dose of 200 µg/kg. The in vitro results of ivermectin for reducing SARS-CoV-2 viral load are promising and show that Ivermectin kills SARS-CoV-2 within 48 hours. A hypothesized mechanism of action for this drug is a likely inhibition of IMPα/β1-mediated nuclear import of viral proteins as demonstrated for other RNA viruses. However, controlled and randomized studies are needed to prove its effectiveness in COVID-19 in humans. In a single in vivo study with published results, patients confirmed to be infected with SARS-CoV-2 received at least one dose of ivermectin at any time during hospitalization. The use of ivermectin was associated with lower mortality during treatment with COVID-19, especially in patients who required increased inspired oxygen or ventilatory support. Additionally, 81 studies with the clinical use of ivermectin in humans are being carried out worldwide according to ClinicalTrials.gov. However, none of these data has been published so far. However, private and public entities in Brazil have been adopting this drug in their protocols as prophylaxis and in the initial phase of the disease. In addition, ivermectin has been used in mass treatment to prevent onchocerciasis and lymphatic filariasis in sub-Saharan Africa for many years. Surprisingly, this region has the lowest proportional mortality rate among the continents, despite the increasing numbers of infected people released by the World Health Organization.

MYCETOME

ONCHOCERCOSE

SCHISTOSOMIASE

Investigation of Intestinal and Blood Parasites in People Returning to Turkey with a History of Traveling Abroad During the Pandemic.

Ekici, A., Gürbüz, E., Ünlü, A., Yıldız, R., Aydemir, S., Halidi, A., Ödemiş, N., Karakuş, S., Yürektürk, Ş., Çiçek, M., Yılmaz, H.

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Türkiye Parazitoloj Derg

<https://doi.org/10.4274/tpd.galenos.2021.02886>

Objective: To investigate intestinal and blood parasites in people who have a history of traveling abroad during the Coronavirus disease-2019 pandemic and returning to Turkey.

Methods: In this study, 104 patients with gastrointestinal system and/or fever complaints who had traveled abroad during the pandemic period and returned to Turkey were

included. Parasitic agents were investigated by taking blood and stool samples from the patients. Additionally, urine samples were obtained from patients with hematuria or dysuria with the suspicion of schistosomiasis. A direct microscopic examination, the Crypto-Giardia immunochromatographic test, and ELISA methods were used in the examination of the stool samples. In order to detect *Plasmodium* species, blood samples were examined by preparing both the rapid diagnostic test and thick drop and thin smear preparations. **Results:** One or more parasite species were detected in 38 (38.5%) of 104 patients included in the study. While intestinal parasites were detected in 16 (32%) of 50 patients who traveled to Iran and 16 (33.3%) of 48 patients who traveled to Northern Iraq, blood parasites were not found. *Schistosoma mansoni* was detected in all 5 of the patients with a history of traveling to Sudan. *Plasmodium falciparum* was detected in 1 patient who traveled to the African continent. **Conclusion:** It is vital to take precautions to prevent parasitic diseases, such as malaria and schistosomiasis, during travels to African countries. During travels to neighboring countries of Turkey, such as Northern Iraq and Iran, hygiene should be paid attention to, so as to prevent contracting intestinal parasitic diseases. In addition, it was concluded that people who plan to travel abroad should have information about the endemic parasitic diseases of the country that they are going to.

The prophylactic and anti-fibrotic activity of phthalimido-thiazole derivatives in schistosomiasis mansoni.

Laranjeira Miranda Filho, C., de Oliveira Barbosa, M., Rodrigues Oliveira, A., Ferreira Pinto, A., Araújo, D., Lucena, J., de Araújo, R., de Oliveira, S., Lima Leite, A.
23-05-2022

Parasitol Res

<https://doi.org/10.1007/s00436-022-07533-4>

Schistosomiasis mansoni is considered a serious public health problem. As praziquantel is the only drug recommended by the World Health Organization for the treatment and control of schistosomiasis, the development of new drugs is of great significance. In this work, we present the antischistosomal activity of a small set of phthalimido-thiazole derivatives against *Schistosoma mansoni*. The effects of those derivatives on the viability of larvae juveniles and adult parasites, production and development of eggs, mortality of schistosomules in vitro by counting worms, and stages of eggs of infected animals in acute and chronic phases were evaluated, resulting in the identification of new multistage antischistosomal compounds. Additionally, a study of liver fibrogenesis was released. The phthalimido-thiazole derivatives, compounds 2b-d, 2h-j, had shown activity on schistosomules, achieving 100% mortality even at 5 mg/mL, in the first 24 h. In the chronic phase of schistosomiasis infection, compound 2i promoted a reduction in the number of immature eggs, an increase in the number of non-viable parasite eggs, a reduction in the average number of eggs in the liver and intestine, decrease in the levels of

hydroxyproline in the liver, and a reduction in the areas of hepatic fibrosis. This compound also promoted an increase of IL-10 and a reduction in the level of TNF- α in the liver. Accordingly, the phthalimido-thiazole scaffold is a new starting point for the development of multistage compounds that affect *S. mansoni* viability, egg formation, and production.

Implication of serum Nitric oxide and IgE in urinary schistosomiasis: the case of Bamendjing, Cameroon.

Nkam, E., Ajonina-Ekoti, I., Oumar, M., Chewa, S., Ntonifor, H.
19-05-2022

Acta Trop

<https://pubmed.ncbi.nlm.nih.gov/35598653>

Background: Urinary schistosomiasis (US), also known as bilharziasis is a waterborne parasitic infection most common in rural areas of developing countries. The infection is associated with haematuria but little or nothing is known about its association with other urinary parameters, induction of Nitric Oxide (NO) and IgE production around the Bamendjing Dam an area highly suspected of *Schistosoma haematobium* infections. The study sought to address this problem for possible future interventions and control.

Materials and methods: Urine samples were collected from 301 randomly selected participants and analysed for the presence of *S. haematobium* using the syringe filtration concentration method. Sera from patients infected with *S. haematobium* and also from some uninfected individuals were analysed for IgE and NO using ELISA and colorimetric methods respectively. **Findings:** The results showed a prevalence of 16.9% (51/301). Sixty percent of the 49 patients with nitrite in their urine, were infected with urinary schistosomiasis (US) (30/49; $p = 0.00$). Meanwhile only 40% of the 15 patients with bilirubinuria were infected with US (6/15; $p = 0.0241$). The risk of patients with US having leucocytes and nitrites was high (OR of 1.3 and 1.7 respectively). Total IgE serum levels were significantly higher in patients with US (648.872 ± 223.142) compared to uninfected individuals (275.682 ± 181.674) ($p = 0.00$). Infected persons had heightened mean NO levels ($2583617.647 \pm 1100678.786$) than non-infected participants ($1689766.667 \pm 1163084.729$). Urinary Schistosomiasis in association with urinary parameters had a significant impact on mean IgE levels ($F = 4.248$, $p = 0.022$). Patients infected with Urinary Schistosomiasis alone had significantly higher mean total IgE levels than non-infected participants ($p = 0.004$). **Conclusion:** Apart from haematuria, this study has demonstrated that Urinary Schistosomiasis is prevalent among inhabitants around the Bamendjing Dam and results in an increase of other urine parameters such as leucocytes and nitrates and high levels of serum NO and total serum IgE in patients. These parameters are important in the screening of patients for treatment and control of urinary schistosomiasis.

Oncolytic Myxoma virus infects and damages the tegument of the human parasitic flatworm *Schistosoma mansoni*.

Rahman, M., McFadden, G., Ruthel, G., Herbert, D., Freedman,

B., Greenberg, R., Bais, S.

19-05-2022

Exp Parasitol

<https://pubmed.ncbi.nlm.nih.gov/35598646>

Schistosomiasis is a devastating disease caused by parasitic flatworms of the genus *Schistosoma*. Praziquantel (PZQ), the current treatment of choice, is ineffective against immature worms and cannot prevent reinfection. The continued reliance on a single drug for treatment increases the risk of the development of PZQ-resistant parasites. Reports of PZQ insusceptibility lends urgency to the need for new therapeutics. Here, we report that Myxoma virus (MYXV), an oncolytic pox virus which is non-pathogenic in all mammals except leporids, infects and replicates in *S. mansoni* schistosomula, juveniles, and adult male and female worms. MYXV infection results in the shredding of the tegument and reduced egg production in vitro, identifying MYXV as the first viral pathogen of schistosomes. MYXV is currently in preclinical studies to manage multiple human cancers, supporting its use in human therapeutics. Our findings raise the exciting possibility that MYXV virus represents a novel and safe class of potential anthelmintic therapeutics.

A novel use of a geometric morphometric technique to distinguish human parasite eggs of twelve different species.

Suwandittakul, N., Mungthin, M., Kuntawong, K., Laojun, S., Pimsuka, S., Chaiphongpachara, T.

17-05-2022

Exp Parasitol

<https://pubmed.ncbi.nlm.nih.gov/35594932>

Copro-microscopic diagnostic methods are the most common approach for screening patients with parasitic infections. However, expertise is required to identify helminthic eggs from fecal specimens. Consequently, new methods are required. Novel technologies have recently been developed for the classification of organisms, including geometric morphometric (GM) approaches. In this study, the outline-based GM approach was used to distinguish the eggs of 12 common human parasite species, including *Ascaris lumbricoides*, *Trichuris trichiura*, *Enterobius vermicularis*, hookworm, *Capillaria philippinensis*, *Opisthorchis* spp., *Fasciola* spp., *Paragonimus* spp., *Schistosoma mekongi*, *Taenia* spp., *Hymenolepis diminuta* and *Hymenolepis nana*. The GM analysis revealed that the size cannot be used as the main variable in the identification of parasite species at the egg stage, producing only 30.18% overall accuracy. However, comparisons of shape based on the Mahalanobis distances between pairs of parasite species showed significant differences in all pairs ($p < 0.05$). The shape analysis produced 84.29% overall accuracy. This is the first time that outline-based GM has been preliminarily confirmed as a valuable approach to support copro-microscopic analysis, in order to effectively screen helminth eggs. However, further studies with a larger set of helminth eggs and artefacts should be carried out to increase confidence in the identification of parasite species in the absence of local experts.

Review of 2022 WHO guidelines on the control and elimination of schistosomiasis.

Revue de littérature

Lo, N., Bezerra, F., Colley, D., Fleming, F., Homeida, M., Kabatereine, N., Kabole, F., King, C., Mafe, M., Midzi, N., Mutapi, F., Mwanga, J., Ramzy, R., Satrija, F., Stothard, J., Traoré, M., Webster, J., Utzinger, J., Zhou, X., Danso-Appiah, A., Eusebi, P., Loker, E., Obonyo, C., Quansah, R., Liang, S., Vaillant, M., Murad, M., Hagan, P., Garba, A.

17-05-2022

Lancet Infect Dis

<https://pubmed.ncbi.nlm.nih.gov/35594896>

Schistosomiasis is a helminthiasis infecting approximately 250 million people worldwide. In 2001, the World Health Assembly (WHA) 54.19 resolution defined a new global strategy for control of schistosomiasis through preventive chemotherapy programmes. This resolution culminated in the 2006 WHO guidelines that recommended empirical treatment by mass drug administration with praziquantel, predominately to school-aged children in endemic settings at regular intervals. Since then, school-based and community-based preventive chemotherapy programmes have been scaled-up, reducing schistosomiasis-associated morbidity. Over the past 15 years, new scientific evidence-combined with a more ambitious goal of eliminating schistosomiasis and an increase in the global donated supply of praziquantel-has highlighted the need to update public health guidance worldwide. In February, 2022, WHO published new guidelines with six recommendations to update the global public health strategy against schistosomiasis, including expansion of preventive chemotherapy eligibility from the predominant group of school-aged children to all age groups (2 years and older), lowering the prevalence threshold for annual preventive chemotherapy, and increasing the frequency of treatment. This Review, written by the 2018-2022 Schistosomiasis Guidelines Development Group and its international partners, presents a summary of the new WHO guideline recommendations for schistosomiasis along with their historical context, supporting evidence, implications for public health implementation, and future research needs.

Community-wide prevalence and intensity of soil-transmitted helminthiasis and *Schistosoma mansoni* in two districts of Sierra Leone.

Tupps, C., Kargbo-Labour, I., Paye, J., Dhakal, S., Hodges, M., Jones, A., Davlin, S., Sonnie, M., Manah, S., Imtiaz, R., Zhang, Y.

20-05-2022

PLoS Negl Trop Dis

<https://doi.org/10.1371/journal.pntd.0010410>

In Sierra Leone, nationally powered school-based surveys have documented significant progress in the control of soil-transmitted helminthiasis (STH) and schistosomiasis. In order to assess the district-level prevalence and intensity of infection among key at-risk groups outside of school age children (SAC), we conducted a multi-stage, cluster-sample household survey in Bo and Kenema districts in May 2018.

From both districts, we examined 1,282 pre-school age children (PSAC), 730 school age children (SAC), and 517 adults over 14 years (including 387 women of reproductive age, or WRA) for STH and *Schistosoma mansoni* infection using Kato Katz technique. In Bo, STH prevalence was 8.0% (95% Upper Confidence Limit 10.2%) in PSAC, 6.4% (95% Upper Confidence Limit 9.0%) in SAC, 14.1% (95% Upper Confidence Limit 17.4%) in all adults and 11.9% (95% Upper Confidence Limit 17.4%) in WRA. In Kenema, STH prevalence was 18.1% (95% Upper Confidence Limit 20.5%) in PSAC, 17.3% (95% Upper Confidence Limit 20.7%) in SAC, and 16.9% (95% Upper Confidence Limit 20.5%) in all adults and 16.9% (95% Upper Confidence Limit 22.6%) in WRA. Hookworm species were the most prevalent of STH in both districts overall. The overall prevalence of *S. mansoni* was <10% in Bo and <20% in Kenema, and was similar across age groups. No moderate or heavy intensity STH infections or heavy intensity *S. mansoni* infections, as per World Health Organization (WHO) classification, were detected in either district. Sanitation variables, such as toilet access and quality, were independently associated with STH and *S. mansoni* infection. In Kenema, STH prevalence in SAC was within the WHO-defined range for annual treatment, whereas a previous nationally-powered survey estimated it to lie within the range of treatment once per two years. By utilizing community-based sampling, we were able to assess prevalence among WRA and make recommendations based on current guidance from WHO. To continue toward elimination of STH and *S. mansoni* as a public health problem, resources should be mobilized to increase access to and uptake of improved sanitation at community and household levels.

NAD-catabolizing ectoenzymes of *Schistosoma mansoni*.

Nation, C., Da'Dara, A., Skelly, P.

20-05-2022

Biochem J

<https://pubmed.ncbi.nlm.nih.gov/35593185>

Infection with schistosomes (blood flukes) can result in the debilitating disease schistosomiasis. These parasites survive in their host for many years, and we hypothesize that proteins on their tegumental surface, interacting with the host microenvironment, facilitate longevity. One such ectoenzyme - the nucleotide pyrophosphatase/phosphodiesterase SmNPP5 can cleave ADP (to prevent platelet aggregation) and NAD (likely preventing Treg apoptosis). A second tegumental ectoenzyme, the glycohydrolase SmNACE, also catabolizes NAD. Here, we undertake a comparative biochemical characterization of these parasite ectoenzymes. Both are GPI-linked and exhibit different optimal pH ranges. While SmNPP5 requires divalent cations, SmNACE does not. The Km values of the two enzymes for NAD at physiological pH differ: SmNPP5, Km=340µM±44; SmNACE, Km=49µM±4. NAD cleavage by each enzyme yields different products. SmNPP5 cleaves NAD to form nicotinamide mononucleotide (NMN) and AMP, whereas SmNACE cleaves NAD to generate nicotinamide (NAM) and adenosine diphosphate ribose (ADPR). Each enzyme can

process the other's reaction product. Thus, SmNACE cleaves NMN (to yield NAM and ribose phosphate) and SmNPP5 cleaves ADPR (yielding AMP and ribose phosphate). Metabolomic analysis of plasma containing adult worms supports the idea that these cleavage pathways are active in vivo. We hypothesize that a primary function of SmNPP5 is to cleave NAD to control host immune cell function and a primary function of SmNACE is to cleave NMN to generate the vital nutrient nicotinamide (vitamin B3) for convenient uptake by the worms. Chemical inhibition of one or both ectoenzymes could upset worm metabolism and control schistosome infection.

Climate Change and Cascading Risks from Infectious Disease.

Revue de littérature

Semenza, J., Rocklöv, J., Ebi, K.

19-05-2022

Infect Dis Ther

<https://doi.org/10.1007/s40121-022-00647-3>

Climate change is adversely affecting the burden of infectious disease throughout the world, which is a health security threat. Climate-sensitive infectious disease includes vector-borne diseases such as malaria, whose transmission potential is expected to increase because of enhanced climatic suitability for the mosquito vector in Asia, sub-Saharan Africa, and South America. Climatic suitability for the mosquitoes that can carry dengue, Zika, and chikungunya is also likely to increase, facilitating further increases in the geographic range and longer transmission seasons, and raising concern for expansion of these diseases into temperate zones, particularly under higher greenhouse gas emission scenarios. Early spring temperatures in 2018 seem to have contributed to the early onset and extensive West Nile virus outbreak in Europe, a pathogen expected to expand further beyond its current distribution, due to a warming climate. As for tick-borne diseases, climate change is projected to continue to contribute to the spread of Lyme disease and tick-borne encephalitis, particularly in North America and Europe. Schistosomiasis is a water-borne disease and public health concern in Africa, Latin America, the Middle East, and Southeast Asia; climate change is anticipated to change its distribution, with both expansions and contractions expected. Other water-borne diseases that cause diarrheal diseases have declined significantly over the last decades owing to socioeconomic development and public health measures but changes in climate can reverse some of these positive developments. Weather and climate events, population movement, land use changes, urbanization, global trade, and other drivers can catalyze a succession of secondary events that can lead to a range of health impacts, including infectious disease outbreaks. These cascading risk pathways of causally connected events can result in large-scale outbreaks and affect society at large. We review climatic and other cascading drivers of infectious disease with projections under different climate change scenarios. Supplementary file1 (MP4 328467 KB).

Characterization of aspartyl aminopeptidase from *Schistosoma japonicum*.

Shang, Z., Guo, Q., Zhou, X., Yue, Y., Zhou, K., Tang, L., Zhang, Z., Fu, Z., Liu, J., Lin, J., Xu, B., Zhang, M., Hong, Y.

16-05-2022

Acta Trop

<https://pubmed.ncbi.nlm.nih.gov/35584779>

The tegument of schistosomes is the interface between the worm and the host environment. Some molecules distributed on the tegument participate in host-parasite interactions. Aspartyl aminopeptidase (AAP), identified on the tegument of *Schistosoma japonicum* (*S. japonicum*), facilitate protein turnover by acting in concert with other aminopeptidases. In this study, the gene encoding *S. japonicum* aspartyl aminopeptidase (SjAAP) was cloned, expressed and characterized. Quantitative real-time PCR analysis showed that SjAAP was expressed in all studied developmental stages. The transcript level was higher in 8, 14, 21, and 28 days old worms than the other detected stages. Moreover, the level of expression in 42-day-old male worms was significantly higher than that in females. The recombinant SjAAP (rSjAAP) was expressed as both supernatant and inclusion bodies in *Escherichia coli* BL21 cells. The enzymatic activity of rSjAAP was 4.45 U/mg. The K_m and V_{max} values for H-Asp-pNA hydrolysis were discovered to be 5.93 mM and 0.018 mM·min⁻¹. Immunofluorescence analysis revealed that SjAAP is primarily distributed on the tegument and parenchyma of schistosomes. Western blot showed that rSjAAP possessed good immunogenicity. Although specific antibodies were produced in BALB/c mice vaccinated with rSjAAP emulsified with ISA 206 adjuvant, no significant reduction of worm burden and number of eggs in the liver was observed. Therefore, rSjAAP may not be suitable to act as a potential vaccine candidate against schistosomiasis japonica in mice. However, this study provides some foundation for further exploration of the biological function of this molecule.

iNOS is essential to maintain a protective Th1/Th2 response and the production of cytokines/chemokines against *Schistosoma japonicum* infection in rats.

Shen, J., Yu, S., Peng, M., Lai, D., Hide, G., Wu, Z., Lun, Z.

18-05-2022

PLoS Negl Trop Dis

<https://doi.org/10.1371/journal.pntd.0010403>

Humans and a wide range of mammals are generally susceptible to *Schistosoma* infection, while some rodents such as *Rattus* rats and *Microtus* spp are not. We previously demonstrated that inherent high expression levels of nitric oxide (NO), produced by inducible nitric oxide synthase (iNOS), plays an important role in blocking the growth and development of *Schistosoma japonicum* in wild-type rats. However, the potential regulatory effects of NO on the immune system and immune response to *S. japonicum* infection in rats are still unknown. In this study, we used iNOS-knockout (KO) rats to determine the role of iNOS-derived NO

in the immune system and immunopathological responses to *S. japonicum* infection in rats. Our data showed that iNOS deficiency led to weakened immune activity against *S. japonicum* infection. This was characterized by the impaired T cell responses and a significant decrease in *S. japonicum*-elicited Th2/Th1 responses and cytokine and chemokine-producing capability in the infected iNOS-KO rats. Unlike iNOS-KO mice, Th1-associated cytokines were also decreased in the absence of iNOS in rats. In addition, a profile of pro-inflammatory and pro-fibrogenic cytokines was detected in serum associated with iNOS deficiency. The alterations in immune responses and cytokine patterns were correlated with a slower clearance of parasites, exacerbated granuloma formation, and fibrosis following *S. japonicum* infection in iNOS-KO rats. Furthermore, we have provided direct evidence that high levels of NO in rats can promote the development of pulmonary fibrosis induced by egg antigens of *S. japonicum*, but not inflammation, which was negatively correlated with the expression of TGF- β 3. These studies are the first description of the immunological and pathological profiles in iNOS-KO rats infected with *S. japonicum* and demonstrate key differences between the responses found in mice. Our results significantly enhance our understanding of the immunoregulatory effects of NO on defensive and immunopathological responses in rats and the broader nature of resistance to pathogens such as *S. japonicum*.

Analysis of rhodopsin G protein-coupled receptor orthologs reveals semiochemical peptides for parasite (*Schistosoma mansoni*) and host (*Biomphalaria glabrata*) interplay.

Phan, P., Liang, D., Zhao, M., Wyeth, R., Fogarty, C., Duke, M., McManus, D., Wang, T., Cummins, S.

17-05-2022

Sci Rep

<https://doi.org/10.1038/s41598-022-11996-x>

Schistosomiasis is a medically significant disease caused by helminth parasites of the genus *Schistosoma*. The schistosome life cycle requires chemically mediated interactions with an intermediate (aquatic snail) and definitive (human) host. Blocking parasite development within the snail stage requires improved understanding of the interactions between the snail host and the *Schistosoma* water-borne free-living form (miracidium). Innovations in snail genomics and aquatic chemical communication provide an ideal opportunity to explore snail-parasite coevolution at the molecular level. Rhodopsin G protein-coupled receptors (GPCRs) are of particular interest in studying how trematode parasites navigate towards their snail hosts. The potential role of GPCRs in parasites makes them candidate targets for new antihelminthics that disrupt the intermediate host life-cycle stages, thus preventing subsequent human infections. A genomic-bioinformatic approach was used to identify GPCR orthologs between the snail *Biomphalaria glabrata* and miracidia of its obligate parasite *Schistosoma mansoni*. We show that 8 *S. mansoni* rhodopsin GPCRs expressed within the miracidial stage share overall amino acid similarity with 8

different *B. glabrata* rhodopsin GPCRs, particularly within transmembrane domains, suggesting conserved structural features. These GPCRs include an orphan peptide receptor as well as several with strong sequence homologies with rhabdomeric opsin receptors, a serotonin receptor, a sulfakinin (SK) receptor, an allatostatin-A (buccalin) receptor and an FMRamide receptor. Buccalin and FMRFa peptides were identified in water conditioned by *B. glabrata*, and we show synthetic buccalin and FMRFa can stimulate significant rates of change of direction and turn-back responses in *S. mansoni* miracidia. Ortholog GPCRs were identified in *S. mansoni* miracidia and *B. glabrata*. These GPCRs may detect similar ligands, including snail-derived odorants that could facilitate miracidial host finding. These results lay the foundation for future research elucidating the mechanisms by which GPCRs mediate host finding which can lead to the potential development of novel anti-schistosome interventions.

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

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

16-05-2022

Parasitology

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

Schistosoma mansoni is the main causative agent of intestinal schistosomiasis which affects millions of people worldwide. At the larval stage, miracidia are released into bodies of water where they utilize their motility to successfully infect their intermediate host, snails. Here, we revisit the motility and survival of *S. mansoni* miracidia throughout its life span. Briefly, miracidia motility was monitored at 30-min and 60-min intervals under the presence/absence of natural/artificial light. Based on a subjective evaluation of activity, body shape and transparency, 6 categories of miracidia activity were established from its fully active stage to its immobile larva stage. The estimated life span of miracidia was 5.8 and 3.5 h in the experiments with 60-min and 30-min observation intervals, respectively. Death was defined by an absence of cilia and body movement. When mobility was used as a proxy for infectivity, infective miracidia were detected at 2.5 and 4.5 h, respectively. The present miracidia motility and survival re-evaluation supports parameters optimization for computational modelling of schistosomiasis transmission dynamics. Target control interventions, especially at late stages next to transmission interruption, may greatly benefit from improved modelling studies.

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

Using quantitative PCR to identify opportunities to strengthen soil-transmitted helminth control in Solomon Islands: A cross-sectional epidemiological survey.

Le, B., Clarke, N., Hii, S., Byrne, A., Zendejas-Heredia, P., Lake, S., Sokana, O., Khattak, A., Romani, L., Engelman, D., Nasi, T., Boara, D., Kaldor, J., Steer, A., Traub, R., Nery, S.
23-05-2022

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Background: The Kato-Katz microscopy technique is the global standard for assessment of soil-transmitted helminth (STH) burden. However, major limitations include its poor sensitivity, requirement for rapid sample processing, and inability to differentiate hookworm species nor detect *Strongyloides* spp. infections. We assessed the prevalence and intensity of STH species in Solomon Islands by conducting a province-wide survey using quantitative PCR (qPCR) for diagnosis, which can provide much better characterisation of STH burden than microscopy. **Methodology/principal findings:** We conducted a cross-sectional survey in 18 villages in Western Province to detect infections with six STH species and quantify intensity with three. We used linear mixed model regression to identify potential water, sanitation, and hygiene (WASH) and environmental risk factors for infection. We collected stool specimens from 830 village residents. Overall STH prevalence was 63.3% (range 27.5 to 91.5% across villages), led by *Necator americanus* (54.5% [range 17.5-89.4%]), followed by *Ancylostoma ceylanicum* (15.5% [range 2.8-45.8%]), *Trichuris trichiura* (9.1% [range 0-79.2%]), and *Strongyloides* spp. (3.2% [range 0-29.2%]). Most infections were of light intensity for *N. americanus* (85.7%) and *T. trichiura* (90.7%). Owning a household latrine was associated with a lower risk of *N. americanus* infection (AOR 0.41, 95% CI 0.24-0.68) while greater precipitation was linked to more common *T. trichiura* infection (AOR 1.14, 95% CI 1.04-1.25). **Conclusion/significance:** In this first large-scale population survey of STH in the Pacific using qPCR, we found evidence that ivermectin should be incorporated into STH control programmes because of the presence of *T. trichiura* and *Strongyloides* spp., both of which are poorly responsive to albendazole. Furthermore, One Health strategies are needed for improved *A. ceylanicum* and *Strongyloides* spp. control, WASH access and use should be improved to complement deworming programmes, and control efforts should ideally be expanded to entire communities. **Trial registration:** ClinicalTrials.gov Australian and New Zealand Clinical Trials Registry ACTRN12618001086257.

Retrospective Analysis of the Distribution of Intestinal Parasites in Patients Admitted to Dicle University Faculty of Medicine Between the Years 2011-2020.

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Turkiye Parazitol Derg

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Objective: The purpose of this study was to determine and evaluate retrospectively the distribution of intestinal parasites detected in patients who applied to Dicle University Medical Faculty Parasitology Laboratory between 2011-2020.

Methods: Stool samples sent to the parasitology laboratory for parasite examination were examined by the native-Lugol method and the samples sent with cellophane tape were examined microscopically for parasite examination. In addition, modified acid-fast and trichrome staining methods were used to identify protozoan. **Results:** Parasites were detected in 5.99% of 60.501 stool samples sent to the parasitology laboratory. *Blastocystis* spp. (57.62%) was detected with the highest rate among positive samples, followed by 31.93% *Giardia intestinalis*, 3.75% *Entamoeba histolytica/dispar*, 2.37% *Hymenolepis nana*, 1.57% *Fasciola* spp., 0.91% *Taenia saginata*, 0.72% *Enterobius vermicularis*, 0.52% *Cryptosporidium* spp., 0.42% *Cyclospora cayetanensis*, 0.19 *Ascaris lumbricoides* were detected. **Conclusion:** Although the incidence of intestinal parasite infections in our study decreased over a ten-year period, it continues to maintain its importance. Therefore, to reduce the prevalence of intestinal parasites; It is important to safeguarding clean water resources, solve infrastructure problems, and inform the public about sanitation rules.

A novel use of a geometric morphometric technique to distinguish human parasite eggs of twelve different species.

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17-05-2022

Exp Parasitol

<https://pubmed.ncbi.nlm.nih.gov/35594932>

Copro-microscopic diagnostic methods are the most common approach for screening patients with parasitic infections. However, expertise is required to identify helminthic eggs from fecal specimens. Consequently, new methods are required. Novel technologies have recently been developed for the classification of organisms, including geometric morphometric (GM) approaches. In this study, the outline-based GM approach was used to distinguish the eggs of 12 common human parasite species, including *Ascaris lumbricoides*, *Trichuris trichiura*, *Enterobius vermicularis*, hookworm, *Capillaria philippinensis*, *Opisthorchis* spp., *Fasciola* spp., *Paragonimus* spp., *Schistosoma mekongi*, *Taenia* spp., *Hymenolepis diminuta* and *Hymenolepis nana*. The GM analysis revealed that the size cannot be used as the main variable in the identification of parasite species at the egg stage, producing only 30.18% overall accuracy. However,

comparisons of shape based on the Mahalanobis distances between pairs of parasite species showed significant differences in all pairs ($p < 0.05$). The shape analysis produced 84.29% overall accuracy. This is the first time that outline-based GM has been preliminarily confirmed as a valuable approach to support copro-microscopic analysis, in order to effectively screen helminth eggs. However, further studies with a larger set of helminth eggs and artefacts should be carried out to increase confidence in the identification of parasite species in the absence of local experts.

Community-wide prevalence and intensity of soil-transmitted helminthiasis and *Schistosoma mansoni* in two districts of Sierra Leone.

Tupps, C., Kargbo-Labour, I., Paye, J., Dhakal, S., Hodges, M., Jones, A., Davlin, S., Sonnie, M., Manah, S., Imtiaz, R., Zhang, Y. 20-05-2022

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In Sierra Leone, nationally powered school-based surveys have documented significant progress in the control of soil-transmitted helminthiasis (STH) and schistosomiasis. In order to assess the district-level prevalence and intensity of infection among key at-risk groups outside of school age children (SAC), we conducted a multi-stage, cluster-sample household survey in Bo and Kenema districts in May 2018. From both districts, we examined 1,282 pre-school age children (PSAC), 730 school age children (SAC), and 517 adults over 14 years (including 387 women of reproductive age, or WRA) for STH and *Schistosoma mansoni* infection using Kato Katz technique. In Bo, STH prevalence was 8.0% (95% Upper Confidence Limit 10.2%) in PSAC, 6.4% (95% Upper Confidence Limit 9.0%) in SAC, 14.1% (95% Upper Confidence Limit 17.4%) in all adults and 11.9% (95% Upper Confidence Limit 17.4%) in WRA. In Kenema, STH prevalence was 18.1% (95% Upper Confidence Limit 20.5%) in PSAC, 17.3% (95% Upper Confidence Limit 20.7%) in SAC, and 16.9% (95% Upper Confidence Limit 20.5%) in all adults and 16.9% (95% Upper Confidence Limit 22.6%) in WRA. Hookworm species were the most prevalent of STH in both districts overall. The overall prevalence of *S. mansoni* was <10% in Bo and <20% in Kenema, and was similar across age groups. No moderate or heavy intensity STH infections or heavy intensity *S. mansoni* infections, as per World Health Organization (WHO) classification, were detected in either district. Sanitation variables, such as toilet access and quality, were independently associated with STH and *S. mansoni* infection. In Kenema, STH prevalence in SAC was within the WHO-defined range for annual treatment, whereas a previous nationally-powered survey estimated it to lie within the range of treatment once per two years. By utilizing community-based sampling, we were able to assess prevalence among WRA and make recommendations based on current guidance from WHO. To continue toward elimination of STH and *S. mansoni* as a public health problem, resources should be mobilized to increase access to and uptake of improved sanitation at community and household levels.

GALE

Crusted scabies in a child with Down syndrome.

Cebeci, F., Erdemir, V., Gürel, M., Akdeniz, N., Aslan Kayıran, M.

23-05-2022

J Cosmet Dermatol

<https://doi.org/10.1111/jocd.15105>

MORSURES DE SERPENT

What the snake leaves in its wake: Functional limitations and disabilities among snakebite victims in Ghanaian communities.

Aglanu, L., Amuasi, J., Schut, B., Steinhorst, J., Beyuo, A., Dari, C., Agbogbately, M., Blankson, E., Punguyire, D., Lalloo, D., Blessmann, J., Abass, K., Harrison, R., Stienstra, Y.

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Background: The estimated five million snakebites per year are an important health problem that mainly affect rural poor populations. The global goal is to halve both mortality and morbidity from this neglected tropical disease by 2030. Data on snakebite morbidity are sparse and mainly obtained from hospital records. **Methods:** This community-based study was conducted among 379 rural residents with or without a history of snakebite in the Ashanti and Upper West regions of Ghana. All participants in the snakebite group were bitten at least six months before the day of survey. The World Health Organisation Disability Assessment Schedule 2.0 (WHODAS 2.0) and the Buruli Ulcer Functional Limitation Score were used to obtain patient-reported measure of functioning and disability. Long-term consequences were evaluated based on the severity of the symptoms at the time of the snakebite.

Findings: The median (IQR) time since the snakebite was 8.0 (3.5-16.5) years. The relative risk of disability was 1.54 (95% CI, 1.17-2.03) in the snakebite group compared to the community controls. Among patients with clinical symptoms suggesting envenoming at the time of bite, 35% had mild/moderate disabilities compared to 20% in the control group. The disability domains mainly affected by snakebite envenoming were cognition level, mobility, life activities and participation in society. A combination of the severity of symptoms at the time of the bite, age, gender and region of residence most accurately predicted the odds of having functional limitations and disabilities. **Conclusion:** The burden of snakebite in the community includes long-term disabilities of mild to moderate severity, which need to be considered when designing appropriate public health interventions. Estimating the total burden of snakebite is complicated by geographic differences in types of snakes and their clinical manifestations.