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Veille scientifique
Maladies tropicales négligées

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Cysticercose

Aggregation of Taenia solium cysticerci in pigs: Implications for transmission and control.

Kabululu ML, Johansen MV, Lightowlers M, Trevisan C, Braae UC, Ngowi HA.
23-05-2023
Parasite Epidemiol Control.
https://pubmed.ncbi.nlm.nih.gov/37261135/

Parasite aggregation within hosts is a fundamental feature of parasite distributions, whereby the majority of parasites are harboured by a minority of hosts. Parasite aggregation can influence their transmission and hence control. In this narrative review, possible sources of aggregation of *Taenia solium* cysticerci in pigs are discussed, along with implications for control of the parasite. While heavy *T. solium* infections in pigs could most likely be associated with ingestion of high doses of infective parasite eggs, consistent with coprophagic behaviour of pigs, lighter infections indicate a role of indirect routes of transmission to pigs, mostly from lower infection doses. Light infections are likely to be missed by commonly used diagnostic methods - tongue examination or meat inspection - and end up in the food chain. Hence, they entail a 'hidden' risk and are of a particular public health concern, especially in areas where meat is consumed raw or undercooked. To be effective and sustainable, control strategies against *T. solium* likely require a broader understanding of, and consideration for parasite transmission dynamics. More importantly, a holistic One Health approach incorporating interventions on humans, pigs and the environment will likely have a larger, more successful and sustainable impact.

Cysticercosis Mimicking Fibroadenoma of the Breast in a Young Female: A Case Report From North Central Nigeria.

Ezike KN, Okwudire-Ejeh IA, Dallang BC, Ndaiya R.
26-04-2023
Cureus.
https://pubmed.ncbi.nlm.nih.gov/37252499/

The parasitic infestation, cysticercosis, arises when humans are infested with the larvae (cysticerci) of the pork tapeworm, *Taenia solium* (*T. solium*). Epidemiologically, cysticercosis presents a worldwide distribution due in part to endemicity in developing countries in Latin America, Asia, and sub-Saharan Africa, and increased migration from these countries to more developed countries in Europe and North America. Cysticercosis may be asymptomatic or may manifest clinical symptoms and signs depending on which part of the body cysticerci are found, including skeletal and heart muscle, skin, subcutaneous tissues, the lungs, liver, the central nervous system (CNS), and less commonly, the oral mucosa and breast. We report a case of a mass in the left breast in an 11-year-old Nigerian girl, which was diagnosed clinically and on ultrasonography as fibroadenoma but was confirmed on histology to be cysticercosis. Cysticercosis should be included in the differential diagnoses of breast lumps in persons of all ages and sex, especially in endemic areas and in places with significant immigration from endemic areas.

Acute cysticercosis caused by Cysticercus tenuicollis in lambs.

Abdollahi M, Lotfollahzadeh S, Shokrpoor S, Ashrafi Tamai I.
29-05-2023
J Vet Intern Med.
https://pubmed.ncbi.nlm.nih.gov/37246792/

Differential Protein Expression of Taenia crassiceps ORF Strain in the Murine Cysticercosis Model Using Resistant (C57BL/6) Mice.

Jiménez L, Díaz-Zaragoza M, Hernández M, Navarro L, Hernández-Ávila R, Encarnación-Guevara S, Ostoa-Saloma P, Landa A.
04-05-2023
Pathogens.
https://pubmed.ncbi.nlm.nih.gov/37242348/

A cysticercosis model of *Taenia crassiceps* ORF strain in susceptible BALB/c mice revealed a Th2 response after 4 weeks, allowing for the growth of the parasite, whereas resistant C57BL/6 mice developed a sustained Th1 response, limiting parasitic growth. However, little is known about how cysticerci respond to an immunological environment in resistant mice. Here, we show that the Th1 response, during infection in resistant C57BL/6 mice, lasted up to 8 weeks and kept parasitemia low. Proteomics analysis of parasites during this Th1 environment showed an average of 128 expressed proteins; we chose 15 proteins whose differential expression varied between 70 and 100%. A total of 11 proteins were identified that formed a group whose expression increased at 4 weeks and decreased at 8 weeks, and another group with proteins whose expression was high at 2 weeks and decreased at 8 weeks. These identified proteins participate in tissue repair, immunoregulation and parasite establishment. This suggests that *T. crassiceps* cysticerci in mice resistant under the Th1 environment express proteins that control damage and help to establish a parasite in the host. These proteins could be targets for drugs or vaccine development.

Cysticercosis: Unearthing the worm.

Narayan B, Priya B, Urs AB.
Jan-Mar 2023
J Oral Maxillofac Pathol.
https://pubmed.ncbi.nlm.nih.gov/37234322/

Cysticercosis, a helminthic disease caused by *T. Solium*, is a major health concern in developing and underdeveloped nations of the world. If left untreated, it may lead to severe neurological and ophthalmic complications. The diagnosis of oral cysticercosis depends on the identification of the larva in the biopsied tissue. However, an accurate diagnosis can be challenging, if the larva is dead because of which it cannot be identified. In such a scenario, step by step approach to unearth the worm is discussed here.

Neurocysticercosis-related seizures: Imaging biomarkers.

Ratcliffe C, Adan G, Marson A, Solomon T, Saini J, Sinha S, Keller SS.
Mai-2023
Seizure.
https://pubmed.ncbi.nlm.nih.gov/37060627/

Dengue, chikungunya et maladie à virus Zika

Dengue Shock Syndrome with Acute Liver Failure- A Stormy Presentation of Congenital Dengue.

Subashri P, G B, Rao PVR.
31-05-2023
Indian J Pediatr.
https://pubmed.ncbi.nlm.nih.gov/37256450/

Chikungunya virus infection induces ultrastructural changes and impaired neuronal differentiation of human neurospheres.

de Lima Cavalcanti TYV, Azevedo EAN, Lima MC, Saraiva KLA, Franca RFO.
11-05-2023
Front Microbiol.
https://pubmed.ncbi.nlm.nih.gov/37250062/

Chikungunya virus (CHIKV) is an arthropod-borne virus recently associated with large outbreaks in many parts of the world. Infection is typically manifested as a febrile and self-limited illness, characterized by joint pain and myalgia, albeit severe neurological manifestations are also reported. Although CHIKV is not recognized as a truly neurotropic virus, neurons, astrocytes, and oligodendrocytes are susceptible to infection *in vitro*. Here we employed a model of 3D cell culture to obtain neurospheres from ATRA/BNDF differentiated human neuroblastoma cells. We demonstrate that CHIKV is able to establish a productive infection, resulting in ultrastructural changes in cell morphology and impaired neuronal differentiation. Ultrastructural analysis of neurospheres infected with CHIKV during neuronal differentiation revealed diminished neuron dendrite formation, accumulation of viral particles associated with the plasma membrane, numerous cell vacuoles, and swollen mitochondria. Apoptotic cells were significantly increased at 72 h post-infection. Compared to Zika virus, a well-characterized neurotropic arbovirus, CHIKV infection resulted in a more discrete, albeit detectable upregulation of IL-6 levels. Finally, we found that CHIKV infection resulted in an altered profile expression, mainly downregulation, of a group of transcription factors named Hox genes. Altogether our findings highlight important features of CHIKV in the CNS, as well as the feasibility of neurospheres as robust experimental models that can support further studies for novel pharmacological interventions.

Neonatal Chikungunya - An Emerging Tale of Neonatal Encephalopathy.

Kr A, Bandiya P, Hs N.
30-05-2023
Indian J Pediatr.
https://pubmed.ncbi.nlm.nih.gov/37248382/

Entomological surveillance of invasive Aedes mosquitoes in Mazandaran Province, northern Iran from 2014 to 2020.

Nikookar SH, Charkame A, Nezammahalleh A, Moradi-Asl E, Enayati A, Fazeli-Dinan M, Sedaghat MM, Zaim M.
29-05-2023
Sci Rep.
https://pubmed.ncbi.nlm.nih.gov/37248286/

Genetic Diversity and Dispersal of DENGUE Virus among Three Main Island Groups of the Philippines during 2015-2017.

Sy AK, Koo C, Privaldos KJR, Quinones MAT, Igoy MAU, Villanueva SYAM, Hibberd ML, Ng LC, Hapuarachchi HC.
28-04-2023
Viruses.
https://pubmed.ncbi.nlm.nih.gov/37243165/

Dengue has been one of the major public health concerns in the Philippines for more than a century. The annual dengue case burden has been increasing in recent years, exceeding 200,000 in 2015 and 2019. However, there is limited information on the molecular epidemiology of dengue in the Philippines. We, therefore, conducted a study to understand the genetic composition and dispersal of DENV in the Philippines from 2015 to 2017 under UNITEDengue. Our analyses included 377 envelope (*E*) gene sequences of all 4 serotypes obtained from infections in 3 main island groups (Luzon, Visayas, and Mindanao) of the Philippines. The findings showed that the overall diversity of DENV was generally low. DENV-1 was relatively more diverse than the other serotypes. Virus dispersal was evident among the three main island groups, but each island group demonstrated a distinct genotype composition. These observations suggested that the intensity of virus dispersal was not substantive enough to maintain a uniform heterogeneity among island groups so that each island group behaved as an independent epidemiological unit. The analyses suggested Luzon as one of the major sources of DENV emergence and CAR, Calabarzon, and CARAGA as important hubs of virus dispersal in the Philippines. Our findings highlight the importance of virus surveillance and molecular epidemiological analyses to gain deep insights into virus diversity, lineage dominance, and dispersal patterns that could assist in understanding the epidemiology and transmission risk of dengue in endemic regions.

Monodelphis domestica as a Fetal Intra-Cerebral Inoculation Model for Zika Virus Pathogenesis.

Thomas J, Garcia J, Terry M, Mahaney S, Quintanilla O, Silva DC, Morales M, VandeBerg JL.
19-05-2023
Pathogens.
https://pubmed.ncbi.nlm.nih.gov/37242404/

The prevalence of IGM antibodies to Zika virus in pregnant women in Northern Nigeria.

Adekola HA, Ojo DA, Balogun SA, Dipeolu MA, Mohammed M, Adejo DS, Aliyu RM, Abdullahi MA, Madugu NH.
18-05-2023
Vopr Virusol.
https://pubmed.ncbi.nlm.nih.gov/37264846/

Introduction: Zika virus (ZIKV) infection during pregnancy can result in severe outcomes for both the pregnant woman and the developing fetus. The objective of this study was to investigate the prevalence of Zika virus infection among pregnant women who sought healthcare services at Ahmadu Bello University Teaching Hospital. Materials and methods: Serum samples were collected and analyzed using Enzyme Linked Immunoassay and RT-qPCR methods, while a structured questionnaire was used to gather relevant information about the participants. Results: The results showed that 53 out of the 180 pregnant women tested positive for Anti-Zika IgM antibodies, which represents a 29.4% prevalence rate. Subsequent RT-qPCR analysis found that only 6 out of the 53 positive samples contained Zika virus RNA. Fever and headache were the most commonly reported symptoms related to the infection. Conclusion: These findings indicate a potential outbreak of Zika fever in Northern Nigeria emphasizing the importance for pregnant women to take precautions to avoid getting infected.

Vertical dispersal of Aedes albopictus within multi-story buildings in downtown Shanghai, China.

Jin S, Fan J, Cao H, Zhang Z, Leng P, Gao Q.
01-06-2023
Parasit Vectors.
https://pubmed.ncbi.nlm.nih.gov/37264465/

Background: Shanghai has numerous high-rise apartment and office buildings, but the effects of these high-rise spaces on the vertical dispersal, oviposition and blood feeding behavior of Aedes albopictus are unknown. Methods: In six multi-story building blocks in downtown Shanghai, 174 mosq-ovitraps (MOT) were placed both indoors and outdoors for Ae. albopictus collection at different vertical heights from the 1st to 6th floors and a terrace on the 8th floor. Collections were made for 4 months. The human landing catch (HLC) method for Ae. albopictus monitoring was also conducted on 6 consecutive days on six floors of two of the six buildings to study the feeding behavior of Ae. albopictus at different heights. Results: Both MOTs and HLCs collected Ae. albopictus at all monitored heights. The vertical distribution, oviposition pattern and biting behavior varied significantly among the seven heights (1st-6th floors and 8th floor) (mosq-ovitrap index (MOI): $X^2 = 140.616$, df = 6, $P < 0.001$; HLC: $F_{(5, 138)} = 15.111$, $P < 0.001$). The MOI at low heights (1st + 2nd floors) was significantly higher than that at medium (3rd + 4th floor, $P < 0.001$) and high heights (5th + 6th floors, $P < 0.001$), and there was no significant difference in the MOI for the 3rd-6th floors. The outdoor MOIs were significantly higher than indoor MOIs at all heights (outdoor 23.09% vs. indoor 9.58%, $X^2 = 74.121$, df = 1, $P < 0.001$). Aedes albopictus HLC density on the ground floor was significantly higher than that on all other heights (5.04 vs. 0.13, 0.29, 0.58, 0.79 and 1.50 per half hour, $P < 0.05$), while no difference was detected among the heights above the ground floor ($P > 0.05$). Conclusions: Aedes albopictus is more common near the ground level, but it can easily disperse to higher floors in the multi-story buildings of urban Shanghai. No significant differences in Ae. albopictus density were detected within the 3rd-6th floors using MOT or HLC. This suggests that Ae. albopictus might also disperse to areas above the 6th floor and seek hosts there. Aedes albopictus prefers to oviposit outdoors; however, Ae. albopictus was also able to inhabit, oviposit and engage in blood-feeding behavior indoors on different floors. The three-dimensional dispersal pattern of Ae. albopictus in urban areas could facilitate arbovirus transmission and increase the difficulty of dengue control.

Accuracy of Dengue, Chikungunya, and Zika diagnoses by primary healthcare physicians in Tegucigalpa, Honduras.

Mejía MFÁ, Shu PY, Ji DD.
01-06-2023
BMC Infect Dis.
https://pubmed.ncbi.nlm.nih.gov/37264307/

Different outcomes of neonatal and adult Zika virus infection on startle reflex and prepulse inhibition in mice.

Souza INO, Andrade BS, Frost PS, Neris RLS, Gavino-Leopoldino D, Da Poian AT, Assunção-Miranda I, Figueiredo CP, Clarke JR, Neves GA.
30-05-2023
Behav Brain Res.
https://pubmed.ncbi.nlm.nih.gov/37263423/

Zika virus (ZIKV) infection causes severe neurological consequences in both gestationally-exposed infants and adults. Sensorial gating deficits strongly correlate to the motor, sensorial and cognitive impairments observed in ZIKV-infected patients. However, no startle response or prepulse inhibition (PPI) assessment has been made in patients or animal models. In this study, we identified different outcomes according to the age of infection and sex in mice: neonatally infected animals presented an increase in PPI and delayed startle latency. However, adult-infected male mice presented lower startle amplitude, while a PPI impairment was observed 14 days after infection in both sexes. Our data further the understanding of the functional impacts of ZIKV on the developing and mature nervous system, which could help explain other behavioral and cognitive alterations caused by the virus. With this study, we support the startle reflex testing in ZIKV-exposed patients, especially infants,

allowing for early detection of functional neuromotor damage and early intervention.

Expression of recombinant dengue virus type 1 non-structural protein 1 in mammalian cells and preliminary assessment of its suitability to detect human IgG antibodies elicited by viral infection.

Malnero CM, Azevedo RC, Bergmann IE, de Meneses MDF, Cavalcanti AC, Ibáñez LI, Malirat V.
30-05-2023
J Immunol Methods.
https://pubmed.ncbi.nlm.nih.gov/37263391/

Diagnosis of Acute Dengue Virus Infection Using Enzyme-Linked Immunosorbent Assay and Real-Time PCR.

Iqbal G, Javed H, Raza FA, Gohar UF, Fatima W, Khurshid M.
22-05-2023
Can J Infect Dis Med Microbiol.
https://pubmed.ncbi.nlm.nih.gov/37261378/

Dengue fever is a viral infection caused by the dengue virus and is a growing concern for public health worldwide, particularly in tropical and subtropical regions. This study aimed to assess the diagnostic accuracy of a commercially available NS1 ELISA kit for dengue fever in Pakistan using multiplex qRT-PCR as the gold standard. The study recruited 1236 suspected cases of dengue fever admitted to public sector hospitals in Lahore, Pakistan. Of the suspected cases, 610 (49.3%) were confirmed positive for DENV infection through qRT-PCR, with all four serotypes detected. DENV-2 was the most prevalent serotype, detected in 95.7% of cases. The NS1 ELISA kit detected 71.1% of the positive cases. However, the diagnostic accuracy of the NS1 ELISA kit was found to be only 64.89%. Of the 610 confirmed cases, 68% were male and 32% were female, with a median age of 30 years. Dengue fever was diagnosed in 91.8% of cases, while 8.2% were diagnosed with dengue hemorrhagic fever (DHF). DHF patients had a higher prevalence of abdominal pain, hemorrhagic manifestations, and thrombocytopenia. The cocirculation of all four DENV serotypes in Lahore is concerning and could lead to more severe forms of the disease, such as DHF or dengue shock syndrome, in the future. The study highlights the low diagnostic accuracy of commercially available NS1 ELISA kits and emphasizes the importance of using molecular methods to confirm acute dengue infections. Given the increasing prevalence of dengue fever in developing countries like Pakistan, more accurate and reliable diagnostic tools are needed for effective disease management and control.

Infectious Causes of Acute Encephalitis Syndrome in India: Decadal Change and the Way Forward.

Tandale BV, Narang R, Kumar GV, Jain M, Tomar SJ, Deshmukh PS.
30-05-2023
Indian Pediatr.
https://pubmed.ncbi.nlm.nih.gov/37260063/

The diagnosis and management of encephalitis were largely based on clinical grounds and minimal laboratory investigations. Japanese encephalitis (JE) was considered as the probable diagnosis in most encephalitis cases. However, reports of JE in adults and the elderly are increasing after the JE vaccine introduction among children in 2006. The Nipah virus (NiV) emerged in 2002 and continues to afflict humans in new geographic areas. Many other infections cause encephalitis, including Chandipura, chikungunya, dengue, and West Nile. Significant advances in diagnostic testing like multiplex testing panels and metagenomic approaches along with sequencing have helped in the detection of new etiologies. Recent years have witnessed an increase in climate-sensitive zoonotic diseases with encephalitis. This highlights the importance of the One Health approach in studying the impact of climate change-associated infectious diseases on human health. The government of India's efforts to develop health research infrastructure would help future responses to emerging infectious disease epidemics.

N-Butanol Extract of Glycyrrhizae Radix et Rhizoma Inhibits Dengue Virus through Targeting Envelope Protein.

Shi LZ, Chen X, Cao HH, Tian CY, Zou LF, Yu JH, Lu ZB, Zhao W, Liu JS, Yu LZ.
Fév-2023
Pharmaceuticals (Basel).
https://pubmed.ncbi.nlm.nih.gov/37259408/

Background: At present, about half of the world's population is at risk of being infected with dengue virus (DENV). However, there are no specific drugs to prevent or treat DENV infection. Glycyrrhizae Radix et Rhizome, a well-known traditional Chinese medicine, performs multiple pharmacological activities, including exerting antiviral effects. The aim of this study was to investigate the anti-DENV effects of *n*-butanol extract from Glycyrrhizae Radix et Rhizome (GRE). Methods: Compounds analysis of GRE was conducted via ultra-performance liquid chromatography/tandem mass spectrometry (UHPLC-MS/MS). The antiviral activities of GRE were determined by the CCK-8 assay, plaque assay, qRT-PCR, Western blotting, and the immunofluorescence assay. The DENV-infected suckling mice model was constructed to explore the antiviral effects of GRE in vivo. Results: Four components in GRE were analyzed by UHPLC-MS/MS, including glycyrrhizic acid, glycyrrhetnic acid, liquiritigenin, and isoliquiritigenin. GRE inhibited the attachment process of the virus replication cycle and reduced the expression of the E protein in cell models. In the in vivo study, GRE significantly relieved clinical symptoms and prolong survival duration. GRE also significantly decreased viremia, reduced the viral load in multiple organs, and inhibited the release of pro-inflammatory cytokines in DENV-infected suckling mice.

Conclusions: GRE exhibited significant inhibitory activities in the adsorption stage of the DENV-2 replication cycle by

targeting the envelope protein. Thus, GRE might be a promising candidate for the treatment of DENV infection.

Hemophagocytic lymphohistiocytosis as a rare complication of dengue haemorrhagic fever: a case report.

Pradeep C, Karunathilake P, Abeyagunawardena S, Ralapanawa U, Jayalath T.
01-06-2023
J Med Case Rep.
https://pubmed.ncbi.nlm.nih.gov/37259116/

Immunoinformatics Vaccine Design for Zika Virus.

Antonelli AC, Almeida VP, da Fonseca SG.
2023
Methods Mol Biol.
https://pubmed.ncbi.nlm.nih.gov/37258930/

Aetiology of Acute Undifferentiated Fever Among Children Under the Age of Five in Vietnam: A Prospective Study.

Tran XD, Hoang VT, Dang TTD, Vu TP, To MM, Tran TK, Do MD, Nguyen DC, Nguyen QT, Colson P, Parola P, Marty P, Gautret P.
31-05-2023
J Epidemiol Glob Health.
https://pubmed.ncbi.nlm.nih.gov/37258852/

Background: To investigate the aetiology of acute undifferentiated fever (AUF) among children under the age of five in Vietnam. Methods: This prospective study was conducted in the Thai Binh paediatric hospital, between July 2020 and July 2021 among children with AUF at admission. Real-time PCR testing 18 microbial pathogens were done on blood samples. Results: 286 children were included, with median age of 16 months. 64.7% were male. 53.9% were positive for at least one pathogen by PCR. Enterovirus, human herpesvirus 6, adenovirus, and varicella zoster virus PCR were positive for 31.1, 12.6, 1.4, and 1.0% patients, respectively. Other pathogens tested negative by PCR. During the hospital stay, based on clinical criteria 47.2% children secondarily presented with signs of respiratory tract infections, 18.9% had hand, foot and mouth disease, 4.6% had chickenpox. 4.2% presented signs of central nervous system infections, 1.0% had dengue (antigenic test) and 1.0% had signs of gastrointestinal infection. Finally, 23.1% patients presented a fever with or without a rash and no other symptoms and ultimately received a diagnosis of AUF. Conclusion: Real-time PCR of blood is useful for detecting pathogens and diagnosing infectious causes of AUF. Further prospective studies with blood and urine culture testing and PCR investigation of not only blood but also cerebrospinal fluid, throat, and skin samples according to symptoms would be of interest to confirm the predominance of viral infections in children with AUF and to guide therapeutic options.

Reddit and Google Activity Related to Non-COVID Epidemic Diseases Surged at Start of COVID-19 Pandemic: Retrospective Study.

Cummins JA, Lipworth AD.
15-05-2023
JMIR Form Res.
https://pubmed.ncbi.nlm.nih.gov/37256832/

[Health and sanitation: an evaluation of public policies for the prevention, control, and contingency of arboviruses in Brazil].

Faria MTDS, Ribeiro NRS, Dias AP, Gomes UAF, Moura PM.
Juin2023
Cien Saude Colet.
https://pubmed.ncbi.nlm.nih.gov/37255153/

Severe dengue in children associates with dysregulation of lipid homeostasis, complement cascade and retinol transport.

Panwar A, Kumar R, Goel R, Aggarwal S, Saraswat S, Bansal P, Gonmei Z, Toteja G, Yadav A, Lodha R, Singh N, Medigeshi G.
Juin-2023
Clin Transl Med.
https://pubmed.ncbi.nlm.nih.gov/37254651/

Risk of dengue, Zika, and chikungunya transmission in the metropolitan area of Cucuta, Colombia: cross-sectional analysis, baseline for a cluster-randomised controlled trial of a novel vector tool for water containers.

Carrillo MA, Cardenas R, Yañez J, Petzold M, Kroeger A.
30-05-2023
BMC Public Health.
https://pubmed.ncbi.nlm.nih.gov/37254133/

Background: Arbovirus diseases such as dengue, Zika, and chikungunya are a public health threat in tropical and subtropical areas. In the absence of a vaccine or specific treatment, vector management (in this case the control of the primary vector Aedes aegypti) is the best practice to prevent the three diseases. A good understanding of vector behaviour, ecology, human mobility and water use can help design effective vector control programmes. This study collected baseline information on these factors for identifying the arbovirus transmission risk and assessed the requirements for a large intervention trial in Colombia. Methods: Baseline surveys were conducted in 5,997 households, randomly selected from 24 clusters (neighbourhoods with on average 2000 houses and 250 households inspected) in the metropolitan area of Cucuta, Colombia. The study established population characteristics including water management and mobility as well as larval-pupal indices which were estimated and compared in all clusters. Additionally, the study estimated disease incidence from two sources: self-reported dengue cases in the household survey and cases notified by the national surveillance system. Results: In all 24 study

clusters similar social and demographic characteristics were found but the entomological indicators and estimated disease incidence rates varied. The entomological indicators showed a high vector infestation: House Index = 25.1%, Container Index = 12.3% and Breteau Index = 29.6. Pupae per person Index (PPI) as an indicator of the transmission risk showed a large range from 0.22 to 2.04 indicating a high transmission risk in most clusters. The concrete ground tanks for laundry - mostly outdoors and uncovered- were the containers with the highest production of Ae. aegypti as 86.3% of all 17,613 pupae were identified in these containers. Also, the annual incidence of dengue was high: 841.6 self-reported cases per 100,000 inhabitants and the dengue incidence notified by the National surveillance system was 1,013.4 cases per 100,000 in 2019. Only 2.2% of the households used container water for drinking. 40.3% of the study population travelled during the day (when Aedes mosquitoes bite) outside their clusters. Conclusions: The production of Ae. aegypti mosquitoes occurred almost exclusively in concrete ground tanks for laundry (lavadero), the primary intervention target. The baseline study provides necessary evidence for the design and implementation of a cluster randomized intervention trial in Colombia.

Factors Associated with Chikungunya Infection among Pregnant Women in Grenada, West Indies.

Kiener M, Cudjoe N, Evans R, Mapp-Alexander V, Tariq A, Macpherson C, Noël T, Gérardin P, Waechter R, LaBeaud AD.
30-05-2023
Am J Trop Med Hyg.
https://pubmed.ncbi.nlm.nih.gov/37253436/

Discovery and structure-activity relationship of Morita-Baylis-Hillman adducts as larvicides against dengue mosquito vector, Aedes aegypti (Diptera: Culicidae).

Ricardo Dos Santos Correia P, Duarte de Freitas J, André Zeoly L, Silva Porto R, José da Paz Lima D.
05-05-2023
Bioorg Med Chem.
https://pubmed.ncbi.nlm.nih.gov/37253304/

An economic evaluation of Wolbachia deployments for dengue control in Vietnam.

Turner HC, Quyen DL, Dias R, Huong PT, Simmons CP, Anders KL.
30-05-2023
PLoS Negl Trop Dis.
https://pubmed.ncbi.nlm.nih.gov/37253037/

Introduction: Dengue is a major public health challenge and a growing problem due to climate change. The release of Aedes aegypti mosquitoes infected with the intracellular bacterium Wolbachia is a novel form of vector control against dengue. However, there remains a need to evaluate the benefits of such an intervention at a large scale. In this paper, we evaluate the potential economic impact and cost-effectiveness of scaled Wolbachia deployments as a form of dengue control in Vietnam-targeted at the highest burden urban areas. Methods: Ten settings within Vietnam were identified as priority locations for potential future Wolbachia deployments (using a population replacement strategy). The effectiveness of Wolbachia deployments in reducing the incidence of symptomatic dengue cases was assumed to be 75%. We assumed that the intervention would maintain this effectiveness for at least 20 years (but tested this assumption in the sensitivity analysis). A cost-utility analysis and cost-benefit analysis were conducted. Results: From the health sector perspective, the Wolbachia intervention was projected to cost US$420 per disability-adjusted life year (DALY) averted. From the societal perspective, the overall cost-effectiveness ratio was negative, i.e. the economic benefits outweighed the costs. These results are contingent on the long-term effectiveness of Wolbachia releases being sustained for 20 years. However, the intervention was still classed as cost-effective across the majority of the settings when assuming only 10 years of benefits. Conclusion: Overall, we found that targeting high burden cities with Wolbachia deployments would be a cost-effective intervention in Vietnam and generate notable broader benefits besides health gains.

Dengue virus NS5 degrades ERC1 during infection to antagonize NF-kB activation.

Gonzalez Lopez Ledesma MM, Costa Navarro G, Pallares HM, Paletta A, De Maio F, Iglesias NG, Gebhard L, Oviedo Rouco S, Ojeda DS, de Borba L, Giraldo M, Rajsbaum R, Ceballos A, Krogan NJ, Shah PS, Gamarnik AV.
06-06-2023
Proc Natl Acad Sci U S A.
https://pubmed.ncbi.nlm.nih.gov/37252973/

Clinico-Serological Profile of Infective Causes of Acute Hepatitis in Children Admitted to a Tertiary Care Centre.

Gupta HB, Deshpande T, Choraria N, Patel P, Sethia SG, Sethia S.
28-04-2023
Cureus.
https://pubmed.ncbi.nlm.nih.gov/37252557/

Background: Hepatitis is a major cause of healthcare burden in India. Hepatitis A is the most common cause of acute viral hepatitis in the pediatric population whereas hepatitis E virus (HEV) is the most important cause of epidemic hepatitis. Various other causes of acute infective hepatitis in children are dengue, malaria, and enteric fever. The aim of the present study is to understand the clinico-serological profile in cases of acute infective hepatitis in children. Methodology: The present study is a cross-sectional study that was carried out from 1 September 2017 to 31 March 2019. A total of 89 children in the age group 1-18 years with clinically suspected acute infective hepatitis and subsequent confirmation on laboratory tests were included in the study. Results: Hepatitis A (48.3%) was found to be the most common

aetiology followed by dengue (22.5%) and hepatitis E (12.4%). No cases of hepatitis B or hepatitis C were found. The most common presenting complaint was fever (90%) and the most common clinical finding was icterus (69.7%). The sensitivity of icterus for the diagnosis of hepatitis was found to be 70%. Lab investigations showed a significant association between different etiologies of infective hepatitis with packed cell volume (PCV), white blood cell (WBC) count, and platelet count. Levels of aspartate aminotransferase (AST) and alanine transaminase (ALT) were raised in samples of patients with hepatitis A, hepatitis E, and combined hepatitis A and E infection as compared to other causes. All cases of hepatitis A and E were diagnosed with positive IgM antibody tests to the respective viral antigens. The most common complication was hepatic encephalopathy which was seen in patients with hepatitis A, dengue, and septicemia. Around 99% of patients recovered well and were discharged. One death occurred in a case of septicemia with septic shock with multiple organ dysfunction syndrome (MODS). Conclusion: The most common cause of infective hepatitis in children is hepatitis A. Other causes like dengue, malaria, and typhoid should also be kept in mind. The absence of icterus does not rule out hepatitis. Lab investigations including serology are important to confirm the diagnosis of various causes of hepatitis. Timely immunization against hepatitis is strongly recommended.

Vaccine development for mosquito-borne viral diseases.

Huang Z, Zhang Y, Li H, Zhu J, Song W, Chen K, Zhang Y, Lou Y.
12-05-2023
Front Immunol.
https://pubmed.ncbi.nlm.nih.gov/37251387/

Enhancing the therapeutic activity of hyperimmune IgG against chikungunya virus using FcγRIIIa affinity chromatography.

Fox JM, Roy V, Gunn BM, Bolton GR, Fremont DH, Alter G, Diamond MS, Boesch AW.
12-05-2023
Front Immunol.
https://pubmed.ncbi.nlm.nih.gov/37251375/

Serological survey on bovine viral diarrhea virus in man and evaluation of relation with Zika virus-associated microcephaly.

Giangaspero M, Okabayashi T.
Avr-2023
Open Vet J.
https://pubmed.ncbi.nlm.nih.gov/37251263/

Background: In 2015, an unprecedented epidemic of microcephaly occurred in Brazil. Preliminary observations suggested the involvement of cofactors in the etiopathology of Zika virus-associated microcephaly. Bovine viral diarrhea virus (BVDV) was identified in fetal samples with microcephaly, originating in the state of Paraíba, and two virus sequences, obtained from the amniotic fluid collected from mothers with babies affected by Zika and microcephaly, have been characterized as two different species of BVDV, types 1 and 2. Aim: The involvement of BVDV as a co-factor in the etiopathogenesis of Zika virus-associated microcephaly was explored. Methods: A serological screening using an ELISA test was undertaken to detect antibodies against BVDV among patients referred to the Central Laboratory of Natal, Rio Grande do Norte, encompassing microcephalic babies and their mothers, mothers and pregnants not associated with microcephaly and general patients as a control group. Results: Two samples were positive out of 382 tested (0.52%). No specific relation with birth defects could be established. Conclusions: The study might suggest serological evidence of BVDV in humans. Further studies and the application of improved diagnostic tests adapted to humans are necessary to clarify the epidemiological extent and impact of BVDV.

Design, synthesis and biological evaluation of novel lipophilic 2, 5-disubstituted tetrazole analogues of muramyl dipeptide as NOD2 agonists.

Mhamane TB, Sambyal S, Vemireddy S, Paturu RSR, Katragadda SB, Syed S, Khan A, Halmuthur M SK.
06-06-2023
Bioorg Med Chem.
https://pubmed.ncbi.nlm.nih.gov/37207469/

A focused library of six new 2, 5-disubstituted tetrazole (2, 5-DST) analogues of N-acetylmuramyl-l-alanyl-d-isoglutamine (MDP) as potential immunomodulators were synthesized by the bioisosteric replacement of α-amide of d-isoglutamine with 5-substituted tetrazole (5-ST). Another parameter 'lipophilicity' was also considered to improve the pharmacological properties of MDP through the alkylation of 5-substituted tetrazole during synthesis. In total, six 2, 5-DST analogues of MDP were synthesized and bio-evaluated for the study of human NOD2 stimulation activity in the innate immune response. Interestingly, among the varied lengths of the alkyl chain in 2, 5-disubstituted tetrazole derivatives, the tetrazole analogues 12b bearing the -Butyl (C4) and 12c having -Octyl (C8) chain showed the best NOD2 stimulation potency equivalent with reference compound MDP. These analogues were evaluated for their adjuvanticity against dengue antigen and analogues 12b and 12c have elicited a potent humoral and cell mediated response.

NeuN distribution in brain structures of normal and Zika-infected suckling mice.

Santamaría G, Rengifo AC, Torres-Fernández O.
Juin-2023
J Mol Histol.
https://pubmed.ncbi.nlm.nih.gov/37199896/

Viral Protein Accumulation of Zika Virus Variants Links with Regulation of Innate Immunity for Differential Control of Viral Replication, Spread, and Response to Interferon.

Lu AY, Gustin A, Newhouse D, Gale M Jr.

31-05-2023
J Virol.
https://pubmed.ncbi.nlm.nih.gov/37162358/

Asian lineage Zika virus (ZIKV) strains emerged globally, causing outbreaks linked with critical clinical disease outcomes unless the virus is effectively restricted by host immunity. We have previously shown that retinoic acid-inducible gene-I (RIG-I) senses ZIKV to trigger innate immunity to direct interferon (IFN) production and antiviral responses that can control ZIKV infection. However, ZIKV proteins have been demonstrated to antagonize IFN. Here, we conducted *in vitro* analyses to assess how divergent prototypic ZIKV variants differ in virologic properties, innate immune regulation, and infection outcome. We comparatively assessed African lineage ZIKV/Dakar/1984/ArD41519 (ZIKV/Dakar) and Asian lineage ZIKV/Malaysia/1966/P6740 (ZIKV/Malaysia) in a human epithelial cell infection model. *De novo* viral sequence determination identified amino acid changes within the ZIKV/Dakar genome compared to ZIKV/Malaysia. Viral growth analyses revealed that ZIKV/Malaysia accumulated viral proteins and genome copies earlier and to higher levels than ZIKV/Dakar. Both ZIKV strains activated RIG-I/IFN regulatory factor (IRF3) and NF-κB pathways to induce inflammatory cytokine expression and types I and III IFNs. However, ZIKV/Malaysia, but not ZIKV/Dakar, potently blocked downstream IFN signaling. Remarkably, ZIKV/Dakar protein accumulation and genome replication were rescued in RIG-I knockout (KO) cells late in acute infection, resulting in ZIKV/Dakar-mediated blockade of IFN signaling. We found that RIG-I signaling specifically restricts viral protein accumulation late in acute infection where early accumulation of viral proteins in infected cells confers enhanced ability to limit IFN signaling, promoting viral replication and spread. Our results demonstrate that RIG-I-mediated innate immune signaling imparts restriction of ZIKV protein accumulation, which permits IFN signaling and antiviral actions controlling ZIKV infection. IMPORTANCE ZIKV isolates are classified under African or Asian lineages. Infection with emerging Asian lineage-derived ZIKV strains is associated with increased incidence of neurological symptoms that were not previously reported during infection with African or preemergent Asian lineage viruses. In this study, we utilized *in vitro* models to compare the virologic properties of and innate immune responses to two prototypic ZIKV strains from distinct lineages: African lineage ZIKV/Dakar and Asian lineage ZIKV/Malaysia. Compared to ZIKV/Dakar, ZIKV/Malaysia accumulates viral proteins earlier, replicates to higher levels, and robustly blocks IFN signaling during acute infection. Early accumulation of ZIKV/Malaysia NS5 protein confers enhanced ability to antagonize IFN signaling, dampening innate immune responses to promote viral spread. Our data identify the kinetics of viral protein accumulation as a major regulator of host innate immunity, influencing host-mediated control of ZIKV replication and spread. Importantly, these findings provide a novel framework for evaluating the virulence of emerging variants.

Perspectives on the current antiviral developments towards RNA-dependent RNA polymerase (RdRp) and methyltransferase (MTase) domains of dengue virus non-structural protein 5 (DENV-NS5).

Sreekanth GP.
05-08-2023
Eur J Med Chem.
https://pubmed.ncbi.nlm.nih.gov/37159959/

Vitamin D modulates expression of antimicrobial peptides and proinflammatory cytokines to restrict Zika virus infection in macrophages.

Fernandez GJ, Ramírez-Mejía JM, Castillo JA, Urcuqui-Inchima S.
Juin-2023
Int Immunopharmacol.
https://pubmed.ncbi.nlm.nih.gov/37150017/

Although the impact of Zika virus (ZIKV) infection on human health has been well documented, we still have no vaccine or effective treatment. This fact highlights the importance of searching for alternative therapy for treating ZIKV. To search for ZIKV antivirals, we examined the effect of vitamin D in monocyte-derived macrophages (MDMs) differentiated in the presence of vitamin D (D3-MDM) and explored the molecular mechanisms by analyzing transcriptional profiles. Our data show the restriction of ZIKV infection in D3-MDMs as compared to MDMs. Transcriptional profiles show that vitamin D alters about 19% of Zika response genes (8.2% diminished and 10.8% potentiated). Among the genes with diminished expression levels, we found proinflammatory cytokines and chemokines such as IL6, TNF, IL1A, IL1B, and IL12B, CCL1, CCL4, CCL7, CXCL3, CXCL6, and CXCL8. On the other hand, genes with potentiated expression were related to degranulation such as Lysozyme, cathelicidin (CAMP), and Serglycin. Since the CAMP gene encodes the antimicrobial peptide LL-37, we treated MDMs with LL-37 and infected them with ZIKV. The results showed a decrease in the proportion of infected cells. Our data provide new insights into the role of vitamin D in restricting ZIKV infection in macrophages that are mediated by induction of cathelicidin/LL-37 expression and downregulation of proinflammatory genes. Results highlight the biological relevance of vitamin D-inducible peptides as an antiviral treatment for Zika fever.

Long-Term Safety Analysis of the ChAdOx1-nCoV-19 Corona Virus Vaccine: Results from a Prospective Observational Study in Priority Vaccinated Groups in North India.

Kaur U, Fatima Z, Maheshwari K, Sahni V, Dehade A, Kl A, Yadav AK, Kansal S, Jaisawal V, Chakrabarti SS.
Juin-2023
Drug Saf.
https://pubmed.ncbi.nlm.nih.gov/37133805/

Introduction: Various vaccines for protection against COVID-19 were provided emergency approval in late 2020 to early 2021. There is a scarcity of long-term safety data

for many of these. **Objective:** The main aim of this study is to provide the one-year safety results of the ChAdOx1-nCoV-19/AZD1222 vaccine and determine the risk factors of adverse events of special interest (AESIs) and persistent AESIs. **Methods:** This was a prospective observational study conducted from February 2021 to April 2022 in a tertiary hospital in North India and its two associated centers. Health care workers, other frontline workers, and the elderly vaccinated with the ChAdOx1-nCoV-19 vaccine constituted the study population. Individuals were contacted telephonically at pre-decided intervals for one year and health issues of significant concern were recorded. Atypical adverse events developing after a booster dose of the COVID-19 vaccine were assessed. Regression analysis was conducted to determine risk factors of AESI occurrence and determinants of AESIs persisting for at least one month at the time of final telephonic contact. **Results:** Of 1650 individuals enrolled, 1520 could be assessed at one-year post-vaccination. COVID-19 occurred in 44.1% of participants. Dengue occurred in 8% of participants. The majority of the AESIs belonged to the MedDRA® SOC of musculoskeletal disorders (3.7% of 1520). Arthropathy (knee joint involvement) was the most common individual AESI (1.7%). Endocrinal disorders such as thyroid abnormalities and metabolic disorders such as newly diagnosed diabetes developed in 0.4% and 0.3% of individuals, respectively. Regression analysis showed females, individuals with a pre-vaccination history of COVID-19, diabetes, hypothyroidism, and arthropathy had 1.78-, 1.55-, 1.82-, 2.47- and 3.9-times higher odds of AESI development. Females and individuals with hypothyroidism were at 1.66- and 2.23-times higher risk of persistent AESIs. Individuals receiving the vaccine after COVID-19 were at 2.85- and 1.94 times higher risk of persistent AESIs compared, respectively, to individuals with no history of COVID-19 and individuals developing COVID-19 after the vaccine. Among participants receiving a booster dose of the COVID-19 vaccine (n = 185), 9.7% developed atypical adverse events of which urticaria and new-onset arthropathy were common. **Conclusion:** Nearly half of the ChAdOx1-nCoV-19 vaccine recipients developed COVID-19 over one year. Vigilance is warranted for AESIs such as musculoskeletal disorders. Females, individuals with hypothyroidism, diabetes, and pre-vaccination history of COVID-19 are at higher risk of adverse events. Vaccines received after natural SARS-CoV-2 infection may increase the risk of persistence of adverse events. Sex and endocrinal differences and timing of the COVID-19 vaccine with respect to natural infection should be explored as determinants of AESIs in the future. Pathogenetic mechanisms of vaccine-related adverse events should be investigated along with comparisons with an unvaccinated arm to delineate the overall safety profile of COVID-19 vaccines.

Colocalization of Chikungunya Virus with Its Receptor MXRA8 during Cell Attachment, Internalization, and Membrane Fusion.

Feng F, Bouma EM, Hu G, Zhu Y, Yu Y, Smit JM, Diamond MS, Zhang R.

31-05-2023
J Virol.
https://pubmed.ncbi.nlm.nih.gov/37133449/

Applying a multi-strain dengue model to epidemics data.

de Araújo RGS, Jorge DCP, Dorn RC, Cruz-Pacheco G, Esteva MLM, Pinho STR.
Juin-2023
Math Biosci.
https://pubmed.ncbi.nlm.nih.gov/37127090/

Future perspectives of emerging novel drug targets and immunotherapies to control drug addiction.

Malik JA, Agrewala JN.
Juin-2023
Int Immunopharmacol.
https://pubmed.ncbi.nlm.nih.gov/37099943/

Substance Use Disorder (SUD) is one of the major mental illnesses that is terrifically intensifying worldwide. It is becoming overwhelming due to limited options for treatment. The complexity of addiction disorders is the main impediment to understanding the pathophysiology of the illness. Hence, unveiling the complexity of the brain through basic research, identification of novel signaling pathways, the discovery of new drug targets, and advancement in cutting-edge technologies will help control this disorder. Additionally, there is a great hope of controlling the SUDs through immunotherapeutic measures like therapeutic antibodies and vaccines. Vaccines have played a cardinal role in eliminating many diseases like polio, measles, and smallpox. Further, vaccines have controlled many diseases like cholera, dengue, diphtheria, Haemophilus influenza type b (Hib), human papillomavirus, influenza, Japanese encephalitis, etc. Recently, COVID-19 was controlled in many countries by vaccination. Currently, continuous effort is done to develop vaccines against nicotine, cocaine, morphine, methamphetamine, and heroin. Antibody therapy against SUDs is another important area where serious attention is required. Antibodies have contributed substantially against many serious diseases like diphtheria, rabies, Crohn's disease, asthma, rheumatoid arthritis, and bladder cancer. Antibody therapy is gaining immense momentum due to its success rate in cancer treatment. Furthermore, enormous advancement has been made in antibody therapy due to the generation of high-efficiency humanized antibodies with a long half-life. The advantage of antibody therapy is its instant outcome. This article's main highlight is discussing the drug targets of SUDs and their associated mechanisms. Importantly, we have also discussed the scope of prophylactic measures to eliminate drug dependence.

February 2023 Updates of the Advisory Committee on Immunization Practices.

Gaviria-Agudelo C, Yonts AB, Kimberlin DW, O'Leary ST, Paulsen GC.
31-05-2023
J Pediatric Infect Dis Soc.

https://pubmed.ncbi.nlm.nih.gov/37094832/

Cellular uptake of metal oxide-based nanocomposites and targeting of chikungunya virus replication protein nsP3.

Bhatia P, Singh VA, Rani R, Nath M, Tomar S.
Juil-2023
J Trace Elem Med Biol.
https://pubmed.ncbi.nlm.nih.gov/37075567/

DMKPs provide a generalizable strategy for studying genes required for reproduction or viability in nontraditional model organisms.

Laursen WJ, Busby R, Sarkissian T, Chang EC, Garrity PA.
26-05-2023
Genetics.
https://pubmed.ncbi.nlm.nih.gov/37036394/

The advent of CRISPR/Cas9-mediated genome editing has expanded the range of animals amenable to targeted genetic analysis. This has accelerated research in animals not traditionally studied using molecular genetics. However, studying genes essential for reproduction or survival in such animals remains challenging, as they lack the tools that aid genetic analysis in traditional genetic model organisms. We recently introduced the use of distinguishably marked knock-in pairs (DMKPs) as a strategy for rapid and reliable genotyping in such species. Here we show that DMKPs also facilitate the maintenance and study of mutations that cannot be maintained in a homozygous state, a group which includes recessive lethal and sterile mutations. Using DMKPs, we disrupt the zero population growth locus in Drosophila melanogaster and in the dengue vector mosquito Aedes aegypti. In both species, DMKPs enable the maintenance of zero population growth mutant strains and the reliable recovery of zero population growth mutant animals. Male and female gonad development is disrupted in fly and mosquito zero population growth mutants, rendering both sexes sterile. In Ae. aegypti, zero population growth mutant males remain capable of inducing a mating refractory period in wild-type females and of competing with wild-type males for mates, properties compatible with zero population growth serving as a target in mosquito population suppression strategies. DMKP is readily generalizable to other species amenable to CRISPR/Cas9-mediated gene targeting, and should facilitate the study of sterile and lethal mutations in multiple organisms not traditionally studied using molecular genetics.

Dengue Virus 2 NS2B Targets MAVS and IKKε to Evade the Antiviral Innate Immune Response.

Nie Y, Deng D, Mou L, Long Q, Chen J, Wu J.
28-05-2023
J Microbiol Biotechnol.
https://pubmed.ncbi.nlm.nih.gov/36788451/

Dengue virus (DENV) is a widespread arbovirus. To efficiently establish infection, DENV evolves multiple strategies to hijack the host innate immune response. Herein, we examined the inhibitory effects of DENV serotype 2 (DENV2) nonstructural proteins on RIG-I-directed antiviral immune response. We found that DENV2 NS2A, NS2B, NS4A, and NS4B significantly inhibited RIG-I-mediated IFN-β promoter activation. The roles of NS2B in RIG-I-directed antiviral immune response are unknown. Our study further showed that NS2B could dose-dependently suppress RIG-I/MAVS-induced activation of IFN-β promoter. Consistently, NS2B significantly decreased RIG-I- and MAVS-induced transcription of *IFNB1*, *ISG15*, and *ISG56*. Mechanistically, NS2B was found to interact with MAVS and IKKε to impair RIG-I-directed antiviral response. Our findings demonstrated a previously uncharacterized function of NS2B in RIG-I-mediated antiviral response, making it a promising drug target for anti-DENV treatments.

The ^{1}H, ^{15}N and ^{13}C resonance assignments of dengue virus capsid protein with the deletion of the intrinsically disordered N-terminal region.

Barbosa GM, Morando MA, Da Poian AT, Almeida FCL.
Juin-2023
Biomol NMR Assign.
https://pubmed.ncbi.nlm.nih.gov/36723824/

Antiviral Activity of Pyrimidine Containing Compounds: Patent Review.

Farghaly TA, Harras MF, Alsaedi AMR, Thakir HA, Mahmoud HK, Katowah DF.
2023
Mini Rev Med Chem.
https://pubmed.ncbi.nlm.nih.gov/36545712/

Persistence of Immunogenicity of a Purified Inactivated Zika Virus Vaccine Candidate in Healthy Adults: 2 Years of Follow-up Compared With Natural Infection.

Acosta CJ, Diaz C, Nordio F, Han HH, Moss KJ, Bohning K, Kumar P, Liu M, Patel H, Pacciarini F, Mwangi V, Walter E, Powell TD, El Sahly HM, Baldwin WR, Santangelo J, Anderson EJ, Dubin G.
29-05-2023
J Infect Dis.
https://pubmed.ncbi.nlm.nih.gov/36484441/

Antibodies Produced in Response to a Live-Attenuated Dengue Vaccine Are Functional in Activating the Complement System.

Nascimento EJM, Norwood B, Kpamegan E, Parker A, Fernandes J, Perez-Guzman E, Tricou V, Braun R, Sharma M, Dean HJ.
29-05-2023
J Infect Dis.

https://pubmed.ncbi.nlm.nih.gov/36461942/

Modelling the impact of climate change on dengue outbreaks and future spatiotemporal shift in Pakistan.

Saeed A, Ali S, Khan F, Muhammad S, Reboita MS, Khan AW, Goheer MA, Khan MA, Kumar R, Ikram A, Jabeen A, Pongpanich S.
Juin-2023
Environ Geochem Health.
https://pubmed.ncbi.nlm.nih.gov/36367603/

Climate change has a significant impact on the intensity and spread of dengue outbreaks. The objective of this study is to assess the number of dengue transmission suitable days (DTSD) in Pakistan for the baseline (1976-2005) and future (2006-2035, 2041-2070, and 2071-2099) periods under Representative Concentration Pathway (RCP4.5 and RCP8.5) scenarios. Moreover, potential spatiotemporal shift and future hotspots of DTSD due to climate change were also identified. The analysis is based on fourteen CMIP5 models that have been downscaled and bias-corrected with quantile delta mapping technique, which addresses data stationarity constraints while preserving future climate signal. The results show a higher DTSD during the monsoon season in the baseline in the study area except for Sindh (SN) and South Punjab (SP). In future periods, there is a temporal shift (extension) towards pre- and post-monsoon. During the baseline period, the top ten hotspot cities with a higher frequency of DTSD are Karachi, Hyderabad, Sialkot, Jhelum, Lahore, Islamabad, Balakot, Peshawar, Kohat, and Faisalabad. However, as a result of climate change, there is an elevation-dependent shift in DTSD to high-altitude cities, e.g. in the 2020s, Kotli, Muzaffarabad, and Drosh; in the 2050s, Garhi Dopatta, Quetta, and Zhob; and in the 2080s, Chitral and Bunji. Karachi, Islamabad, and Balakot will remain highly vulnerable to dengue outbreaks for all the future periods of the twenty-first century. Our findings also indicate that DTSD would spread across Pakistan, particularly in areas where we have never seen dengue infections previously. The good news is that the DTSD in current hotspot cities is projected to decrease in the future due to climate change. There is also a temporal shift in the region during the post- and pre-monsoon season, which provides suitable breeding conditions for dengue mosquitos due to freshwater; therefore, local authorities need to take adaption and mitigation actions.

Topical Mosquito Repellent Formulations for Enhanced Repellency Time and Reduced Toxicity.

Higuchi CT, Filho NA, Lopes PS, Grice JE, Leite-Silva VR.
2023
Curr Drug Deliv.
https://pubmed.ncbi.nlm.nih.gov/35984015/

Concomitant knockdown resistance allele, L982W + F1534C, in Aedes aegypti has the potential to impose fitness costs without selection pressure.

Uemura N, Furutani S, Tomita T, Itokawa K, Komagata O, Kasai S.
Juin-2023
Pestic Biochem Physiol.
https://pubmed.ncbi.nlm.nih.gov/37247997/

Prediction of dengue cases using the attention-based long short-term memory (LSTM) approach.

Majeed MA, Shafri HZM, Wayayok A, Zulkafli Z.
25-05-2023
Geospat Health.
https://pubmed.ncbi.nlm.nih.gov/37246539/

This research proposes a 'temporal attention' addition for long-short term memory (LSTM) models for dengue prediction. The number of monthly dengue cases was collected for each of five Malaysian states i.e. Selangor, Kelantan, Johor, Pulau Pinang, and Melaka from 2011 to 2016. Climatic, demographic, geographic and temporal attributes were used as covariates. The proposed LSTM models with temporal attention was compared with several benchmark models including a linear support vector machine (LSVM), a radial basis function support vector machine (RBFSVM), a decision tree (DT), a shallow neural network (SANN) and a deep neural network (D-ANN). In addition, experiments were conducted to analyze the impact of look-back settings on each model performance. The results showed that the attention LSTM (A-LSTM) model performed best, with the stacked, attention LSTM (SA-LSTM) one in second place. The LSTM and stacked LSTM (S-LSTM) models performed almost identically but with the accuracy improved by the attention mechanism was added. Indeed, they were both found to be superior to the benchmark models mentioned above. The best results were obtained when all attributes were included in the model. The four models (LSTM, S-LSTM, A-LSTM and SA-LSTM) were able to accurately predict dengue presence 1-6 months ahead. Our findings provide a more accurate dengue prediction model than previously used, with the prospect of also applying this approach in other geographic areas.

Prescriptive, descriptive or predictive models: What approach should be taken when empirical data is limited? Reply to comments on "Mathematical models for Dengue fever epidemiology: A 10-year systematic review".

Aguiar M, Anam V, Blyuss KB, Estadilla CDS, Guerrero BV, Knopoff D, Kooi BW, Mateus L, Srivastav AK, Steindorf V, Stollenwerk N.
19-05-2023
Phys Life Rev.
https://pubmed.ncbi.nlm.nih.gov/37245453/

Prevalence of dengue virus in Haripur district, Khyber Pakhtunkhwa, Pakistan.

Qureshi H, Khan MI, Bae SJ, Akhtar S, Khattak AA, Haider A, Nisar A.
06-05-2032
J Infect Public Health.

https://pubmed.ncbi.nlm.nih.gov/37244095/

Natural Products and Derivatives as Potential Zika virus Inhibitors: A Comprehensive Review.

Pereira RS, Santos FCP, Campana PRV, Costa VV, de Pádua RM, Souza DG, Teixeira MM, Braga FC.
20-05-2023
Viruses.
https://pubmed.ncbi.nlm.nih.gov/37243296/

Zika virus (ZIKV) is an arbovirus whose infection in humans can lead to severe outcomes. This article reviews studies reporting the anti-ZIKV activity of natural products (NPs) and derivatives published from 1997 to 2022, which were carried out with NPs obtained from plants (82.4%) or semisynthetic/synthetic derivatives, fungi (3.1%), bacteria (7.6%), animals (1.2%) and marine organisms (1.9%) along with miscellaneous compounds (3.8%). Classes of NPs reported to present anti-ZIKV activity include polyphenols, triterpenes, alkaloids, and steroids, among others. The highest values of the selectivity index, the ratio between cytotoxicity and antiviral activity (SI = CC_{50}/EC_{50}), were reported for epigallocatechin gallate (SI ≥ 25,000) and anisomycin (SI ≥ 11,900) obtained from *Streptomyces* bacteria, dolastane (SI = 1246) isolated from the marine seaweed *Canistrocarpus cervicorni*, and the flavonol myricetin (SI ≥ 862). NPs mostly act at the stages of viral adsorption and internalization in addition to presenting virucidal effect. The data demonstrate the potential of NPs for developing new anti-ZIKV agents and highlight the lack of studies addressing their molecular mechanisms of action and pre-clinical studies of efficacy and safety in animal models. To the best of our knowledge, none of the active compounds has been submitted to clinical studies.

Idiotope-Driven T-Cell/B-Cell Collaboration-Based T-Cell Epitope Prediction Using B-Cell Receptor Repertoire Sequences in Infectious Diseases.

Nakamura Y, Moi ML, Shiina T, Shin-I T, Suzuki R.
17-05-2023
Viruses.
https://pubmed.ncbi.nlm.nih.gov/37243272/

The Dimeric Peptide (KKYRYHLKPF)2K Shows Broad-Spectrum Antiviral Activity by Inhibiting Different Steps of Chikungunya and Zika Virus Infection.

Ayusso GM, Lima MLD, da Silva Sanches PR, Santos IA, Martins DOS, da Conceição PJP, Carvalho T, da Costa VG, Bittar C, Merits A, Santos-Filho NA, Cilli EM, Jardim ACG, de Freitas Calmon M, Rahal P.
14-05-2023
Viruses.
https://pubmed.ncbi.nlm.nih.gov/37243254/

A Dual-Approach Strategy to Optimize the Safety and Efficacy of Anti-Zika Virus Monoclonal Antibody Therapeutics.

Sun H, Yang M, Lai H, Neupane B, Teh AY, Jugler C, Ma JK, Steinkellner H, Bai F, Chen Q.
11-05-2023
Viruses.
https://pubmed.ncbi.nlm.nih.gov/37243242/

Genetic Analysis of Dengue Virus in Severe and Non-Severe Cases in Dhaka, Bangladesh, in 2018-2022.

Rahim R, Hasan A, Phadungsombat J, Hasan N, Ara N, Biswas SM, Nakayama EE, Rahman M, Shioda T.
10-05-2023
Viruses.
https://pubmed.ncbi.nlm.nih.gov/37243230/

Dengue virus (DENV) infections have unpredictable clinical outcomes, ranging from asymptomatic or minor febrile illness to severe and fatal disease. The severity of dengue infection is at least partly related to the replacement of circulating DENV serotypes and/or genotypes. To describe clinical profiles of patients and the viral sequence diversity corresponding to non-severe and severe cases, we collected patient samples from 2018 to 2022 at Evercare Hospital Dhaka, Bangladesh. Serotyping of 495 cases and sequencing of 179 cases showed that the dominant serotype of DENV shifted from DENV2 in 2017 and 2018 to DENV3 in 2019. DENV3 persisted as the only representative serotype until 2022. Co-circulation of clades B and C of the DENV2 cosmopolitan genotype in 2017 was replaced by circulation of clade C alone in 2018 with all clones disappearing thereafter. DENV3 genotype I was first detected in 2017 and was the only genotype in circulation until 2022. We observed a high incidence of severe cases in 2019 when the DENV3 genotype I became the only virus in circulation. Phylogenetic analysis revealed clusters of severe cases in several different subclades of DENV3 genotype I. Thus, these serotype and genotype changes in DENV may explain the large dengue outbreaks and increased severity of the disease in 2019.

Allosteric Inhibitors of Zika Virus NS2B-NS3 Protease Targeting Protease in "Super-Open" Conformation.

Meewan I, Shiryaev SA, Kattoula J, Huang CT, Lin V, Chuang CH, Terskikh AV, Abagyan R.
30-04-2023
Viruses.
https://pubmed.ncbi.nlm.nih.gov/37243192/

Identification of Key Residues in Dengue Virus NS1 Protein That Are Essential for Its Secretion.

Tan BEK, Beard MR, Eyre NS.
30-04-2023
Viruses.
https://pubmed.ncbi.nlm.nih.gov/37243188/

Dengue virus (DENV) non-structural protein 1 (NS1) is involved in multiple aspects of the DENV lifecycle. Importantly, it is secreted from infected cells as a hexameric lipoparticle that mediates vascular damage that is a hallmark of severe dengue. Although the secretion of

NS1 is known to be important in DENV pathogenesis, the exact molecular features of NS1 that are required for its secretion from cells are not fully understood. In this study, we employed random point mutagenesis in the context of an NS1 expression vector encoding a C-terminal HiBiT luminescent peptide tag to identify residues within NS1 that are essential for its secretion. Using this approach, we identified 10 point mutations that corresponded with impaired NS1 secretion, with in silico analyses indicating that the majority of these mutations are located within the β-ladder domain. Additional studies on two of these mutants, V220D and A248V, revealed that they prevented viral RNA replication, while studies using a DENV NS1-NS5 viral polyprotein expression system demonstrated that these mutations resulted in a more reticular NS1 localisation pattern and failure to detect mature NS1 at its predicted molecular weight by Western blotting using a conformation-specific monoclonal antibody. Together, these studies demonstrate that the combination of a luminescent peptide tagged NS1 expression system with random point mutagenesis enables rapid identification of mutations that alter NS1 secretion. Two such mutations identified via this approach revealed residues that are essential for correct NS1 processing or maturation and viral RNA replication.

Phylogenetic Reconstructions Reveal the Circulation of a Novel Dengue Virus-1V Clade and the Persistence of a Dengue Virus-2 III Genotype in Northeast Brazil.

Fritsch H, Moreno K, Lima IAB, Santos CS, Costa BGG, de Almeida BL, Dos Santos RA, Francisco MVLO, Sampaio MPS, de Lima MM, Pereira FM, Fonseca V, Tosta S, Xavier J, de Oliveira C, Adelino T, de Mello ALES, Gräf T, Alcantara LCJ, Giovanetti M, de Siqueira IC.
28-04-2023
Viruses.
https://pubmed.ncbi.nlm.nih.gov/37243159/

Repurposing of Doramectin as a New Anti-Zika Virus Agent.

Zhu Y, Liang M, Yu J, Zhang B, Zhu G, Huang Y, He Z, Yuan J.
27-04-2023
Viruses.
https://pubmed.ncbi.nlm.nih.gov/37243154/

Zika virus (ZIKV), belonging to the *Flavivirus* family and mainly transmitted by mosquitoes, causes a variety of adverse outcomes, including Guillain-Barré syndrome, microcephaly, and meningoencephalitis. However, there are no approved vaccines or drugs available for ZIKV. The discovery and research on drugs for ZIKV are still essential. In this study, we identified doramectin, an approved veterinary antiparasitic drug, as a novel anti-ZIKV agent (EC_{50} value from 0.85 μM to 3.00 μM) with low cytotoxicity (CC_{50} > 50 μM) in multiple cellular models. The expression of ZIKV proteins also decreased significantly under the treatment of doramectin. Further study showed that doramectin directly interacted with the key enzyme for ZIKV genome replication, RNA-dependent RNA polymerase (RdRp), with a stronger affinity (K_d = 16.9 μM), which may be related to the effect on ZIKV replication. These results suggested that doramectin might serve as a promising drug candidate for anti-ZIKV.

Noncoding RNA of Zika Virus Affects Interplay between Wnt-Signaling and Pro-Apoptotic Pathways in the Developing Brain Tissue.

Slonchak A, Chaggar H, Aguado J, Wolvetang E, Khromykh AA.
26-04-2023
Viruses.
https://pubmed.ncbi.nlm.nih.gov/37243147/

Zika virus (ZIKV) has a unique ability among flaviviruses to cross the placental barrier and infect the fetal brain causing severe abnormalities of neurodevelopment known collectively as congenital Zika syndrome. In our recent study, we demonstrated that the viral noncoding RNA (subgenomic flaviviral RNA, sfRNA) of the Zika virus induces apoptosis of neural progenitors and is required for ZIKV pathogenesis in the developing brain. Herein, we expanded on our initial findings and identified biological processes and signaling pathways affected by the production of ZIKV sfRNA in the developing brain tissue. We employed 3D brain organoids generated from induced human pluripotent stem cells (ihPSC) as an ex vivo model of viral infection in the developing brain and utilized wild type (WT) ZIKV (producing sfRNA) and mutant ZIKV (deficient in the production of sfRNA). Global transcriptome profiling by RNA-Seq revealed that the production of sfRNA affects the expression of >1000 genes. We uncovered that in addition to the activation of pro-apoptotic pathways, organoids infected with sfRNA-producing WT, but not sfRNA-deficient mutant ZIKV, which exhibited a strong down-regulation of genes involved in signaling pathways that control neuron differentiation and brain development, indicating the requirement of sfRNA for the suppression of neurodevelopment associated with the ZIKV infection. Using gene set enrichment analysis and gene network reconstruction, we demonstrated that the effect of sfRNA on pathways that control brain development occurs via crosstalk between Wnt-signaling and proapoptotic pathways.

Effect of Viral Strain and Host Age on Clinical Disease and Viral Replication in Immunocompetent Mouse Models of Chikungunya Encephalomyelitis.

Anderson EJ, Knight AC, Heise MT, Baxter VK.
26-04-2023
Viruses.
https://pubmed.ncbi.nlm.nih.gov/37243143/

The alphavirus chikungunya virus (CHIKV) represents a reemerging public health threat as mosquito vectors spread and viruses acquire advantageous mutations. Although primarily arthritogenic in nature, CHIKV can produce neurological disease with long-lasting sequelae that are difficult to study in humans. We therefore evaluated immunocompetent mouse strains/stocks for their susceptibility to intracranial infection with three different CHIKV strains, the East/Central/South African

(ECSA) lineage strain SL15649 and Asian lineage strains AF15561 and SM2013. In CD-1 mice, neurovirulence was age- and CHIKV strain-specific, with SM2013 inducing less severe disease than SL15649 and AF15561. In 4-6-week-old C57BL/6J mice, SL15649 induced more severe disease and increased viral brain and spinal cord titers compared to Asian lineage strains, further indicating that neurological disease severity is CHIKV-strain-dependent. Proinflammatory cytokine gene expression and CD4+ T cell infiltration in the brain were also increased with SL15649 infection, suggesting that like other encephalitic alphaviruses and with CHIKV-induced arthritis, the immune response contributes to CHIKV-induced neurological disease. Finally, this study helps overcome a current barrier in the alphavirus field by identifying both 4-6-week-old CD-1 and C57BL/6J mice as immunocompetent, neurodevelopmentally appropriate mouse models that can be used to examine CHIKV neuropathogenesis and immunopathogenesis following direct brain infection.

Chikungunya Virus Infection and Gonotrophic Cycle Shape Aedes aegypti Oviposition Behavior and Preferences.

Mulatier M, Boullis A, Dollin C, Cebrián-Torrejón G, Vega-Rúa A.
25-04-2023
Viruses.
https://pubmed.ncbi.nlm.nih.gov/37243130/

NS1 Protein N-Linked Glycosylation Site Affects the Virulence and Pathogenesis of Dengue Virus.

Fang E, Li M, Liu X, Hu K, Liu L, Zhang Z, Li X, Peng Q, Li Y.
08-05-2023
Vaccines (Basel).
https://pubmed.ncbi.nlm.nih.gov/37243063/

Characterization of an Aedes ADP-Ribosylation Protein Domain and Role of Post-Translational Modification during Chikungunya Virus Infection.

Kumar R, Mehta D, Nayak D, Sunil S.
16-05-2023
Pathogens.
https://pubmed.ncbi.nlm.nih.gov/37242388/

Poly ADP-ribose polymerases (PARPs) catalyze ADP-ribosylation, a subclass of post-translational modification (PTM). Mono-ADP-ribose (MAR) moieties bind to target molecules such as proteins and nucleic acids, and are added as part of the process which also leads to formation of polymer chains of ADP-ribose. ADP-ribosylation is reversible; its removal is carried out by ribosyl hydrolases such as PARG (poly ADP-ribose glycohydrolase), TARG (terminal ADP-ribose protein glycohydrolase), macrodomain, etc. In this study, the catalytic domain of *Aedes aegypti* tankyrase was expressed in bacteria and purified. The tankyrase PARP catalytic domain was found to be enzymatically active, as demonstrated by an in vitro poly ADP-ribosylation (PARylation) experiment. Using in vitro ADP-ribosylation assay, we further demonstrate that the chikungunya virus (CHIKV) nsp3 (non-structural protein 3) macrodomain inhibits ADP-ribosylation in a time-dependent way. We have also demonstrated that transfection of the CHIKV nsP3 macrodomain increases the CHIKV viral titer in mosquito cells, suggesting that ADP-ribosylation may play a significant role in viral replication.

Comparative Analysis of Human Hepatic Lesions in Dengue, Yellow Fever, and Chikungunya: Revisiting Histopathological Changes in the Light of Modern Knowledge of Cell Pathology.

Ribeiro YP, Falcão LFM, Smith VC, de Sousa JR, Pagliari C, Franco ECS, Cruz ACR, Chiang JO, Martins LC, Nunes JAL, Vilacoert FSDS, Santos LCD, Furlaneto MP, Fuzii HT, Bertonsin Filho MV, da Costa LD, Duarte MIS, Furlaneto IP, Martins Filho AJ, Aarão TLS, Vasconcelos PFDC, Quaresma JAS.
04-05-2023
Pathogens.
https://pubmed.ncbi.nlm.nih.gov/37242350/

Arboviruses, such as yellow fever virus (YFV), dengue virus (DENV), and chikungunya virus (CHIKV), present wide global dissemination and a pathogenic profile developed in infected individuals, from non-specific clinical conditions to severe forms, characterised by the promotion of significant lesions in different organs of the harbourer, culminating in multiple organ dysfunction. An analytical cross-sectional study was carried out via the histopathological analysis of 70 samples of liver patients, collected between 2000 and 2017, with confirmed laboratory diagnoses, who died due to infection and complications due to yellow fever (YF), dengue fever (DF), and chikungunya fever (CF), to characterise, quantify, and compare the patterns of histopathological alterations in the liver between the samples. Of the histopathological findings in the human liver samples, there was a significant difference between the control and infection groups, with a predominance of alterations in the midzonal area of the three cases analysed. Hepatic involvement in cases of YF showed a greater intensity of histopathological changes. Among the alterations evaluated, cell swelling, microvesicular steatosis, and apoptosis were classified according to the degree of tissue damage from severe to very severe. Pathological abnormalities associated with YFV, DENV, and CHIKV infections showed a predominance of changes in the midzonal area. We also noted that, among the arboviruses studied, liver involvement in cases of YFV infection was more intense.

Mechanism of Immune Evasion in Mosquito-Borne Diseases.

Bhattacharjee S, Ghosh D, Saha R, Sarkar R, Kumar S, Khokhar M, Pandey RK.
23-04-2023
Pathogens.
https://pubmed.ncbi.nlm.nih.gov/37242305/

Toxic Determination of Cry11 Mutated Proteins Obtained Using Rational Design and Its Computational Analysis.

Suárez-Barrera MO, Herrera-Pineda DF, Rondón-Villarreal P, Pinzón-Reyes EH, Ochoa R, Visser L, Rueda-Forero NJ.
22-05-2023
Int J Mol Sci.
https://pubmed.ncbi.nlm.nih.gov/37240424/

The Diagnostic Potential of RNA Aptamers against the NS1 Protein of Dengue Virus Serotype 2.

Thevendran R, Rogini S, Leighton G, Mutombwera A, Shigdar S, Tang TH, Citartan M.
15-05-2023
Biology (Basel).
https://pubmed.ncbi.nlm.nih.gov/37237536/

Dengue infection, caused by the dengue virus, is a global threat which requires immediate attention and appropriate disease management. The current diagnosis of dengue infection is largely based on viral isolation, RT-PCR and serology-based detection, which are time-consuming and expensive, and require trained personnel. For early diagnosis of dengue, the direct detection of a dengue antigenic target is efficacious, and one such target is NS1. NS1-based detection is primarily antibody-centric and is beset by drawbacks pertaining to antibodies such as the high cost of synthesis and large batch-to-batch variation. Aptamers are potential surrogates of antibodies and are much cheaper, without exhibiting batch-to-batch variation. Given these advantages, we sought to isolate RNA aptamers against the NS1 protein of dengue virus serotype 2. A total of 11 cycles of SELEX were carried out, resulting in two potent aptamers, DENV-3 and DENV-6, with dissociation constant values estimated at 37.57 ± 10.34 nM and 41.40 ± 9.29 nM, respectively. These aptamers can be further miniaturized to TDENV-3 and TDENV-6a with an increased LOD upon their usage in direct ELASA. Moreover, these truncated aptamers are highly specific against the dengue NS1 while showing no cross-reactivity against the NS1 of the Zika virus, the E2 protein of the Chikungunya virus or the LipL32 protein of Leptospira, with target selectivity retained even in human serum. The usage of TDENV-3 as the capturing probe and TDENV-6a as the detection probe underpinned the development of an aptamer-based sandwich ELASA for the detection of dengue NS1. The sensitivity of the sandwich ELASA was further improved with the stabilization of the truncated aptamers and the repeated incubation strategy, which enabled a LOD of 2 nM when used with the target NS1 spiked in human serum diluted at 1:2000.

Detection of Anti-ZIKV NS1 IgA, IgM, and Combined IgA/IgM and Identification of IL-4 and IL-10 as Potential Biomarkers for Early ZIKV and DENV Infections in Hyperendemic Regions, Thailand.

Petphong V, Kosoltanapiwat N, Limkittikul K, Maneekan P, Chatchen S, Jittmittraphap A, Sriburin P, Chattanadee S, Leaungwutiwong P.
17-05-2023
Trop Med Infect Dis.
https://pubmed.ncbi.nlm.nih.gov/37235332/

The frequency of Zika virus (ZIKV)-specific IgA and IgM and the cytokine expression profile of ZIKV-infected patients in hyperendemic areas remain unclear. This study investigated the rates of ZIKV non-structural protein 1 (NS1)-specific IgA and IgM and evaluated serum cytokine levels of ZIKV and Dengue virus (DENV) cases in Thailand to identify potential diagnostic biomarkers, elucidate the immunity against ZIKV and DENV, and investigate the association between cytokine levels and ZIKV symptoms. Low rates of positivity for ZIKV NS1-specific IgA and IgM were detected in our study. ZIKV NS1 IgA/M (11%, 11/101) in combination was more frequently detected than ZIKV NS1 IgM (2%, 2/101) or ZIKV NS1 IgA (4%, 4/96) alone, especially in acute ZIKV cases with previous DENV exposure (14%, 10/72). Cytokine analysis showed that both ZIKV and DENV infections induced polyfunctional immunity, and the latter triggered more prolonged responses. The existence of significant differences in IL-4 and IL-10 levels between acute ZIKV and acute DENV cases suggested that IL-4 ($p = 0.0176$) and IL-10 ($p = 0.0003$) may represent biomarkers for acute ZIKV and acute DENV infections, respectively. Analysis of the association between increased cytokine levels and ZIKV symptoms indicated that CXCL10 ($p = 0.0029$) was associated with exanthema, while IL-5 ($p = 0.0496$) was linked to headache. The detection of ZIKV NS1 IgA and IgM in combination may enhance the diagnosis of early ZIKV infection, particularly when levels of IgM or IgA alone are low or undetectable. IL-4 and IL-10 may serve as targets for the development of diagnostic tools to detect ZIKV and DENV infections early, respectively, in flavivirus-endemic regions.

Spatial Analysis of Dengue Clusters at Department, Municipality and Local Scales in the Southwest of Colombia, 2014-2019.

Marceló-Díaz C, Lesmes MC, Santamaría E, Salamanca JA, Fuya P, Cadena H, Muñoz-Laiton P, Morales CA.
02-05-2023
Trop Med Infect Dis.
https://pubmed.ncbi.nlm.nih.gov/37235310/

Dengue is an arbovirus transmitted by mosquitoes of the genus *Aedes* and is one of the 15 main public health problems in the world, including Colombia. Where limited financial resources create a problem for management, there is a need for the department to prioritize target areas for public health implementation. This study focuses on a spatio-temporal analysis to determine the targeted area to manage the public health problems related to dengue cases. To this end, three phases at three different scales were carried out. First, for the departmental scale, four risk clusters were identified in Cauca (RR ≥ 1.49) using the Poisson model, and three clusters were identified through Getis-Ord Gi* hotspots analysis; among them, Patía municipality presented significantly high incidence rates in the time window (2014-2018). Second, on the municipality scale, altitude and minimum temperature were observed to be more relevant than precipitation; considering posterior means, no spatial autocorrelation for the Markov Chain Monte Carlo was found (Moran test < 1.0), and convergence was reached for b_1-b_{105} with

20,000 iterations. Finally, on the local scale, a clustered pattern was observed for dengue cases distribution (nearest neighbour index, NNI = 0.202819) and the accumulated number of pupae (G = 0.70007). Two neighbourhoods showed higher concentrations of both epidemiological and entomological hotspots. In conclusion, the municipality of Patía is in an operational scenario of a high transmission of dengue.

Dengue as a Disease Threatening Global Health: A Narrative Review Focusing on Latin America and Brazil.

Lessa CLS, Hodel KVS, Gonçalves MS, Machado BAS.
23-04-2023
Trop Med Infect Dis.
https://pubmed.ncbi.nlm.nih.gov/37235289/

Aminotransferases in Relation to the Severity of Dengue: A Systematic Review.

Kalluru PKR, Mamilla M, Valisekka SS, Mandyam S, Calderon Martinez E, Posani S, Sharma S, Gopavaram RR, Gargi B, Gaddam A, Reddy S.
24-05-2023
Cureus.
https://pubmed.ncbi.nlm.nih.gov/37234451/

A systematic review was conducted to investigate the relationship between aminotransferases and the severity of dengue infection, which is a prevalent and significant infection in tropical and subtropical regions. Aminotransferases are enzymes that are often elevated in dengue due to the liver's physiological and immunological response to the infection. This review focused on analyzing various studies that examined the correlation between aminotransferase levels and the severity of dengue. Extensive literature searches were performed using ("dengue*" OR "dengue fever*" OR "dengue haemorrhagic fever*" OR "dengue shock syndrome*") AND ("alanine aminotransferase*" OR "aspartate aminotransferase*") on PubMed. The selected articles were thoroughly reviewed, encompassing epidemiology, pathogenesis, and clinical manifestations of dengue. The consistent findings across the studies indicated that aminotransferases can serve as predictive markers for dengue severity. Therefore, early assessment of liver enzyme levels is crucial in dengue cases, and elevated levels should be closely monitored to prevent adverse outcomes.

A Comparative Analysis of Effectiveness of Recombinant Interleukin-11 Versus Papaya Leaf Extract for Treatment of Thrombocytopenia: A Review.

Mishra KP, Bakshi J, Sharma G, Singh S, Panjwani U.
Juil-2023
Indian J Clin Biochem.
https://pubmed.ncbi.nlm.nih.gov/37234180/

Integrated Plan of Insecticide Resistance Surveillance in Mosquito Vectors in France.

Devillers J, David JP, Barrès B, Alout H, Lapied B, Chouin S, Dusfour I, Billault C, Mekki F, Attig I, Corbel V.
12-05-2023
Insects.
https://pubmed.ncbi.nlm.nih.gov/37233085/

Machine Learning Modeling of Aedes albopictus Habitat Suitability in the 21st Century.

Georgiades P, Proestos Y, Lelieveld J, Erguler K.
09-05-2023
Insects.
https://pubmed.ncbi.nlm.nih.gov/37233075/

Mosquito Blood Feeding Prevention Using an Extra-Low DC Voltage Charged Cloth.

Luan K, McCord MG, West AJ, Cave G, Travanty NV, Apperson CS, Roe RM.
23-04-2023
Insects.
https://pubmed.ncbi.nlm.nih.gov/37233033/

Mosquito vector-borne diseases such as malaria and dengue pose a major threat to human health. Personal protection from mosquito blood feeding is mostly by treating clothing with insecticides and the use of repellents on clothing and skin. Here, we developed a low-voltage, mosquito-resistant cloth (MRC) that blocked all blood feeding across the textile and was flexible and breathable. The design was based on mosquito head and proboscis morphometrics, the development of a novel 3-D textile with the outer conductive layers insulated from each other with an inner, non-conductive woven mesh, and the use of a DC (direct current; extra-low-voltage) resistor-capacitor. Blockage of blood feeding was measured using host-seeking *Aedes aegypti* adult female mosquitoes and whether they could blood feed across the MRC and an artificial membrane. Mosquito blood feeding decreased as voltage increased from 0 to 15 volts. Blood feeding inhibition was 97.8% at 10 volts and 100% inhibition at 15 volts, demonstrating proof of concept. Current flow is minimal since conductance only occurs when the mosquito proboscis simultaneously touches the outside layers of the MRC and is then quickly repelled. Our results demonstrated for the first time the use of a biomimetic, mosquito-repelling technology to prevent blood feeding using extra-low energy consumption.

Investigating the antiviral therapeutic potentialities of marine polycyclic lamellarin pyrrole alkaloids as promising inhibitors for SARS-CoV-2 and Zika main proteases (Mpro).

Pereira F, Bedda L, Tammam MA, Alabdullah AK, Arafa R, El-Demerdash A.
26-05-2023
J Biomol Struct Dyn.
https://pubmed.ncbi.nlm.nih.gov/37232419/

Genotyping of dengue virus from infected tissue samples embedded in paraffin.

Rivera JA, Rengifo AC, Rosales-Munar A, Díaz-Herrera TH, Ciro JU, Parra E, Alvarez-Díaz DA, Laiton-Donato K, Caldas ML.
25-05-2023
Virol J.
https://pubmed.ncbi.nlm.nih.gov/37232419/

Effect of voluntary human mobility restrictions on vector-borne diseases during the COVID-19 pandemic in Japan: A descriptive epidemiological study using a national database (2016 to 2021).

Hibiya K, Shinzato A, Iwata H, Kinjo T, Tateyama M, Yamamoto K, Fujita J.
25-05-2023
PLoS One.
https://pubmed.ncbi.nlm.nih.gov/37228070/

Mosquito gene targeted RNAi studies for vector control.

Yadav M, Dahiya N, Sehrawat N.
25-05-2023
Funct Integr Genomics.
https://pubmed.ncbi.nlm.nih.gov/37227504/

Vector-borne diseases are serious public health concern. Mosquito is one of the major vectors responsible for the transmission of a number of diseases like malaria, Zika, chikungunya, dengue, West Nile fever, Japanese encephalitis, St. Louis encephalitis, and yellow fever. Various strategies have been used for mosquito control, but the breeding potential of mosquitoes is such tremendous that most of the strategies failed to control the mosquito population. In 2020, outbreaks of dengue, yellow fever, and Japanese encephalitis have occurred worldwide. Continuous insecticide use resulted in strong resistance and disturbed the ecosystem. RNA interference is one of the strategies opted for mosquito control. There are a number of mosquito genes whose inhibition affected mosquito survival and reproduction. Such kind of genes could be used as bioinsecticides for vector control without disturbing the natural ecosystem. Several studies have targeted mosquito genes at different developmental stages by the RNAi mechanism and result in vector control. In the present review, we included RNAi studies conducted for vector control by targeting mosquito genes at different developmental stages using different delivery methods. The review could help the researcher to find out novel genes of mosquitoes for vector control.

Investigating the folding dynamics of NS2B protein of Zika virus.

Kumar A, Kumar P, Mishra PM, Giri R.
Juil-2023
Virology.
https://pubmed.ncbi.nlm.nih.gov/37210794/

NS2B protein of the Zika virus acts as a co-factor for NS3 protease and also involves in remodeling NS3 protease structure. Therefore, we investigated the overall dynamics of NS2B protein. We find surprising similarities between selected flavivirus NS2B model structures predicted from Alphafold2. Further, the simulated ZIKV NS2B protein structure shows a disordered cytosolic domain (residues 45-95) as a part of a full-length protein. Since only the cytosolic domain of NS2B is sufficient for the protease activity, we also investigated the conformational dynamics of only ZIKV NS2B cytosolic domain (residues 49-95) in the presence of TFE, SDS, Ficoll, and PEG using simulation and spectroscopy. The presence of TFE induces α-helix in NS2B cytosolic domain (residues 49-95). On the other hand, the presence of SDS, ficoll, and PEG does not induce secondary structural change. This dynamics study could have implications for some unknown folds of the NS2B protein.

Exploring allosteric hits of the NS2B-NS3 protease of DENV2 by structure-guided screening.

Gangopadhyay A, Saha A.
Juin-2023
Comput Biol Chem.
https://pubmed.ncbi.nlm.nih.gov/37141792/

Dracunculose

Genomics of turions from the Greater Duckweed reveal its pathways for dormancy and re-emergence strategy.

Pasaribu B, Acosta K, Aylward A, Liang Y, Abramson BW, Colt K, Hartwick NT, Shanklin J, Michael TP, Lam E.
Juil-2023
New Phytol.
https://pubmed.ncbi.nlm.nih.gov/37149888/

Over 15 families of aquatic plants are known to use a strategy of developmental switching upon environmental stress to produce dormant propagules called turions. However, few molecular details for turion biology have been elucidated due to the difficulties in isolating high-quality nucleic acids from this tissue. We successfully developed a new protocol to isolate high-quality transcripts and carried out RNA-seq analysis of mature turions from the Greater Duckweed Spirodela polyrhiza. Comparison of turion transcriptomes to that of fronds, the actively growing leaf-like tissue, were carried out. Bioinformatic analysis of high confidence, differentially expressed transcripts between frond and mature turion tissues revealed major pathways related to stress tolerance, starch and lipid metabolism, and dormancy that are mobilized to reprogram frond meristems for turion differentiation. We identified the key genes that are likely to drive starch and lipid accumulation during turion formation, as well as those in pathways for starch and lipid utilization upon turion germination. Comparison of genome-wide cytosine methylation levels also revealed evidence for epigenetic changes in the formation of turion tissues. Similarities between turions and seeds provide evidence that key regulators for seed maturation and germination were retooled for their function in turion biology.

Empirical and Mechanistic Modeling of Release Kinetics of Heavy Metals and Their Chemical Distribution in the Rhizosphere and Non-rhizosphere Soils Under Vegetable Cultivation.

Fakhri R, Jalali M, Ranjbar F.
Mai-2023
Arch Environ Contam Toxicol.
https://pubmed.ncbi.nlm.nih.gov/37084006/

Biochemical processes in the rhizosphere affect the availability and distribution of heavy metals (HMs) in various forms. Rhizosphere soil (RS) and non-rhizosphere soil (NRS) samples were collected from 10 fields under tarragon (Artemisia dracunculus L.) cultivation to investigate the release kinetics and distribution of HMs including cadmium (Cd), cobalt (Co), copper (Cu), iron (Fe), and zinc (Zn) in five fractions. The cumulative amounts of Cu and Fe released after 88 h were in the following ranges, respectively: 1.31-2.76 and 3.24-6.35 mg kg^{-1} in RS and 1.41-2.72 and 3.15-5.27 mg kg^{-1} in NRS. The parabolic diffusion and pseudo-second-order equations provided the best fit to the release kinetics data of Cu and Fe, respectively. The cation exchange model (CEM) based on Gaines-Thomas selectivity coefficients implemented in the PHREEQC program could well simulate the release of Cu and Fe suggesting that cation exchange was the dominant mechanism in the release of Fe and Cu from soils by 0.01 M $CaCl_2$. Cadmium was predominantly found in fraction F2, while other HMs were mainly present in fraction F5. According to the risk assessment code, there was a very high risk for Cd, a medium risk for Co and Cu, a very low risk for Fe, and a low risk for Zn. Correlation analysis showed that soil physicochemical properties were effective in the distribution and transformation of HMs. Significant positive correlations between five fractions indicated that different forms of HMs can potentially transform into each other.

Effect of effective microorganisms (EM) treated taro (Colocasia esculenta) root on the growth performance of broiler chickens.

Yesuf YK, Lejamo SB, Abduljebar TH.
Juin2023
Anim Biotechnol.
https://pubmed.ncbi.nlm.nih.gov/34665682/

Echinococcose

Multifocal hydatidosis with extensive involvement of the sacrum and the femoral head.

Feki A, Abid C, Ben Djemaa S, Gassara Z, Mariam E, Kallel MH, Rim A, Fourati H, Baklouti S.
29-05-2023
Clin Case Rep.
https://pubmed.ncbi.nlm.nih.gov/37260616/

Key clinical message: Hydatidosis is a parasitic infection caused by the larval form of "Echinococcus granulosis." Bone localization is rare even in endemic areas. We report an unusual case of an extensive hydatidosis of the right sacrum and femur with muscle involvement. Abstract: We report the case of a man, with a history of visceral hydatidosis, who developed after 14 years an extensive hydatidosis of the sacrum and femur with muscle involvement. The treatment of visceral hydatidosis was chemotherapy with albendazole for a long term. Conservative surgical treatment is considered for bone locations.

Molecular characterization of cattle and sheep isolates of Echinococcus granulosus from elazig province in Turkey and expression analysis of the non-coding RNAs, egr-miR-7, egr-miR-71 and egr-miR-96.

Irehan B, Celik F, Koroglu E, Tektemur A, Simsek S.
29-05-2023
Exp Parasitol.
https://pubmed.ncbi.nlm.nih.gov/37257717/

Cystic Echinococcosis (CE) is a common zoonotic disease seen in human and animals worldwide, caused by the larval form of Echinococcus granulosus. In this study, E. granulosus s.l. species and haplotypes were determined in hydatid cysts isolated from cattle and sheep, and the expression levels of egr-miR-7, egr-miR-71 and egr-miR-96 miRNAs were compared in different cyst structures. A total of 82 (cattle, n = 41; sheep, n = 41) hydatid cyst isolates (germinal membranes and/or protoscoleces) were collected from a slaughterhouse in Elazig province of Turkey. After mt-CO1 gene sequences were made, 81 out of 82 hydatid cyst isolates were determined as E. granulosus s.s. (G1 and G3), while an isolate of cattle origin was determined as Echinococcus canadensis (G6/7). A total of 26 nucleotide polymorphisms and 29 haplotype groups were identified in the samples. miRNA expressions in germinal membranes of sterile cysts and germinal membrane and protoscoleces of fertile cysts were investigated by qRT-PCR and Real Time PCR analyses. It was determined that miRNAs were expressed at high levels in 79.31% of the 29 haplotype groups and at low levels in the remaining 10.34%. In 10 fertile samples of sheep origin, egr-miR-7, egr-miR-71 and egr-miR-96 miRNAs were found to be 44, 168, and 351-fold higher in expression, respectively, in the germinal membrane compared to the protoscoleces. Especially egr-miR-96 may have the potential to be used as biomarkers in the diagnosis of active CE.

Cardiac Hydatid Cyst: An Uncommon Cause of Complete Atrioventricular Block.

Moraes RP, Brida MS, Reis RM, Silva RS, Farias CB.
26-05-2023
Arq Bras Cardiol.
https://pubmed.ncbi.nlm.nih.gov/37255128/

Hydatidosis is a zoonosis caused by Echinococcus granulosus, leading to the formation of cysts on involved organs. Cardiac involvement is rare and can cause a wide range of complications secondary to rupture,

embolization, or compression. Its diagnosis is challenging, and is generally confirmed through data related to clinical manifestations, environmental exposure, and laboratory and imaging exams. Surgical removal is necessary in most cases, in which an association with antiparasite therapy is recommended. The present article describes a case of a cardiac hydatid cyst associated with a complete atrioventricular block (AVB) in a young adult patient, with the need for a pacemaker implant, an atypical presentation, and scarce reports in the literature.

Corrigendum: Comparing copromicroscopy to intestinal scraping to monitor red fox intestinal helminths with zoonotic and veterinary importance.

Marchiori E, Obber F, Celva R, Marcer F, Danesi P, Maurizio A, Cenni L, Massolo A, Citterio CV, Cassini R.
11-05-2023
Front Vet Sci.
https://pubmed.ncbi.nlm.nih.gov/37252385/

Study of the saiga helminth fauna and Ural sheep in the western region of Kazakhstan.

Kushaliyev K, Ussenov Z, Alimbekov S, Millakaev O, Kozhayeva A, Khairushev A.
Avr-2023
Open Vet J.
https://pubmed.ncbi.nlm.nih.gov/37251266/

Retrospective Analysis of Serology and Radiology Results in Patients with Suspected Cystic Echinococcosis Through 3 Years Period.

Özmen Çapın BB, Can B, Kurşun M, Cimşit C, Karahasan A.
29-06-2023
Turkiye Parazitol Derg.
https://pubmed.ncbi.nlm.nih.gov/37249110/

[Echinococcus granulosus cyst fluid(EgCF) inhibits the migration and phagocytic function of mouse macrophages induced by LPS via inducing cytoskeletal rearrangement].

He F, Dong D, Chen Y, Liao Y, Lin K, Meng J, Wu X, Chen X.
Mai-2023
Xi Bao Yu Fen Zi Mian Yi Xue Za Zhi.
https://pubmed.ncbi.nlm.nih.gov/37248831/

Objective To investigate the effect of Echinococcus granulosus cyst fluid(EgCF) on the cytoskeletal rearrangement and phagocytosis and the migration of macrophages induced by lipopolysaccharide(LPS). Methods Peritoneal macrophages of C57BL/6 mice were isolated and cultured in vitro, and divided into control group and LPS group and LPS combined with EgCF group. After 48 hours of treatment, filamentous actin (F-actin) changes were observed with rhodamine-labelled phalloidin staining and fluorescence microscopy; Transwell™ chamber was used to test cell migration ability and flow cytometry to test cell phagocytosis. After 1 hour of treatment, PI3K and AKT, phosphorylated AKT (p-AKT), Rac1, guanosine triphospho-Rac1 (GTP-Rac1), WASP and Arp2 protein expressions were detected with Western blot analysis. Results Compared with the control group, after LPS stimulation, macrophages were deformed significantly; pseudopodia increased; actin cytoskeleton increased and was more distributed in pseudopodia; the ability of migration and phagocytosis were significantly improved, and the expression of PI3K, p-AKT, GTP-Rac1, WASP and Arp2 proteins significantly increased. EgCF treatment caused cell shrinkage and disappearance of pseudopodia protrusions of LPS-activated cells, and led to the reduced phagocytic and migratory of cells; the protein expression of PI3K, p-AKT, GTP-Rac1, WASP and Arp2 decreased significantly compared with the LPS group. Conclusion LPS induces the migration and enhances phagocytosis of macrophages while EgCF inhibits these effects, which is related to actin cytoskeleton rearrangement.

Primary cervical hydatid cyst: A rare case report.

Rahimi MT, Hares R, Rahman H, Shinwari MA, Khaliqi S, Hares S.
24-05-2023
Int J Surg Case Rep.
https://pubmed.ncbi.nlm.nih.gov/37244108/

Introduction and importance: Hydatid cyst is a zoonotic parasitic disease caused by Echinococcus granulosis. Occurrence in the head and neck is quite uncommon even in endemic areas. The diagnosis of an isolated cystic neck mass is still a challenge due to the presence of similar congenital cystic lesions and benign tumors in the neck. Imaging is useful, but sometimes they cannot identify a definitive diagnosis. The treatment of choice is exclusively surgical excision, combined with chemotherapy. Histopathology confirms the definitive diagnosis. **Case presentation:** We present a case of an 8-year-old boy with no history of surgery or trauma, who complained of an isolated left posterior neck mass since one year. All radiological items lead to suspect a cystic lymphangioma. Excisional biopsy under general anesthesia was done. The cystic mass was totally resected and the diagnosis was further confirmed by histopathology. **Clinical discussion:** Cervical hydatid cyst is mostly a misdiagnosed condition, majority of hydatid cyst cases are asymptomatic and vary on the basis of their locations. The differential diagnosis includes cystic lymphangioma, branchial cleft cyst, bronchogenic, thoracic duct, esophageal duplication cysts, pseudocysts and benign tumors. **Conclusion:** Isolated cervical hydatid cyst is rarely reported yet, it must be considered in any cases of cystic cervical mass, particularly in endemic areas. Imaging modalities are sensitive in diagnosing cystic lesions, yet sometimes they cannot identify the exact etiology of the lesion. Furthermore, Prevention of hydatid disease is more favorable than surgical excision.

A case of pediatric primary osteolytic extradural and complicated hydatid cyst revealed by a skull vault swelling.

Borni M, Abdelmouleh S, Taallah M, Blibeche H, Ayadi A, Boudawara MZ.
27-05-2023
Childs Nerv Syst.
https://pubmed.ncbi.nlm.nih.gov/37243810/

Hydatidosis is a parasitic infestation whose etiological agent is the larva of the cestode Echinococcus granulosus. It is a zoonosis, and the human being behaves as an accidental intermediate host in the parasitic cycle with pediatric predominance. The most frequent clinical presentation is hepatic, followed by pulmonary, with cerebral hydatidosis being extremely rare. Imaging is characteristic, generally dealing with single cystic lesion, usually unilocular and less frequently multilocular, located mainly intraaxially. Extradural hydatid cyst, whether primary or secondary, remains very rare or even exceptional. The primary disease remains extremely rare, and its clinical picture is related to the number, size, and location of the lesions. Infection within these cerebral hydatid cysts remains an extremely rare occurrence, and only few cases were reported previously in the literature. The authors report the nosological review of the clinical, imaging, surgical, and histopathological records of a pediatric primary osteolytic extradural and complicated hydatid cyst in a 5-year-old North African male patient coming from a rural area who presented for progressive onset of a painless left parieto-occipital soft swelling without any neurological disorder with good outcomes after surgery. The authors report this case due the fact that it had not been documented before in the pediatric population and to the success of the specialized treatment.

Circulating Small RNA Profiling of Patients with Alveolar and Cystic Echinococcosis.

Cucher MA, Mariconti M, Manciulli T, Vola A, Rosenzvit MC, Brehm K, Kamenetzky L, Brunetti E.
13-05-2023
Biology (Basel).
https://pubmed.ncbi.nlm.nih.gov/37237528/

Molecular Screening of Echinococcus spp. and Other Cestodes in Wild Carnivores from Central Italy.

Crotti S, Brustenga L, Cruciani D, Bonelli P, D'Avino N, Felici A, Morandi B, Sebastiani C, Spina S, Gobbi M.
27-04-2023
Vet Sci.
https://pubmed.ncbi.nlm.nih.gov/37235401/

Tapeworm infections are among the most relevant parasitic diseases in humans and animals. Tapeworms from the Genus *Echinococcus* are particularly important as they can cause cystic or alveolar echinococcosis. A molecular screening was performed on 279 fecal samples collected from carcasses of wild carnivores from Central Italy using PCR targeting diagnostic fragments of *nad1*, *rrnS*, and *nad5* genes. Samples positive for either *Taenia* spp. or *Echinococcus granulosus* were sequenced to taxonomically identify the parasitic DNA. Of the 279 samples, 134 (48.0%) gave positive results in the multiplex PCR. Only one (0.4%) sample from an Apennine wolf tested positive for *Echinococcus granulosus* sensu stricto (genotype G3), whereas no sample tested positive for *E. multilocularis*. The most frequently detected tapeworms were: *Mesocestoides corti* (syn *M. vogae*) (12.9%), *M. litteratus* (10.8%), *Taenia serialis* (9.3%), and *T. hydatigena* (6.5%), other tapeworms were rarely detected. The results suggest that *Echinococcus* infections in Central Italy do not seem to be sustained by sylvatic cycles, confirming the absence of *E. multilocularis* in Central Italy. The survey corroborates, yet again, the importance of passive surveillance of wild animals that can serve as reservoirs for zoonotic pathogens, especially on wild canids that in other areas are strongly implicated in the transmission of *E. granulosus* and *E. multilocularis*.

Evaluation of the Local Immune Response to Hydatid Cysts in Sheep Liver.

De Biase D, Prisco F, Pepe P, Bosco A, Piegari G, d'Aquino I, Russo V, Papparella S, Maurelli MP, Rinaldi L, Paciello O.
27-04-2023
Vet Sci.
https://pubmed.ncbi.nlm.nih.gov/37235398/

Past and present of diagnosis of echinococcosis: A review (1999-2021).

Alvi MA, Ali RMA, Khan S, Saqib M, Qamar W, Li L, Fu BQ, Yan HB, Jia WZ.
Juil-2023
Acta Trop.
https://pubmed.ncbi.nlm.nih.gov/37080264/

Filariose lymphatique

Population pharmacokinetic model of ivermectin in mass drug administration against lymphaticfilariasis.

Alshehri A, Chhonker YS, Bala V, Edi C, Bjerum CM, Koudou BG, John LN, Mitjà O, Marks M, King CL, Murry DJ.
01-06-2023
PLoS Negl Trop Dis.
https://pubmed.ncbi.nlm.nih.gov/37262040/

Background: Ivermectin (IVM) is a broad-spectrum anthelmintic drug used to treat diseases caused by filarial worms, such as onchocerciasis and lymphatic filariasis (LF). IVM is part of a triple-drug therapy used by the Mass Drug Administration (MDA) as a preventive strategy to eradicate LF in sub-Saharan Africa. The drug shows high variability in drug exposure in previous pharmacokinetic studies. This study aims to build a population pharmacokinetic (PopPK) model to identify and quantify the possible sources of the variability of IVM exposure after a single-oral dose in LF-infected subjects and healthy

individuals. **Methodology / principal findings:** In this analysis, 724 samples were collected from treatment-naïve Wuchereria bancrofti-infected (n = 32) and uninfected (n = 24) adults living in Côte d'Ivoire who had received one dose of IVM as a part of triple-drug therapy. PopPK analysis was conducted using Phoenix NLME 8.3 software. The Monte Carlo simulation based on the final model was performed to simulate drug exposure among different dosing groups (200 µg/kg, 18 mg, and 36 mg). A two-compartment model with zero-order dose input into the absorption compartment with a lag time function followed by first-order absorption and linear elimination best described the IVM's pharmacokinetic (PK) parameters. The final model identifies that the PK parameters of IVM are not affected by LF infection. Sex was a significant covariate on the peripheral volume of distribution (Vp/F, 53% lower in men than in women). IVM drug exposure shows linear pharmacokinetic behavior among the simulated dosing groups with similar drug exposure based on sex. **Conclusion/significance:** We have developed a PopPk model to describe and identify possible sources of the variability of IVM exposure. To our knowledge, this is the first PopPK study of IVM in patients with LF.

Extracellular vesicles secreted by Brugia malayi microfilariae modulate the melanization pathway in the mosquito host.

Loghry HJ, Kwon H, Smith RC, Sondjaja NA, Minkler SJ, Young S, Wheeler NJ, Zamanian M, Bartholomay LC, Kimber MJ.
31-05-2023
Sci Rep.
https://pubmed.ncbi.nlm.nih.gov/37258694/

Vector-borne, filarial nematode diseases cause significant disease burdens in humans and domestic animals worldwide. Although there is strong direct evidence of parasite-driven immunomodulation of mammalian host responses, there is less evidence of parasite immunomodulation of the vector host. We have previously reported that all life stages of Brugia malayi, a filarial nematode and causative agent of Lymphatic filariasis, secrete extracellular vesicles (EVs). Here we investigate the immunomodulatory effects of microfilariae-derived EVs on the vector host Aedes aegypti. RNA-seq analysis of an Ae. aegypti cell line treated with B. malayi microfilariae EVs showed differential expression of both mRNAs and miRNAs. AAEL002590, an Ae. aegypti gene encoding a serine protease, was shown to be downregulated when cells were treated with biologically relevant EV concentrations in vitro. Injection of adult female mosquitoes with biologically relevant concentrations of EVs validated these results in vivo, recapitulating the downregulation of AAEL002590 transcript. This gene was predicted to be involved in the mosquito phenoloxidase (PO) cascade leading to the canonical melanization response and correspondingly, both suppression of this gene using RNAi and parasite EV treatment reduced PO activity in vivo. Our data indicate that parasite-derived EVs interfere with critical immune responses in the vector host, including melanization.

Use of medicinal plants as a remedy against lymphatic filariasis: Current status and future prospect.

Fordjour FA, Osei-Poku P, Genfi AKA, Ainooson KG, Amponsah K, Arthur PK, Stephenson GR, Kwarteng A.
27-05-2023
Health Sci Rep.
https://pubmed.ncbi.nlm.nih.gov/37251521/

Giant scrotal lymphedema after paraffinoma injection: A case report.

Manduaru R, Wallad CK, Ariwicaksono SC.
20-05-2023
Urol Case Rep.
https://pubmed.ncbi.nlm.nih.gov/37250967/

Reduced Type 2 Innate Lymphocyte Cell Frequencies in Patent Wuchereria bancrofti-Infected Individuals.

Tamadaho RSE, Osei-Mensah J, Arndts K, Debrah LB, Debrah AY, Layland LE, Hoerauf A, Pfarr K, Ritter M.
30-04-2023
Pathogens.
https://pubmed.ncbi.nlm.nih.gov/37242335/

Approximately 51 million individuals suffer from lymphatic filariasis (LF) caused mainly by the filarial worm *Wuchereria bancrofti*. Mass drug administration (MDA) programs led to a significant reduction in the number of infected individuals, but the consequences of the treatment and clearance of infection in regard to host immunity remain uncertain. Thus, this study investigates the composition of myeloid-derived suppressor cells (MDSCs), macrophage subsets and innate lymphoid cells (ILCs), in patent (circulating filarial antigen (CFA)+ microfilariae (MF)+) and latent (CFA+MF-) *W. bancrofti*-infected individuals, previously *W. bancrofti*-infected (PI) individuals cured of the infection due to MDA, uninfected controls (endemic normal (EN)) and individuals who suffer from lymphoedema (LE) from the Western Region of Ghana. Frequencies of ILC2 were significantly reduced in *W. bancrofti*-infected individuals, while the frequencies of MDSCs, M2 macrophages, ILC1 and ILC3 were comparable between the cohorts. Importantly, clearance of infection due to MDA restored the ILC2 frequencies, suggesting that ILC2 subsets might migrate to the site of infection within the lymphatic tissue. In general, the immune cell composition in individuals who cured the infection were comparable to the uninfected individuals, showing that filarial-driven changes of the immune responses require an active infection and are not maintained upon the clearance of the infection.

Lymphatic filariasis endgame strategies: Using GEOFIL to model mass drug administration and targeted surveillance and treatment strategies in American Samoa.

Shaw C, McLure A, Graves PM, Lau CL, Glass K.
18-05-2023
PLoS Negl Trop Dis.

https://pubmed.ncbi.nlm.nih.gov/37200375/

Gale

Co-infection patterns in the ectoparasitic community affecting the Iberian ibex Capra pyrenaica.

Fernández-Muñoz MJ, Castillo-Contreras R, Pérez JM, Granados JE, Márquez FJ, López-Montoya AJ.
30-05-2023
Parasit Vectors.
https://pubmed.ncbi.nlm.nih.gov/37254132/

Background: Sarcoptic mange is one of the main parasitic diseases affecting the Iberian ibex Capra pyrenaica. Scabietic animals suffer a decline in body condition and reproductive fitness and in severe cases may die. Although several previous studies of the pathology of this disease and the physiological changes it produces in ibex have been carried out in recent years, our knowledge of the relationship between Sarcoptes scabiei and other ectoparasites of this host is still limited. Methods: We analysed 430 Iberian ibex skin samples. Ectoparasites were removed, counted and identified. Mite (S. scabiei) numbers were obtained after digesting the skin samples in a 5% KOH solution. We modelled mite numbers in terms of host sex and age, site, year, season and the presence of other ectoparasites such as ticks and lice using generalized linear mixed models (GLMMs) and ectoparasite co-occurrence patterns using two different models: the probabilistic model species co-occurrence and the generalized linear latent variable model (GLLVM). Results: The ectoparasite community was mainly composed of S. scabiei, six ticks (Haemaphysalis sulcata, Haemaphysalis punctata, Rhipicephalus bursa, Rhipicephalus turanicus, Dermacentor marginatus and Ixodes ricinus) and two lice (Bovicola crassipes and Linognathus stenopsis). Adult male ibex harboured more mites than females. Mite numbers varied greatly spatially and seasonally and increased with the presence of other parasites. Some positive co-occurrence relationships between pairs of different ectoparasites were observed, particularly between ticks. The presence of S. scabiei negatively affected lice and H. sulcata numbers. Conclusions: Sarcoptic mange has spread above all in ibex populations in and around the Mediterranean Basin, where it is now found in almost a third of its host's range. Mite numbers varied seasonally and spatially and were higher in male hosts. The presence of S. scabiei had a negative effect on lice numbers but favoured the presence of ticks.

Disseminated Scabies During Induction Chemotherapy for Acute Promyelocytic Leukemia.

Bolaman AZ, Eroğlu Küçükdiler AH, Yavaşoğlu İ.
29-06-2023
Turkiye Parazitol Derg.
https://pubmed.ncbi.nlm.nih.gov/37249118/

Identification of Daphne genkwa and Its Vinegar-Processed Products by Ultraperformance Liquid Chromatography-Quadrupole Time-of-Flight Mass Spectrometry and Chemometrics.

Mi H, Zhang P, Yao L, Gao H, Wei F, Lu T, Ma S.
Mai-2023
Molecules.
https://pubmed.ncbi.nlm.nih.gov/37241730/

Crude herbs of *Daphne genkwa* (CHDG) are often used in traditional Chinese medicine to treat scabies baldness, carbuncles, and chilblain owing to their significant purgation and curative effects. The most common technique for processing DG involves the use of vinegar to reduce the toxicity of CHDG and enhance its clinical efficacy. Vinegar-processed DG (VPDG) is used as an internal medicine to treat chest and abdominal water accumulation, phlegm accumulation, asthma, and constipation, among other diseases. In this study, the changes in the chemical composition of CHDG after vinegar processing and the inner components of the changed curative effects were elucidated using optimized ultrahigh-performance liquid chromatography coupled with quadrupole time-of-flight mass spectrometry (UPLC-Q-TOF-MS). Untargeted metabolomics, based on multivariate statistical analyses, was also used to profile differences between CHDG and VPDG. Eight marker compounds were identified using orthogonal partial least-squares discrimination analysis, which indicated significant differences between CHDG and VPDG. The concentrations of apigenin-7-*O*-β-d-methylglucuronate and hydroxygenkwanin were considerably higher in VPDG than those in CHDG, whereas the amounts of caffeic acid, quercetin, tiliroside, naringenin, genkwanines O, and orthobenzoate 2 were significantly lower. The obtained results can indicate the transformation mechanisms of certain changed compounds. To the best of our knowledge, this study is the first to employ mass spectrometry to detect the marker components of CHDG and VPDG.

The current available diagnostic tools and treatments of scabies and scabies variants: An updated narrative review.

Al-Dabbagh J, Younis R, Ismail N.
26-05-2023
Medicine (Baltimore).
https://pubmed.ncbi.nlm.nih.gov/37233429/

Can Ivermectin kill Sarcoptes scabiei during the molting process?

Feng S, Shi M, Yin Z, Di W, Guillot J, Fang F.
17-05-2023
PLoS Negl Trop Dis.
https://pubmed.ncbi.nlm.nih.gov/37196006/

Background: Sarcoptes scabiei is a permanent obligate ectoparasite that lives and reproduces in the epidermis of humans and other mammals worldwide. There is a lack of information on the molting process of Sarcoptes scabiei. Ivermectin is widely used to treat Sarcoptes infection in humans and animals, while the survival of molting

Sarcoptes mites in the presence of ivermectin is unknown. The aim of the present study is to investigate the molting process of Sarcoptes mites and assess the activity of ivermectin during the molting process of Sarcoptes mites. Methodology/principal findings: molting Sarcoptes mites were incubated at 35°C and 80% relative humidity and observed hourly until complete molt. Of the 192 molting mites recorded, the longest molt periods for larvae and nymphs were 23 and 30 h, respectively. The activity of ivermectin on molting Sarcoptes mites was also assessed using two concentrations of the drug (0.1 and 0.05 mg/ml). The exposure time for molting mites was determined by 100% mortality of female mites exposed to the solution of ivermectin. While all female mites were killed after exposure to 0.1 mg/ml ivermectin for 2 h and and 0.05 mg/ml for 7 h, 32% and 36% of molting mites survived and successfully molted, respectively. Conclusions/significance: The present study demonstrated that molting Sarcoptes mites are less susceptible to ivermectin than active mites. As a consequence, mites may survive after two doses of ivermectin given 7 days apart due not only to hatching eggs but also to the resistance of mites during their molting process. Our results provide insight into the optimal therapeutic regimens for scabies and highlight the need for further research on the molting process of Sarcoptes mites.

Permethrin Steal Effect by Unmasked Corneocytic Keratin in Topical Therapy of Scabies.

Scholz L, Fritz C, Chuttke J, Eichner A, Wohlrab J.
2023
Skin Pharmacol Physiol.
https://pubmed.ncbi.nlm.nih.gov/36716721/

Introduction: The use of epicutaneously applied permethrin in the treatment of common scabies is considered to be the first-line therapy. Due to increasing clinical treatment failure, the development of genetic resistance to permethrin in Sarcoptes scabiei var. hominis has been postulated. In addition, metabolic resistance and pharmacokinetic limitations by parasitic digestion and reactive thickening of stratum corneum are suspected to cause a reduction in cutaneous bioavailability. Methods: Since lipophilic permethrin is known to form hydrophobic interactions with proteins via van der Waals interactions, a similar interaction was assumed and investigated for permethrin and the protein keratin. Using keratin particles extracted from animal material, a model for hyperkeratotic and parasitic digested scabies skin was developed. Using fluorescence-labeled keratin and ^{3}H-permethrin, their interaction potential was validated by loading and unloading experiments. Additionally, the impact of keratin to permethrin penetration was investigated based on an in vitro model using Franz diffusion cells. Results: For the first time, keratin particles were introduced as a model for dyskeratotic skin, as we were able to show, the keratin particles' interaction potential with permethrin but no penetration behavior into the stratum corneum. Moreover, comparative penetration experiments of a reference formulation with and without added keratin or keratin-adherent permethrin showed that keratin causes a steal effect for permethrin, leading to a relevant reduction in cutaneous bioavailability in the target compartment. Conclusion: The results provide further evidence for a relevant pharmacokinetic influencing factor in the epicutaneous application of permethrin and a rationale for the necessity of keratolytic pretreatment in hyperkeratotic skin for the effective use of topical permethrin application in scabies.

Helminthiases transmises par le sol (ascaridiose, trichuriase, ankylostomiase)

Extra-intestinal complications of Ascaris lumbricoides infections in India: A systematic review and meta-analysis.

Mewara A, Kanaujia R, Malla N.
02-06-2023
Trans R Soc Trop Med Hyg.
https://pubmed.ncbi.nlm.nih.gov/37264906/

The aber of Ascaris lumbricoides may cause extra-intestinal ascariasis (EIA) involving hepato-biliary-pancreatic (HBP) or other extra-gastro-intestinal (EGI) organs. We performed a systematic review and meta-analysis to study the risk factors and clinical presentations of EIA, and differences in HBP and EGI ascariasis. Medline, Web of Science and Embase were searched for cases of EIA in the English language from India. From 1204 articles, 86 studies (105 cases) were included. The majority of the cases involved the HBP system (78%). Among HBP ascariasis, the most commonly involved site was the bile duct (53.6%). Females had 11.3 times higher odds (95% CI 2.852 to 44.856; p=0.001) of HBP ascariasis, while the pediatric population had lower odds (OR=0.323). Previous gallbladder disease was significantly associated with HBP ascariasis in adults (p=0.046), while a significantly higher number of cases of EGI ascariasis were observed among pediatric patients (p=0.003). Ocular symptoms occurred exclusively in the pediatric population (p=0.017). Overall, death was reported in 3.8% of patients (n=4). This review emphasizes the importance of the complications of EIA. It encourages future research into issues such as the reasons of higher gall bladder ascariasis in females and the implications of Ascaris-related complications following biliary tract interventions. It also suggests considering Ascaris as a differential diagnosis for airway obstuction in intubated critically ill patients.

Efficacy of Single-Dose Albendazole for the Treatment of Soil-Transmitted Helminthic Infections among School Children in Rwanda-A Prospective Cohort Study.

Kabatende J, Barry A, Mugisha M, Ntirenganya L, Bergman U, Bienvenu E, Aklillu E.
17-01-2023
Pharmaceuticals (Basel).
https://pubmed.ncbi.nlm.nih.gov/37259291/

Mass drug administration (MDA) of single-dose albendazole to all at-risk populations as preventive chemotherapy (deworming) is recommended by WHO to halt transmission of soil-transmitted helminth (STH) in endemic countries. We assessed the effectiveness of single-dose albendazole against STH infection in the western province of Rwanda, where STH prevalence remains high despite the implementation of preventive chemotherapy for over a decade. Two weeks before the scheduled MDA, 4998 school children (5-15 years old) were screened for STH infections (*Ascaris lumbricoides*, *Trichuris trichiura*, and hookworm), and 1526 children who tested positive for at least one type of STH parasite were enrolled and received single-dose albendazole (400 mg) through MDA. A follow-up stool exam was performed at three weeks post-treatment using Kato-Katz. Efficacy was assessed by cure rate (CR), defined as the proportion of children who became egg-free, and egg reduction rates (ERRs) at three weeks post-treatment. The CR and ERR for hookworms (CR = 96.7%, ERR = 97.4%) was above, and for *Ascaris lumbricoides* (CR = 95.1%, ERR = 94.6%) was borderline compared with the WHO efficacy threshold (CR and ERR ≥ 95%). However, the CR and ERR for *T. trichiura* (CR = 17.6% ERR = 40.3%) were below the WHO threshold for efficacy (CR and ERR ≥ 50%). Having moderate-to-heavy infection intensity and coinfection with another type of STH parasites were independent risk factors for lower CR and ERR against *Trichirus trichiura* ($p < 0.001$). Single-dose albendazole used in the MDA program is efficacious for the treatment and control for hookworms and *Ascaris lumbricoides* infections but not effective for *Trichirus trichiura*. An alternative treatment regimen is urgently needed to prevent, control, and eliminate STH as a public health problem.

A parasitological study on the possible toilet ruins of the Japanese colonial period in Korea.

Kim J, Seo M, Fujita H, Chai JY, Park JW, Jang JW, Jang IS, Shin DH.
Mai-2023
Parasites Hosts Dis.
https://pubmed.ncbi.nlm.nih.gov/37258267/

What was the main factor in successful control of ascariasis in Korea?

Cho SY, Hong ST.
Mai-2023
Parasites Hosts Dis.
https://pubmed.ncbi.nlm.nih.gov/37258258/

In the l950s, under the legacy of traditional agriculture, Ascaris lumbricoides, spread epidemically in the war-bitten society of Korea. Consensus on the parasite control was drafted in the Parasite Disease Prevention Act, which passed a parliamentary agreement in 1966, and established safe disposal of feces and mass chemotherapy as control strategies. Biannual stool examinations and treating infected schoolchildren were basic scheme of the control activity through which revenue could be secured for organized business. In the 27 years following 1969, a maximum of 16 million stool examinations had been done every year. Cellophane thick smear enabled the task. The infection declined remarkably in the 1970s when industrialization and green revolution proceeded. A population study of A. lumbricoides in the late 1970s helped us better understand its epidemiology. The data also settled down the understandable protest of teachers against the repeated stool examinations. In the 9 years following 1987, the target population was gradually reduced when the egg positive rate was below 0.1%. An article in the Korean Law, stipulating obligatory stool examinations, was made optional. Although the long-term Korean effort of Ascaris control was a success, the effect of mass chemotherapy was not as succinct in terms of lowering reinfection. In the period of control, Korean agricultural technology changed, and the economy grew and supplied sanitary facilities by which the vicious cycle was disconnected. Reduction of morbidity was a benefit of mass chemotherapy, which is the only control method feasible in economically difficult countries. The most important hurdle of parasite control in the 1960s was poverty of general population and limited financial resources in Korea but the society formed a consensus on the priority of intestinal helminthiasis control during the ordeal period. The national consensus in the 1960s was the critical milestone for Ascaris control in Korea. Under the social agreement, application of timely technical and research advancements in parasitology achieved the success of ascariasis elimination. The successful experience of ascariasis elimination in Korea can be a benchmark for countries where neglected tropical diseases are endemically recycled.

Prevalence and Associated Factors of Intestinal Parasites among Food Handlers Working in Food Service Establishments in Northwest Ethiopia, 2022.

Wondimu H, Mihret M.
18-05-2023
J Parasitol Res.
https://pubmed.ncbi.nlm.nih.gov/37252034/

Parasitological and Bacteriological Evaluation of Common Raw Fruits Collected from Two Major Markets in Iwo, Osun State, South-West Nigeria.

Oladosu OO, Olatunde DO, Olatayo AO, Atobatele B.
18-05-2023
Int J Food Sci.
https://pubmed.ncbi.nlm.nih.gov/37250492/

Background: Fruits are a vital part of human nutrition because they contain the growth factors required to maintain normal health. Fruits are also known to harbour a wide range of parasites and bacteria. Consumption of unwashed raw fruits can lead to foodborne pathogens. This study was carried out to examine the presence of parasites and bacteria on fruits sold at two major markets in Iwo, Osun state, South-West Nigeria. Methods: Twelve different fresh fruits and seven different fresh fruits were purchased from different vendors from "Odo-ori" and "Adeeke" markets, respectively. The samples were

transported to the microbiology laboratory of Bowen University, Iwo, Osun state for bacteriological and parasitological analysis. The parasites were concentrated by sedimentation and were examined using a light microscope, while for the microbial analysis, culturing and biochemical tests were also carried out on all the samples. Results: The parasites discovered include *Fasciola hepatica* eggs, *Ascaris lumbricoides* and *Strongyloides stercoralis* larvae, hookworm larvae, and *Taenia* and *Trichuris trichiura* eggs. *Ascaris lumbricoides* was most frequently detected (40.0%). Bacteria isolated from the sampled fruits include *Klebsiella oxytoca*, *Klebsiella pneumoniae*, *Enterobacter aerogenes*, *Escherichia coli*, *Kluyvera ascorbata*, *Proteus mirabilis*, *Staphylococcus intermedius*, *Staphylococcus* sp., *Micrococcus sedentarius*, *Corynebacterium diphtheriae*, and *Streptococcus zooepidemicus*. Conclusion: The presence of parasites and bacteria on the fruits observed indicates that public health diseases may arise from their consumption. Awareness and education among farmers, vendors, and consumers about the importance of personal and food hygiene through proper washing or disinfection of fruits could reduce the risk of parasites and bacterial fruit contamination.

A general framework to support cost-efficient fecal egg count methods and study design choices for large-scale STH deworming programs-monitoring of therapeutic drug efficacy as a case study.

Coffeng LE, Vlaminck J, Cools P, Denwood M, Albonico M, Ame SM, Ayana M, Dana D, Cringoli G, de Vlas SJ, Fenwick A, French M, Kazienga A, Keiser J, Knopp S, Leta G, Matoso LF, Maurelli MP, Montresor A, Mirams G, Mekonnen Z, Corrêa-Oliveira R, Pinto SA, Rinaldi L, Sayasone S, Steinmann P, Thomas E, Vercruysse J, Levecke B.
17-05-2023
PLoS Negl Trop Dis.
https://pubmed.ncbi.nlm.nih.gov/37196017/

Background: Soil-transmitted helminth (STH) control programs currently lack evidence-based recommendations for cost-efficient survey designs for monitoring and evaluation. Here, we present a framework to provide evidence-based recommendations, using a case study of therapeutic drug efficacy monitoring based on the examination of helminth eggs in stool. Methods: We performed an in-depth analysis of the operational costs to process one stool sample for three diagnostic methods (Kato-Katz, Mini-FLOTAC and FECPAKG2). Next, we performed simulations to determine the probability of detecting a truly reduced therapeutic efficacy for different scenarios of STH species (Ascaris lumbricoides, Trichuris trichiura and hookworms), pre-treatment infection levels, survey design (screen and select (SS); screen, select and retest (SSR) and no selection (NS)) and number of subjects enrolled (100-5,000). Finally, we integrated the outcome of the cost assessment into the simulation study to estimate the total survey costs and determined the most cost-efficient survey design. Principal findings: Kato-Katz allowed for both the highest sample throughput and the lowest cost per test, while FECPAKG2 required both the most laboratory time and was the most expensive. Counting of eggs accounted for 23% (FECPAKG2) or ≥80% (Kato-Katz and Mini-FLOTAC) of the total time-to-result. NS survey designs in combination with Kato-Katz were the most cost-efficient to assess therapeutic drug efficacy in all scenarios of STH species and endemicity. Conclusions/significance: We confirm that Kato-Katz is the fecal egg counting method of choice for monitoring therapeutic drug efficacy, but that the survey design currently recommended by WHO (SS) should be updated. Our generic framework, which captures laboratory time and material costs, can be used to further support cost-efficient choices for other important surveys informing STH control programs. In addition, it can be used to explore the value of alternative diagnostic techniques, like automated egg counting, which may further reduce operational costs.

Prevalence, intensity and associated risk factors of soil-transmitted helminth infections among individuals living in Bata district, Equatorial Guinea.

Ribado Meñe G, Dejon Agobé JC, Momo Besahà JC, Abaga Ondo Ndoho F, Abdulla S, Adegnika AA.
17-05-2023
PLoS Negl Trop Dis.
https://pubmed.ncbi.nlm.nih.gov/37196007/

Biliary ascariasis misidentified as a biliary stent in a patient undergoing liver resection.

Chae H, Suh SW, Choi YS, Sohn HJ, Lee SE, Do JH, Park HJ.
Mai-2023
Parasites Hosts Dis.
https://pubmed.ncbi.nlm.nih.gov/37258266/

Ascaris lumbricoides causes one of the most common soil-transmitted helminthiases globally. The worms mostly infect the human small intestine and elicit negligible or nonspecific symptoms, but there are reports of extraintestinal ectopic ascariasis. We describe a rare case of biliary ascariasis mistaken for biliary stent in a 72-year-old female patient with a history of liver resection. She visited our outpatient clinic complaining of right upper quadrant pain and fever for the past week. She had previously undergone left lateral sectionectomy for recurrent biliary and intrahepatic duct stones 2 years ago. Besides mildly elevated gamma-glutamyl transferase levels, her liver function tests were normal. Magnetic resonance cholangiopancreatography revealed a linear filling defect closely resembling an internal stent from the common bile duct to the right intrahepatic bile duct. A live female A. lumbricoides adult worm was removed by endoscopic retrograde cholangiopancreatography (ERCP). Despite a significant decrease of the ascariasis prevalence in Korea, cases of biliary ascariasis are still occasionally reported. In this study, a additional case of biliary ascariasis, which was radiologically misdiagnosed as the biliary stent, was described in a hepatic resection patient by the worm recovery with ERCP in Korea.

Leishmaniose

Antiproliferative activity and ultrastructural changes in promastigote and amastigote forms of Leishmania amazonensis caused by limonene-acylthiosemicarbazide hybrids.

Contato AG, Kaplum V, Scariot DB, Garcia FP, Falzirolli H, Vandresen F, Ueda-Nakamura T, de Oliveira Silva S, Conceição da Silva C, Nakamura CV.
01-06-2023
Chem Biodivers.
https://pubmed.ncbi.nlm.nih.gov/37263974/

Leishmaniasis is a tropical zoonotic disease. It is found in 98 countries, with an estimated 1.3 million people being affected annually. During the life-cycle, the Leishmania parasite alternates between promastigote and amastigote forms. The first line treatment for leishmaniasis are the pentavalent antimonials, such as N-methylglucamine antimoniate (Glucantime®) and sodium stibogluconate (Pentostam®). These drugs are commonly related to be associated with dangerous side effects such as cardiotoxicity, nephrotoxicity, hepatotoxicity, and pancreatitis. Considering these aspects, this work aimed to obtain a new series of limonene-acylthiosemicarbazides hybrids as an alternative for the treatment of leishmaniasis. For this, promastigotes, axenic amastigotes, and intracellular amastigotes of Leishmania amazonensis were used in the antiproliferative assay; J774-A1 macrophages for the cytotoxicity assay; and electron microscopy techniques were performed to analyze the morphology and ultrastructure of parasites. ATZ-S-04 compound showed the best result in both tests. Its IC50, in promastigotes, axenic amastigotes and intracellular amastigotes was 0.35 ± 0.08 µM, 0.49 ± 0.06 µM, and 15.90 ± 2.88 µM, respectively. Cytotoxicity assay determined a CC50 of 16.10 ± 1.76 µM for the same compound. By electron microscopy, it was observed that ATZ-S-04 affected the Golgi complex, in addition to morphological changes in promastigote forms of L. amazonensis.

Complete assembly, annotation of virulence genes and CRISPR editing of the genome of Leishmania amazonensis PH8 strain.

Goes WM, Brasil CRF, Reis-Cunha JL, Coqueiro-Dos-Santos A, Grazielle-Silva V, de Souza Reis J, Souto TC, Laranjeira-Silva MF, Bartholomeu DC, Fernandes AP, Teixeira SMR.
30-05-2023
Genomics.
https://pubmed.ncbi.nlm.nih.gov/37263313/

We report the sequencing and assembly of the PH8 strain of Leishmania amazonensis one of the etiological agents of leishmaniasis. After combining data from long Pacbio reads, short Illumina reads and synteny with the Leishmania mexicana genome, the sequence of 34 chromosomes with 8317 annotated genes was generated. Multigene families encoding three virulence factors, A2, amastins and the GP63 metalloproteases, were identified and compared to their annotation in other Leishmania species. As they have been recently recognized as virulence factors essential for disease establishment and progression of the infection, we also identified 14 genes encoding proteins involved in parasite iron and heme metabolism and compared to genes from other Trypanosomatids. To follow these studies with a genetic approach to address the role of virulence factors, we tested two CRISPR-Cas9 protocols to generate L. amazonensis knockout cell lines, using the Miltefosine transporter gene as a proof of concept.

The leishmaniases in Kenya: A scoping review.

Grifferty G,

Shirley H, O'Brien K, Hirsch JL, Orriols AM, Amechi KL, Lo J, Chanda N, El Hamzaoui S, Kahn J, Yap SV, Watson KE, Curran C, Atef AbdelAlim A, Bose N, Cilfone AL, Wamai R.
01-06-2023
PLoS Negl Trop Dis.
https://pubmed.ncbi.nlm.nih.gov/37262045/

Cutaneous Leishmaniasis in a Non-endemic Area in Mexico.

Martinez Niño MA, Camacho Galván JR, Castillo Cruz UDR, Perez-Coronado G.
27-04-2023
Cureus.
https://pubmed.ncbi.nlm.nih.gov/37261149/

Cytotoxic and Antileishmanial Effects of the Monoterpene β-Ocimene.

Sousa JMS, Nunes TAL, Rodrigues RRL, Sousa JPA, Val MDCA, Coelho FADR, Santos ALSD, Maciel NB, Souza VMR, Machado YAA, Sousa PSA, Araújo AR, Rocha JA, Sousa DP, Silva MVD, Arcanjo DDR, Rodrigues KADF.
26-01-2023
Pharmaceuticals (Basel).
https://pubmed.ncbi.nlm.nih.gov/37259336/

Overexpression of Leishmania major Protein Arginine Methyltransferase 6 reduces parasite infectivity in vivo.

Campagnaro GD, Lorenzon LB, Rodrigues MA, Defina TPA, Pinzan CF, Ferreira TR, Cruz AK.
29-05-2023
Acta Trop.
https://pubmed.ncbi.nlm.nih.gov/37257676/

Arginine methylation is catalysed by Protein Arginine Methyltransferases (PRMTs) and can affect how a target protein functions and how it interacts with other macromolecules, which in turn impacts on cell metabolism and gene expression control. Leishmania parasites express five different PRMTs, and although the presence of each individual PRMT is not essential per se, the imbalanced activity of these PRMTs can impact the virulence of Leishmania parasites in vitro and in vivo. Here we created

a Leishmania major cell line overexpressing PRMT6 and show that similar to what was observed for the T. brucei homologous enzyme, L. major PRMT6 probably has a narrow substrate range. However, its overexpression notably impairs the infection in mice, with a mild reduction in the number of viable parasites in the lymph nodes. Our results indicate that arginine methylation by LmjPRMT6 plays a significant role in the adaptation of the parasite to the environment found in the mammalian host.

Matrix metalloproteinases -2 and -9 expression in dogs with visceral leishmaniasis: A systematic review.

Rocha Da Silva R, de Santana Fontes Vasconcelos F, Nunes de Santana Campos R, Dos Santos Tavares D, Lima Dos Santos P.
29-05-2023
Cytokine.
https://pubmed.ncbi.nlm.nih.gov/37257306/

The matrix metalloproteinases (MMPs) are engaged in the degradation and remodeling of the extracellular matrix and vessels, allowing the progression of pathological processes. Recent studies pointed that MMP -2 and -9 are promising visceral leishmaniasis biomarkers. Thus, the present studystudy aimed to review published scientific literature related to MMP-2 and -9 activity on canine visceral leishmaniasis (CVL). The review followed the PRISMA method, searching for articles in ScienceDirect, PubMed, Scopus, Lilacs, Medline and Google Scholar from inception until 20 March 2022 by employing the following terms: "dog", "matrix metalloproteinases" and "Visceral Leishmaniasis" or "Kala Azar". The selected articles were read in full and only those consistent with the eligibility criteria were included in the review. Of 238 articles from the initial search, only five were deemed eligible, which were conducted between 2010 and 2018. All studies were performed in Brazil. It was observed that there was a higher expression of proMMP-2 in cerebrospinal (CS) fluid and serum and active MMP-2 in different skin areas, mainly in high parasite load areas. As for MMP-9, the pro and active forms were both expressed in CS fluid, serum and different skin areas. The MMP-2 can be considered a biomarker of bad prognostic as it plays an inflammatory role with a greater release in the initial phase of the disease, where MMP-9 is perceived in the chronic phase of CVL. Future research on the subject with greater methodological rigor and bigger sample sizes are mandatory to clarify the role of MMPs on disease progression.

Phylogenetic and biogeographical traits predict unrecognized hosts of zoonotic leishmaniasis.

Glidden CK, Murran AR, Silva RA, Castellanos AA, Han BA, Mordecai EA.
31-05-2023
PLoS Negl Trop Dis.
https://pubmed.ncbi.nlm.nih.gov/37256857/

In vitro effects of lapachol and β-lapachone against Leishmania amazonensis.

Ramos-Milaré ÁCFH, Sydor BG, Brustolin AÁ, Lera-Nonose DSSL, Oyama J, Silva EL, Caetano W, Campanholi KSS, Demarchi IG, Silveira TGV, Lonardoni MVC.
29-05-2023
Braz J Med Biol Res.
https://pubmed.ncbi.nlm.nih.gov/37255095/

Leishmaniasis is a neglected disease that affects millions of people worldwide, and special attention should be given to treatment because the available drugs have limitations, which can lead to low therapeutic adherence and parasitic resistance. This study evaluated the activity of the bioactive naphthoquinones, lapachol and β-lapachone, against Leishmania amazonensis. The cell alterations were evaluated in vitro on promastigote and amastigote forms. The lethal dose (LD50) at 24, 48, and 72 h on the promastigote's forms using lapachol was 75.60, 72.82, and 58.85 µg/mL and for β-lapachone was 0.65, 1.24, and 0.71 µg/mL, respectively. The naphthoquinones significantly inhibited the survival rate of L. amazonensis amastigotes at 83.11, 57.59, and 34.95% for lapachol (82.28, 41.14, and 20.57 µg/mL), and 78.49, 83.25, and 80.22% for β-lapachone (3.26, 1.63, and 0.815 µg/mL). The compounds on the promastigote's forms led to the loss of mitochondrial membrane potential, induced changes in the integrity of the membrane, caused damage to cells suggestive of the apoptotic process, and showed inhibition of tumor necrosis factor (TNF)-α and interleukin (IL)-6 production. The results showed that these naphthoquinones are promising candidates for research on new drugs with anti-Leishmania activity derived from natural products.

Molecular identification of Phlebotomus kandelakii apyrase and assessment of the immunogenicity of its recombinant protein in BALB/c mice.

Fayaz S, Raz A, Bahrami F, Fard-Esfahani P, Parvizi P, Ajdary S.
30-05-2023
Sci Rep.
https://pubmed.ncbi.nlm.nih.gov/37253833/

[Visceral leishmaniasis in Xinjiang Uygur Autonomous Region during the COVID-19 pandemic: a case report].

Maimaitijiang W, Zhai X, Ayixiamu K, Shi G, Wang S, Cheng X, Kaderya E, Zhao J.
25-04-2023
Zhongguo Xue Xi Chong Bing Fang Zhi Za Zhi.
https://pubmed.ncbi.nlm.nih.gov/37253573/

Objective: To perform an epidemiological investigation on a case of visceral leishmaniasis reported from Shule County, Kashi Prefecture, Xinjiang Uygur Autonomous Region in 2021, so as to provide insights into differential diagnosis of visceral leishmaniasis during the COVID-19 pandemic. Methods: The epidemiological history of this case was collected, and the case was diagnosed for

Leishmania infection with the immunochromatographic (rK39) strip test, bone marrow smear microscopy and PCR assay. **Results:** The patient had typical clinical symptoms of leishmaniasis, including irregular fever, hepatosplenomegaly, low serum albumin and elevated globulin. Bone marrow smear microscopy identified *L. donovani* amastigotes, and both rK39 strip test and PCR assay were positive, while the case was tested negative for SARS-CoV-2. COVID-19 was therefore excluded and visceral leishmaniasis was diagnosed. Standard full-dose treatment with sodium stibogluconate was given, and no *Leishmania* was found on blood smears during the reexamination. No recurrence was found during the followup after discharge for hospital. **Conclusions:** During the COVID-19 pandemic, it is recommended to increase the perception of differential diagnosis of visceral leishmaniasis among first-contact doctors, and reinforce the capability of differential diagnosis and health education of visceral leishmaniasis among medical and healthcare institutions at all levels, to prevent missed diagnosis and misdiagnosis of visceral leishmaniasis.

LEISH2b - A phase 2b study to assess the safety, efficacy, and immunogenicity of the Leishmania vaccine ChAd63-KH in post-kala azar dermal leishmaniasis.

Lacey C, Musa A, Khalil ET, Younis B, Osman M, Wiggins R, Keding A, Kaye P.
03-08-2022
Wellcome Open Res.
https://pubmed.ncbi.nlm.nih.gov/37252616/

Steroid-responsive unilateral keratouveitis following systemic treatment in a patient with human immunodeficiency virus and leishmaniasis.

Su E, Lu JE, Voss K.
20-02-2023
Taiwan J Ophthalmol.
https://pubmed.ncbi.nlm.nih.gov/37252162/

In vitro evaluation of antileishmanial activity, mode of action and cellular response induced by vanillin synthetic derivatives against Leishmania species able to cause cutaneous and visceral leishmaniasis.

Freitas CS, Santiago SS, Lage DP, Antinarelli LMR, Oliveira FM, Vale DL, Martins VT, Magalhaes LND, Bandeira RS, Ramos FF, Pereira IAG, de Jesus MM, Ludolf F, Tavares GSV, Costa AV, Ferreira RS, Coimbra ES, Teixeira RR, Coelho EAF.
27-05-2023
Exp Parasitol.
https://pubmed.ncbi.nlm.nih.gov/37247802/

The treatment against leishmaniasis presents problems, mainly due to their toxicity of the drugs, high cost and/or by the emergence of parasite resistant strains. In this context, new therapeutics should be searched. In this study, two novel synthetic derivatives from vanillin: [4-(2-hydroxy-3-(4-octyl-1H-1,2,3-triazol-1-yl)propoxy)-3-methoxybenzaldehyde] or 3s and [4-(3-(4-decyl-1H-1,2,3-triazol-1-yl)-2-hydroxypropoxy)-3-methoxybenzaldehyde] or 3t, were evaluated regarding their antileishmanial activity against distinct parasite species able to cause cutaneous and visceral leishmaniasis. Results showed that compounds 3s and 3t were effective against Leishmania infantum, L. amazonensis and L. braziliensis promastigote and amastigote-like forms, showing selectivity index (SI) of 25.1, 18.2 and 22.9, respectively, when 3s was used against promastigotes, and of 45.2, 7.5 and 15.0, respectively, against amastigote-like stage. Using the compound 3t, SI values were 45.2, 53.0 and 80.0, respectively, against promastigotes, and of 35.9, 46.0 and 58.4, respectively, against amastigote-like forms. Amphotericin B (AmpB) showed SI values of 5.0, 7.5 and 15.0, respectively, against promastigotes, and of 3.8, 5.0 and 7.5, respectively, against amastigote-like stage. The treatment of infected macrophages and inhibition of the infection upon pre-incubation with the molecules showed that they were effective in reducing the infection degree and inhibiting the infection in pre-incubated parasites, respectively, as compared to data obtained using AmpB. The mechanism of action of 3s and 3t was evaluated in L. infantum, revealing that both 3s and 3t altered the parasite mitochondrial membrane potential leading to reactive oxygen species production, increase in lipid corps and changes in the cell cycle, causing the parasite' death. A preliminary assay using the cell culture supernatant from treated and infected macrophages showed that 3s and 3t induced higher IL-12 and lower IL-10 values; suggesting the development of an in vitro Th1-type response in the treated cells. In this context, data indicated that 3s and 3t could be considered therapeutic agents to be tested in future studies against leishmaniasis.

Green Synthesis of Molecules for the Treatment of Neglected Diseases.

Anghinoni JM, Dilelio MC, Shiguemoto CYK, Schumacher RF, Baroni ACM, Lenardão EJ.
26-05-2023
Curr Top Med Chem.
https://pubmed.ncbi.nlm.nih.gov/37246323/

Neglected tropical diseases (NTDs) affect mainly poor and marginalized populations of tropical and subtropical areas in 150 countries. Many of the chemical processes involved in the synthesis of active pharmaceutical ingredients (APIs) are highly polluting and inefficient, both in terms of materials and energy-consuming. In this review, we present the green protocols developed in the last 10 years to access new small molecules with potential applications in the treatment of leishmania, tuberculosis, malaria, and Chagas disease. The use of alternative and efficient energy sources, like microwaves and ultrasound, as well as reactions using green solvents and solvent-free protocols, are discussed in this review.

Design, synthesis and biological evaluation of antiparasitic dinitroaniline-ether phospholipid hybrids.

Roussaki M, Magoulas GE, Fotopoulou T, Santarem N, Barrias E, Pöhner I, Luelmo S, Afroudakis P, Georgikopoulou K, Nevado PT, Eick J, Bifeld E, Corral MJ, Jiménez-Antón MD, Ellinger B, Kuzikov M, Fragiadaki I, Scoulica E, Gul S, Clos J, Prousis KC, Torrado JJ, Alunda JM, Wade RC, de Souza W, Cordeiro da Silva A, Calogeropoulou T.
19-05-2023
Bioorg Chem.
https://pubmed.ncbi.nlm.nih.gov/37244229/

High Selectivity of 8-Hydroxyquinoline on Leishmania (Leishmania) and Leishmania (Viannia) Species Correlates with a Potent Therapeutic Activity In Vivo.

Lima SKS, Jesus JA, Raminelli C, Laurenti MD, Passero LFD.
07-05-2023
Pharmaceuticals (Basel).
https://pubmed.ncbi.nlm.nih.gov/37242490/

Leishmaniasis is a neglected disease caused by protozoa of the genus *Leishmania*, which causes different clinical manifestations. Drugs currently used in the treatment such as pentavalent antimonial and amphotericin B cause severe side effects in patients, and parasite resistance has been reported. Thus, it is necessary and urgent to characterize new and effective alternative drugs to replace the current chemotherapy of leishmaniasis. In this regard, it has been experimentally demonstrated that quinoline derivatives present significative pharmacological and parasitic properties. Thus, the aim of this work was to demonstrate the leishmanicidal activity of 8-hydroxyquinoline (8-HQ) in vitro and in vivo. The leishmanicidal activity (in vitro) of 8-HQ was assayed on promastigote and intracellular amastigote forms of *L. (L.) amazonensis*, *L. (L.) infantum chagasi*, *L. (V.) guyanensis L. (V.) naiffi*, *L. (V.) lainsoni*, and *L. (V.) shawi*. Additionally, the levels of nitric oxide and hydrogen peroxide were analyzed. The therapeutic potential of 8-HQ was analyzed in BALB/c mice infected with a strain of *L. (L.) amazonensis* that causes anergic cutaneous diffuse leishmaniasis. In vitro data showed that at 24 and 72 h, 8-HQ eliminated promastigote and intracellular amastigote forms of all studied species and this effect may be potentialized by nitric oxide. Furthermore, 8-HQ was more selective than miltefosine. Infected animals treated with 8-HQ by the intralesional route dramatically reduced the number of tissue parasites in the skin, and it was associated with an increase in IFN-γ and decrease in IL-4, which correlated with a reduction in inflammatory reaction in the skin. These results strongly support the idea that 8-HQ is an alternative molecule that can be employed in the treatment of leishmaniasis, given its selectivity and multispectral action in parasites from the *Leishmania* genus.

Gel-Free Tools for Quick and Simple Screening of Anti-Topoisomerase 1 Compounds.

Keller JG, Petersen KV, Mizielinski K, Thiesen C, Bjergbæk L, Reguera RM, Pérez-Pertejo Y, Balaña-Fouce R, Trejo A, Masdeu C, Alonso C, Knudsen BR, Tesauro C.
27-03-2023
Pharmaceuticals (Basel).
https://pubmed.ncbi.nlm.nih.gov/37242440/

With the increasing need for effective compounds against cancer or pathogen-borne diseases, the development of new tools to investigate the enzymatic activity of biomarkers is necessary. Among these biomarkers are DNA topoisomerases, which are key enzymes that modify DNA and regulate DNA topology during cellular processes. Over the years, libraries of natural and synthetic small-molecule compounds have been extensively investigated as potential anti-cancer, anti-bacterial, or anti-parasitic drugs targeting topoisomerases. However, the current tools for measuring the potential inhibition of topoisomerase activity are time consuming and not easily adaptable outside specialized laboratories. Here, we present rolling circle amplification-based methods that provide fast and easy readouts for screening of compounds against type 1 topoisomerases. Specific assays for the investigation of the potential inhibition of eukaryotic, viral, or bacterial type 1 topoisomerase activity were developed, using human topoisomerase 1, *Leishmania donovani* topoisomerase 1, monkeypox virus topoisomerase 1, and *Mycobacterium smegmatis* topoisomerase 1 as model enzymes. The presented tools proved to be sensitive and directly quantitative, paving the way for new diagnostic and drug screening protocols in research and clinical settings.

Insights into the Genetic Diversity of Leishmania (Viannia) panamensis in Panama, Inferred via Multilocus Sequence Typing (MLST).

Mendieta D, Vásquez V, Jaén L, Pineda V, Saldaña A, Calzada JE, Samudio F.
22-05-2023
Pathogens.
https://pubmed.ncbi.nlm.nih.gov/37242417/

Roles of ADP-Ribosylation during Infection Establishment by Trypanosomatidae Parasites.

Dowling J, Doig CL.
12-05-2023
Pathogens.
https://pubmed.ncbi.nlm.nih.gov/37242378/

Potential Biomarkers for Asymptomatic Visceral Leishmaniasis among Iraq-Deployed U.S. Military Personnel.

de Araujo FF, Lakhal-Naouar I, Koles N, Raiciulescu S, Mody R, Aronson N.
12-05-2023
Pathogens.
https://pubmed.ncbi.nlm.nih.gov/37242376/

Visceral leishmaniasis (VL) is a chronic infection caused by *Leishmania* (*L.*) *donovani* or *L. infantum* parasites. Despite

having the infection, most individuals never develop the clinical disease and are able to control the parasite and remain asymptomatic. However, some progress to symptomatic VL, leading to death if untreated. The host immune response has a major role in determining the progression and severity of the clinical manifestations in VL; several immune biomarkers of symptomatic VL have been described with interferon-gamma release as a surrogate biomarker of host cellular immunity. However, new biomarkers to identify asymptomatic VL (AVL) are needed for the identification of people at risk for VL activation. In our study, levels of chemokine/cytokine in the supernatants of peripheral mononuclear blood cells (PBMC) from 35 AVL^+ Iraq-deployed participants, stimulated in vitro with soluble *Leishmania* antigen for 72 h, were assessed by a bead-based assay that allows the measurement of multiple analytes. PBMC of AVL-negative military beneficiaries were used as controls. Monocyte Chemoattractant Protein-1, Monokine Induced by Gamma Interferon and Interleukin-8, were detected at high levels in AVL^+ stimulated cultures from Iraq deployers compared to uninfected controls. Measurement of chemokine/cytokine levels can identify cellular immune responses in AVL^+ asymptomatic individuals.

Recent Advances in Chemotherapeutics for Leishmaniasis: Importance of the Cellular Biochemistry of the Parasite and Its Molecular Interaction with the Host.

Singh R, Kashif M, Srivastava P, Manna PP.
12-05-2023
Pathogens.
https://pubmed.ncbi.nlm.nih.gov/37242374/

Use of In-Clinic Diagnostic Kits for the Detection of Seropositivity to Leishmania infantum and Other Major Vector-Borne Pathogens in Healthy Dogs.

Morelli S, Diakou A, Frangipane di Regalbono A, Colombo M, Simonato G, Di Cesare A, Passarelli A, Pezzuto C, Tzitzoudi Z, Barlaam A, Beall M, Chandrashekar R, Pantchev N, Traversa D.
11-05-2023
Pathogens.
https://pubmed.ncbi.nlm.nih.gov/37242366/

Synergistic Antileishmanial Effect of Oregano Essential Oil and Silver Nanoparticles: Mechanisms of Action on Leishmania amazonensis.

Alves AB, da Silva Bortoleti BT, Tomiotto-Pellissier F, Ganaza AFM, Gonçalves MD, Carloto ACM, Rodrigues ACJ, Silva TF, Nakazato G, Kobayashi RKT, Lazarin-Bidóia D, Miranda-Sapla MM, Costa IN, Pavanelli WR, Conchon-Costa I.
29-04-2023
Pathogens.
https://pubmed.ncbi.nlm.nih.gov/37242330/

American tegumentary leishmaniasis, a zoonotic disease caused by the *Leishmania* genus, poses significant challenges in treatment, including administration difficulty, low efficacy, and parasite resistance. Novel compounds or associations offer alternative therapies, and natural products such as oregano essential oil (OEO), extracted from *Origanum vulgare*, have been extensively researched due to biological effects, including antibacterial, antifungal, and antiparasitic properties. Silver nanoparticles (AgNp), a nanomaterial with compelling antimicrobial and antiparasitic activity, have been shown to exhibit potent leishmanicidal properties. We evaluated the in vitro effect of OEO and AgNp-Bio association on *L. amazonensis* and the death mechanisms of the parasite involved. Our results demonstrated a synergistic antileishmanial effect of OEO + AgNp on promastigote forms and *L. amazonensis*-infected macrophages, which induced morphological and ultrastructural changes in promastigotes. Subsequently, we investigated the mechanisms underlying parasite death and showed an increase in NO, ROS, mitochondrial depolarization, accumulation of lipid-storage bodies, autophagic vacuoles, phosphatidylserine exposure, and damage to the plasma membrane. Moreover, the association resulted in a reduction in the percentage of infected cells and the number of amastigotes per macrophage. In conclusion, our findings establish that OEO + AgNp elicits a late apoptosis-like mechanism to combat promastigote forms and promotes ROS and NO production in infected macrophages to target intracellular amastigote forms.

Structure of Leishmania donovani 6-Phosphogluconate Dehydrogenase and Inhibition by Phosphine Gold(I) Complexes: A Potential Approach to Leishmaniasis Treatment.

Berneburg I, Stumpf M, Velten AS, Rahlfs S, Przyborski J, Becker K, Fritz-Wolf K.
11-05-2023
Int J Mol Sci.
https://pubmed.ncbi.nlm.nih.gov/37239962/

As unicellular parasites are highly dependent on NADPH as a source for reducing equivalents, the main NADPH-producing enzymes glucose 6-phosphate dehydrogenase (G6PD) and 6-phosphogluconate dehydrogenase (6PGD) of the pentose phosphate pathway are considered promising antitrypanosomatid drug targets. Here we present the biochemical characterization and crystal structure of *Leishmania donovani* 6PGD (*Ld*6PGD) in complex with NADP(H). Most interestingly, a previously unknown conformation of NADPH is visible in this structure. In addition, we identified auranofin and other gold(I)-containing compounds as efficient *Ld*6PGD inhibitors, although it has so far been assumed that trypanothione reductase is the sole target of auranofin in *Kinetoplastida*. Interestingly, 6PGD from *Plasmodium falciparum* is also inhibited at lower micromolar concentrations, whereas human 6PGD is not. Mode-of-inhibition studies indicate that auranofin competes with 6PG for its binding site followed by a rapid irreversible inhibition. By analogy with other enzymes, this suggests that the gold moiety is responsible for the observed inhibition. Taken together, we identified gold(I)-containing

compounds as an interesting class of inhibitors against 6PGDs from *Leishmania* and possibly from other protozoan parasites. Together with the three-dimensional crystal structure, this provides a valid basis for further drug discovery approaches.

Thiophene-Derived Schiff Base Complexes: Synthesis, Characterization, Antimicrobial Properties, and Molecular Docking.

Nayab S, Alam A, Ahmad N, Khan SW, Khan W, Shams DF, Shah MIA, Ateeq M, Shah SK, Lee H.
12-05-2023
ACS Omega.
https://pubmed.ncbi.nlm.nih.gov/37251197/

Novel thiophene-derived Schiff base ligand **DE**, where **DE** is (*E*)-N^1,N^1-diethyl-N^2-(thiophen-2-ylmethylene)ethane-1,2-diamine, and the corresponding M(II) complexes, **[M(DE)X_2]** (M = Cu or Zn, X = Cl; M = Cd, X = Br), were prepared and structurally characterized. X-ray diffraction studies revealed that the geometry around the center of the M(II) complexes, **[Zn(DE)Cl_2]** and **[Cd(DE)Br_2]**, could be best described as a distorted tetrahedral. *In vitro* antimicrobial screening of **DE** and its corresponding M(II) complexes, **[M(DE)X_2]**, was performed. The complexes were more potent and showed higher activities against *Escherichia coli*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa*, fungi *Candida albicans*, and protozoa *Leishmania major* compared to the ligand. Among the studied complexes, **[Cd(DE)Br_2]** exhibited the most promising antimicrobial activity against all the tested microbes compared to its analogs. These results were further supported by molecular docking studies. We believe that these complexes may significantly contribute to the efficient designing of metal-derived agents to treat microbial infections.

Leishmania Animal Models Used in Drug Discovery: A Systematic Review.

van der Ende J, Schallig HDFH.
16-05-2023
Animals (Basel).
https://pubmed.ncbi.nlm.nih.gov/37238080/

Signalment, Immunological and Parasitological Status and Clinicopathological Findings of Leishmania-Seropositive Apparently Healthy Dogs.

Baxarias M, Jornet-Rius O, Donato G, Mateu C, Alcover MM, Pennisi MG, Solano-Gallego L.
16-05-2023
Animals (Basel).
https://pubmed.ncbi.nlm.nih.gov/37238079/

Leishmaniasis: Immune Cells Crosstalk in Macrophage Polarization.

Almeida FS, Vanderley SER, Comberlang FC, Andrade AG, Cavalcante-Silva LHA, Silva EDS, Palmeira PHS, Amaral IPGD, Keesen TSL.
15-05-2023
Trop Med Infect Dis.
https://pubmed.ncbi.nlm.nih.gov/37235324/

Leishmaniasis is a complex infectious parasitic disease caused by protozoa of the genus *Leishmania*, belonging to a group of neglected tropical diseases. It establishes significant global health challenges, particularly in socio-economically disadvantaged regions. Macrophages, as innate immune cells, play a crucial role in initiating the inflammatory response against the pathogens responsible for this disease. Macrophage polarization, the process of differentiating macrophages into pro-inflammatory (M1) or anti-inflammatory (M2) phenotypes, is essential for the immune response in leishmaniasis. The M1 phenotype is associated with resistance to *Leishmania* infection, while the M2 phenotype is predominant in susceptible environments. Notably, various immune cells, including T cells, play a significant role in modulating macrophage polarization by releasing cytokines that influence macrophage maturation and function. Furthermore, other immune cells can also impact macrophage polarization in a T-cell-independent manner. Therefore, this review comprehensively examines macrophage polarization's role in leishmaniasis and other immune cells' potential involvement in this intricate process.

Alternative Non-Drug Treatment Options of the Most Neglected Parasitic Disease Cutaneous Leishmaniasis: A Narrative Review.

Orabi MAA, Lahiq AA, Awadh AAA, Alshahrani MM, Abdel-Wahab BA, Abdel-Sattar ES.
14-05-2023
Trop Med Infect Dis.
https://pubmed.ncbi.nlm.nih.gov/37235323/

Gene Expression Profiling of Classically Activated Macrophages in Leishmania infantum Infection: Response to Metabolic Pre-Stimulus with Itaconic Acid.

Palacios G, Vega-García E, Valladares B, Pérez JA, Dorta-Guerra R, Carmelo E.
03-05-2023
Trop Med Infect Dis.
https://pubmed.ncbi.nlm.nih.gov/37235312/

Cysteine synthase: multiple structures of a key enzyme in cysteine synthesis and a potential drug target for Chagas disease and leishmaniasis.

Sowerby K, Freitag-Pohl S, Murillo AM, Silber AM, Pohl E.
01-06-2023
Acta Crystallogr D Struct Biol.
https://pubmed.ncbi.nlm.nih.gov/37204818/

Chagas disease is a neglected tropical disease (NTD) caused by Trypanosoma cruzi, whilst leishmaniasis, which is caused by over 20 species of Leishmania, represents a group of NTDs endemic to most countries in the tropical

and subtropical belt of the planet. These diseases remain a significant health problem both in endemic countries and globally. These parasites and other trypanosomatids, including T. theileri, a bovine pathogen, rely on cysteine biosynthesis for the production of trypanothione, which is essential for parasite survival in hosts. The de novo pathway of cysteine biosynthesis requires the conversion of O-acetyl-L-serine into L-cysteine, which is catalysed by cysteine synthase (CS). These enzymes present potential for drug development against T. cruzi, Leishmania spp. and T. theileri. To enable these possibilities, biochemical and crystallographic studies of CS from T. cruzi (TcCS), L. infantum (LiCS) and T. theileri (TthCS) were conducted. Crystal structures of the three enzymes were determined at resolutions of 1.80 Å for TcCS, 1.75 Å for LiCS and 2.75 Å for TthCS. These three homodimeric structures show the same overall fold and demonstrate that the active-site geometry is conserved, supporting a common reaction mechanism. Detailed structural analysis revealed reaction intermediates of the de novo pathway ranging from an apo structure of LiCS and holo structures of both TcCS and TthCS to the substrate-bound structure of TcCS. These structures will allow exploration of the active site for the design of novel inhibitors. Additionally, unexpected binding sites discovered at the dimer interface represent new potential for the development of protein-protein inhibitors.

Hit-to-lead optimization of a pyrazinylpiperazine series against Leishmania infantum and Leishmania braziliensis.

Jacques Dit Lapierre TJW, Cruz MGFML, Brito NPF, Resende DM, Souza FO, Pilau EJ, da Silva MFB, Neves BJ, Murta SMF, Rezende Júnior CO.
05-08-2023
Eur J Med Chem.
https://pubmed.ncbi.nlm.nih.gov/37156183/

Intracellular persistence of Leishmania tarentolae in primary canine macrophage cells.

Louzada-Flores VN, Latrofa MS, Lucente MS, Dambrós BP, Mendoza-Roldan JA, Varotto-Boccazzi I, Cattaneo GM, Späth GF, Buonavoglia A, Otranto D.
Juil-2023
Acta Trop.
https://pubmed.ncbi.nlm.nih.gov/37127215/

Molecular detection of Leishmania (Sauroleishmania) adleri (Trypanosomatida: Trypanosomatidae) in Sergentomyia sp. sand flies (Diptera: Psychodidae) in Mali and Niger.

Krüger A, Balczun C, Scheid PL, Hagen RM, Eisenbarth A.
Juil-2023
Acta Trop.
https://pubmed.ncbi.nlm.nih.gov/37127214/

Phlebotomine sand flies of the genus Sergentomyia are considered to be of minor importance as vectors of Leishmania parasites pathogenic to humans, but are known to transmit lizard parasites of the subgenus Sauroleishmania, including L. (S.) adleri. However, knowledge on the geographic distribution of Sauroleishmania spp. and the infection rates in the vectors is very limited. Therefore, our study aimed (1) to further elucidate the distribution and prevalence of Sauroleishmania spp. in their respective vectors and (2) to assess the potential risk for occasional transmission of Leishmania parasites to international military personnel deployed in camps in Mali and Niger. A total of 1,482 wild-caught sand flies (Sergentomyia spp. and closely related Grassomyia spp.) were screened by real-time PCR for the presence of Leishmania DNA. Thirty-two sand fly pools were tested positive, with six from Mali and 26 from Niger. The DNA of four representative isolates was sequenced. The resulting sequences revealed a homology to L. adleri, which leads to the first report of this species from Mali and Niger to the best of our knowledge. The results suggest that Sergentomyia (Sintonius) clydei might be the natural sand fly vector, while Grassomyia spp. appear to be refractory. No Leishmania sp. pathogenic to humans was detected in these sand flies.

Live attenuated Leishmania infantum centrin deleted mutant (LiCen$^{-/-}$) as a novel vaccine candidate: A field study on safety, immunogenicity, and efficacy against canine leishmaniasis.

Zarei Z, Mohebali M, Dehghani H, Khamesipour A, Tavakkol-Afshari J, Akhoundi B, Abbaszadeh-Afshar MJ, Alizadeh Z, Eskandari SE, Asl AD, Razmi GR.
Juin-2023
Comp Immunol Microbiol Infect Dis.
https://pubmed.ncbi.nlm.nih.gov/37119594/

This study was designed to evaluate the safety, immunogenicity, and efficacy of a single dose of L. infantum (LiCen$^{-/-}$) live attenuated candidate vaccine against canine leishmaniasis (CanL). Eighteen healthy domestic dogs with no anti-Leishmania antibodies and negative leishmanin skin test (LST) were randomly inoculated intravenously with either L. infantum (LiCen$^{-/-}$) vaccine candidate in 10 dogs or phosphate-buffered saline (PBS) in 8 dogs. The safety, immunogenicity, and efficacy rate of L. infantum (LiCen$^{-/-}$) vaccine candidate against CanL were evaluated by different criteria, including clinical manifestations, injection-site lesion, hematology and biochemistry values, anti-Leishmania antibodies using direct agglutination test (DAT), delayed-type hypersensitivity (DTH) using LST, and CD4$^+$ and CD8$^+$ T-cells subsets, as well as by measuring interferon (IFN-γ), interleukin (IL-23), IL-17, and IL-10 cytokines. Spleen aspiration and detection of Leishmania parasite using parasitological examinations (microscopy and culture) were performed in both vaccinated and control groups. Two months after intervention, each dog was challenged intraperitoneally (IP) with wide type (WT) L. infantum. Two-month follow-up post vaccination showed no clinical signs and serious side effects associated with the vaccination. A significant increase was found in the expression of IL-17, CD4$^+$, and CD8$^+$ gene transcripts in PBMCs, as well as increased levels of Th1 cytokines, and reduction of Th2 cytokine. The efficacy of the vaccine

candidate was calculated to be 42.85%. While the time window for assessing the vaccine's effectiveness was too limited to draw any real conclusions but the preliminary results showed a moderate efficacy rate due to inoculation a single dose of L. infantum (LiCen$^{-/-}$) vaccine candidate. Further investigations with more sample sizes and multiple doses of the vaccine candidate using natural challenges in the endemic areas of CanL are recommended.

MiniPCR as a portable equipment for the molecular diagnosis of american cutaneous leishmaniasis.

Castellanos-Gonzalez A, Cossio A, Jojoa J, Moen S, Travi BL.
Juil-2023
Acta Trop.
https://pubmed.ncbi.nlm.nih.gov/37088354/

Leishmaniasis: Omics Approaches to Understand its Biology from Molecule to Cell Level.

Kumari I, Lakhanpal D, Swargam S, Nath Jha A.
2023
Curr Protein Pept Sci.
https://pubmed.ncbi.nlm.nih.gov/36809951/

Leishmaniasis is the second deadliest vector-borne, neglected tropical zoonotic disease and is found in a variety of clinical forms based on genetic background. Its endemic type is present in tropical, sub-tropical and Mediterranean areas around the world which accounts for a lot of deaths every year. Currently, a variety of techniques are available for detection of leishmaniasis each technique having it's own pros and cons. The advancing next-generation sequencing (NGS) techniques are employed to find out novel diagnostic markers based on single nucleotide variants. A total of 274 NGS studies are available in European Nucleotide Archive (ENA) portal (https://www.ebi.ac.uk/ena/browser/home) that focused on wild-type and mutated Leishmania, differential gene expression, miRNA expression, and detection of aneuploidy mosaicism by omics approaches. These studies have provided insights into the population structure, virulence, and extensive structural variation, including known and suspected drug resistance loci, mosaic aneuploidy and hybrid formation under stressed conditions and inside the midgut of the sandfly. The complex interactions occurring within the parasite-host-vector triangle can be better understood by omics approaches. Further, advanced CRISPR technology allows researchers to delete and modify each gene individually to know the importance of genes in the virulence and survival of the disease-causing protozoa. In vitro generation of Leishmania hybrids are helping to understand the mechanism of disease progression in its different stages of infection. This review will give a comprehensive picture of the available omics data of various Leishmania spp. which helped to reveal the effect of climate change on the spread of its vector, the pathogen survival strategies, emerging antimicrobial resistance and its clinical importance.

Steroid and Triterpenoid Compounds with Antiparasitic Properties.

Kuzminac IZ, Savić MP, Ajduković JJ, Nikolić AR.
2023
Curr Top Med Chem.
https://pubmed.ncbi.nlm.nih.gov/36703585/

Lèpre

Self-reported clinical history of misdiagnosed leprosy cases in the State of Mato Grosso, Brzil, 2016-2019.

Neves KVRN, Machado LMG, Lisboa MN, Steinmann P, Ignotti E.
26-05-2023
Cad Saude Publica.
https://pubmed.ncbi.nlm.nih.gov/37255191/

This study aimed to analyze the self-reported clinical history of patients misdiagnosed with leprosy in the State of Mato Grosso, Brazil. This is a cross-sectional study of new leprosy cases diagnosed in the State of Mato Grosso from 2016 to 2019, with individuals who were released from multidrug therapy due to misdiagnosis after starting treatment. Data were collected via telephone interviews. Over the study period, 354 leprosy cases were released from treatment due to misdiagnosis, of which 162 (45.8%) could be interviewed. All interviewees expressed dissatisfaction with their treatment, which prompted them to seek a reevaluation of their diagnosis before they were released due to "misdiagnosis". Among them, 35.8% received a final diagnosis of a musculoskeletal or connective tissue disease - mainly fibromyalgia and degenerative changes in the spine - followed by 13.6% with diagnoses of skin and subcutaneous tissue diseases. For 23.5% of the respondents, no alternative diagnosis was established, whereas 7.4% were later re-diagnosed with leprosy. Fibromyalgia and spinal problems were the most common alternative diagnoses for erroneous leprosy. Although the diagnosis of leprosy is usually clinical and does not require access to technical infrastructure in most cases, some more complex situations require diagnostic support via complementary tests, as well as close collaboration between primary care and reference services.

Case Report: Necrotizing Erythema Nodosum as a Manifestation of Lepromatous Leprosy Relapse 50 Years after the Initial Infection.

Galeano J, Contreras A, Pabón L, Ruiz AC, Serrano-Coll H, Arboleda M.
30-05-2023
Am J Trop Med Hyg.
https://pubmed.ncbi.nlm.nih.gov/37253443/

Leprosy is a chronic infection caused by Mycobacterium leprae and Mycobacterium lepromatosis that preferentially compromises peripheral nerve, skin, and mucous membranes. Colombia achieved the goal of leprosy elimination in 1997. However, in Urabá (Colombia), there has been an increase in leprosy cases

beginning in 2020. This case report shows a leprosy relapse 5 decades after the initial infection debuted as a necrotizing erythema nodosum leprosum. Therefore, long-term follow-up of patients with risk factors for relapse is emphasized, especially those treated before the standard of multidrug therapy (dapsone, clofazimine, and rifampin). This case report stresses the importance the importance of clinical follow-up and surveillance of patients with these events of interest for the public health.

Barriers and Facilitators to Implementing a Digital Adherence Technology for Tuberculosis Treatment Supervision in Uganda: Qualitative Study.

Leddy A, Ggita J, Berger CA, Kityamuwesi A, Sanyu AN, Tinka LK, Crowder R, Turyahabwe S, Katamba A, Cattamanchi A.
30-05-2023
J Med Internet Res.
https://pubmed.ncbi.nlm.nih.gov/37252774/

A Case of Borderline Tuberculoid Leprosy With Type One Lepra Reaction.

Harikrishna GV, Ca J, Doddapaneni S, Bhat N, Bhanu P.
24-04-2023
Cureus.
https://pubmed.ncbi.nlm.nih.gov/37252606/

Leprosy is a chronic infectious disease caused by *Mycobacterium leprae*, which primarily affects the skin and peripheral nerves. The variants that can be identified include tuberculoid (TT), borderline tuberculoid (BT), mid-borderline (BB), borderline lepromatous (BL), and lepromatous forms (LL). Type one lepra reactions are delayed hypersensitivity reactions that are often observed in borderline variants due to an unstable immunological response. They can exacerbate skin lesions and neuritis, leading to a higher risk of disabilities and deformities. Early detection and management would play a major role in limiting morbidity. Here, we present a case of a 46-year-old male diagnosed with borderline tuberculoid leprosy on multidrug therapy who developed features suggestive of type one lepra reaction. Early recognition of this entity helps in mitigating the risk of permanent nerve damage, disability, deformity, and morbidity.

Post-COVID Quality of Life and Sleep Among Younger Healthcare Workers of Designated COVID Care Centers: A Cross-Sectional Study.

Ts P, Kk A, Bhavanam S, Mathew B.
27-04-2023
Cureus.
https://pubmed.ncbi.nlm.nih.gov/37252472/

Introduction Frontline healthcare workers (FLHCWs) have been persuaded to work this coronavirus disease (COVID) pandemic way in and out but the pandemic has not subsided. The persistence of symptoms after COVID infection, especially chest symptoms like early fatigue with breathlessness, has been documented very well. However, FLHCWs have repeatedly caught the COVID infection and have been working in traumatic and helpless situations since the pandemic started. Post-COVID infection, quality of life (QOL) and sleep are greatly affected, regardless of the time elapsed since discharge or recovery. The continuous assessment of COVID-infected persons for post-COVID sequelae is an important and effective step to reduce complications. Materials and methods This was a cross-sectional study conducted for a period of one year at R.L. Jalappa Hospital and Research Center, Kolar, and SNR District Hospital, Kolar, which were designated COVID care centers. FLHCWs working in these centers who had contracted COVID infection at least once, who were more than 18 years and less than 30 years, and who had experience of less than five years irrespective of their vaccination status were included in the study. FLHCWs with COVID-related health illnesses, which needed ICU admission and prolonged hospital admission, were excluded. To assess QOL, the WHO Quality of Life Brief Version (WHOQOL-BREF) questionnaire was used. To assess sleepiness, the Epworth daytime sleepiness scale was used. The study was started after the institutional ethical committee's clearance was obtained. Results A total of 201 healthcare workers (HCWs) completed the survey. Of the participants, 119 (59.2%) were male, 107 (53.2%) were junior residents, 134 (66.7%) were unmarried, and 171 (85.1%) said they followed regular shifts. Male HCWs had higher scores in the psychological, social relationship, and environmental domains of QoL. Consultants had higher scores in all domains of QoL. Married HCWs had higher scores in the physical, psychological, and social relationship domains of QoL. Out of 201 FLHCWs, 67 (33.3%) had moderate excessive daytime sleep, and 25 (12.4%) had severe excessive daytime sleep. Few factors like gender, occupation, duration of work in the hospital, and regular shifts were statistically significant factors associated with daytime sleepiness. Conclusion The present study has shown that even after the COVID vaccination doses received by the HCWs, sleep and Qol have still been impaired among infected younger healthcare staff. Acceptable and righteous efforts must be made by the institutions for proper policymaking to manage such infectious outbreaks in the future.

Children deserve simple, short, safe, and effective treatment for rifampicin-resistant tuberculosis.

Garcia-Prats AJ, Hoddinott G, Howell P, Hughes J, Jean-Philippe P, Kim S, Palmer M, Schaaf HS, Seddon JA, Svensson E, Hesseling AC.
25-05-2023
Lancet Infect Dis.
https://pubmed.ncbi.nlm.nih.gov/37245523/

Temporal trend, high-risk spatial and spatiotemporal clustering of leprosy indicators in Brazil: A 20-year ecological and population-based study.

Paz WS, Ramos RES, Bezerra LP, Matos DF, Tavares DS, Souza CDF, Bezerra-Santos M, Ximenes RAA.

27-05-2023
Trop Med Int Health.
https://pubmed.ncbi.nlm.nih.gov/37243431/

Objectives: Leprosy still represents a public health concern in Brazil. The country is the only one in America not to reach the global goal of leprosy disease control. Hence, this study aimed to assess the temporal, spatial and space-time patterns of leprosy cases in Brazil of the 20-year time series 2001-2020. Methods: An ecological and population-based analysis was carried out, applying temporal and spatial techniques, and using the detection coefficient of sociodemographic and clinical-epidemiological variables of leprosy new cases in the 5570 municipalities of Brazil. Temporal trends were assessed using a segmented linear regression model. For spatial analysis, global and local Moran indexes were applied, and space-time scan statistics was used to identify risk clusters. Results: The mean detection coefficient was 19.36/100,000 inhabitants, with a higher occurrence among men (21.29/100,000 inhabitants) and in the 60-69 age group (36.31/100,000). A decreasing temporal trend was observed in the country (annual percentage change: -5.20% per year). The North and Midwest regions were the most affected, exhibiting municipalities with a high/high standard, and with the highest annual percentage increase of multibacillary (MB) cases. Leprosy has a heterogeneous distribution throughout Brazil, but with high-risk spatiotemporal clusters, mainly located in the North and Midwest regions. Conclusion: Although Brazil has shown a decreasing temporal trend during the past 20 years, the country is still classified as highly endemic for leprosy, showing an increase in the proportion of new MB cases over the years.

Anti-Adipogenic Activity of Secondary Metabolites Isolated from Smilax sieboldii Miq. on 3T3-L1 Adipocytes.

Jung YW, Lee JA, Lee JE, Cha H, Choi YH, Jeong W, Choi CW, Oh JS, Ahn EK, Hong SS.
16-05-2023
Int J Mol Sci.
https://pubmed.ncbi.nlm.nih.gov/37240212/

Mycobacterium leprae's Infective Capacity Is Associated with Activation of Genes Involved in PGL-I Biosynthesis in a Schwann Cells Infection Model.

Chavarro-Portillo B, Soto CY, Guerrero MI.
13-05-2023
Int J Mol Sci.
https://pubmed.ncbi.nlm.nih.gov/37240073/

Peripheral nerves and Schwann cells (SCs) are privileged and protected sites for initial colonization, survival, and spread of leprosy bacillus. *Mycobacterium leprae* strains that survive multidrug therapy show a metabolic inactivation that subsequently induces the recurrence of typical clinical manifestations of leprosy. Furthermore, the role of the cell wall phenolic glycolipid I (PGL-I) in the *M. leprae* internalization in SCs and the pathogenicity of *M. leprae* have been extensively known. This study assessed the infectivity in SCs of recurrent and non-recurrent *M. leprae* and their possible correlation with the genes involved in the PGL-I biosynthesis. The initial infectivity of non-recurrent strains in SCs was greater (27%) than a recurrent strain (6.5%). In addition, as the trials progressed, the infectivity of the recurrent and non-recurrent strains increased 2.5- and 2.0-fold, respectively; however, the maximum infectivity was displayed by non-recurrent strains at 12 days post-infection. On the other hand, qRT-PCR experiments showed that the transcription of key genes involved in PGL-I biosynthesis in non-recurrent strains was higher and faster (Day 3) than observed in the recurrent strain (Day 7). Thus, the results indicate that the capacity of PGL-I production is diminished in the recurrent strain, possibly affecting the infective capacity of these strains previously subjected to multidrug therapy. The present work opens the need to address more extensive and in-depth studies of the analysis of markers in the clinical isolates that indicate a possible future recurrence.

Effectiveness and safety of multidrug therapy containing clofazimine for paucibacillary leprosy and clarithromycin for rifampicin-resistant leprosy: a systematic review and meta-analysis.

Montezuma T, Vernal S, Andrade EN, Brandão JG, de Oliveira GLA, Gomes CM.
10-05-2023
Front Med (Lausanne).
https://pubmed.ncbi.nlm.nih.gov/37234244/

Introduction: The present study aimed to evaluate leprosy cure and relapse rates as primary outcomes related to two additional strategies for leprosy treatment: clofazimine for paucibacillary (PB) leprosy patients and clarithromycin for patients with rifampicin-resistant leprosy. Methods: We conducted two systematic reviews (protocols CRD42022308272 and CRD42022308260). We searched the PubMed, EMBASE, Web of Science, Scopus, LILACS, Virtual Health Library and Cochrane Library databases, registers of clinical trial databases and gray literature. We included clinical trials evaluating the addition of clofazimine to PB leprosy treatment and the use of clarithromycin for treating patients with rifampicin-resistant leprosy. Risk of bias (RoB) in randomized clinical trials was assessed by the RoB 2 tool and that in non-randomized clinical trials was assessed by the ROBINS-I tool; and the certainty of the evidence was assessed by the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system. A meta-analysis of dichotomous outcomes was performed. Results: For clofazimine, four studies were included. Cure and relapse rates were not different with the addition of clofazimine to PB leprosy treatment and demonstrated very low certainty of evidence. For clarithromycin, six studies were included. Considerable heterogeneity resulted from the difference between comparators, and studies showed no difference in the assessed outcomes with the addition of clarithromycin to rifampicin-resistant leprosy treatment. Mild adverse events were reported for both drugs but did not significantly impact treatment. Discussion: The effectiveness of both drugs still needs to be determined.

Adding clofazimine to PB leprosy treatment may reduce the repercussions of an incorrect operational classification with no apparent relevant side effects.

Live attenuated Leishmania infantum centrin deleted mutant (LiCen-/-) as a novel vaccine candidate: A field study on safety, immunogenicity, and efficacy against canine leishmaniasis.

Zarei Z, Mohebali M, Dehghani H, Khamesipour A, Tavakkol-Afshari J, Akhoundi B, Abbaszadeh-Afshar MJ, Alizadeh Z, Eskandari SE, Asl AD, Razmi GR.
Juin-2023
Comp Immunol Microbiol Infect Dis.
https://pubmed.ncbi.nlm.nih.gov/37119594/

Immunogenicity and protective efficacy of an inactivated Newcastle disease virus vaccine encapsulated in poly-(lactic-co-glycolic acid) nanoparticles.

Ananda Kumar BS, Panickan S, Bindu S, Kumar V, Ramakrishnan S, Saxena S, Shrivastava S, Dandapat S.
Juin-2023
Poult Sci.
https://pubmed.ncbi.nlm.nih.gov/37116285/

$CD11b^{+}Gr\text{-}1^{low}$ cells that accumulate in M.leprae-induced granulomas of the footpad skin of nude mice have the characteristics of monocytic-myeloid-derived suppressor cells.

Jin SH, Lee SB.
Mai-2023
Tuberculosis (Edinb).
https://pubmed.ncbi.nlm.nih.gov/37116235/

$CD11b^{+}Gr\text{-}1^{low}$ cells that are increased in the lungs of a Mycobacterium (M) tuberculosis-infection mouse model have the characteristics of monocytic (M)-myeloid-derived suppressor cells (MDSCs) and harbor M.tuberculosis. Interestingly, a high number of M-MDSCs have also been observed in skin lesions of patients with lepromatous leprosy. We hypothesized that $CD11b^{+}Gr\text{-}1^{low}$ cells might be involved in the pathogenesis of leprosy, as they are in tuberculosis. In the current study, we investigated the issue of whether $CD11b^{+}Gr\text{-}1^{low}$ cells accumulate in Mycobacterium (M) leprae-induced granulomas of the footpad skin of nude mice. Our results show that $CD11b^{+}Gr\text{-}1^{low}$ cells began to accumulate in the 7-month-old M.leprae-induced granulomas and were replaced by other leukocytes, including $CD11b^{+}Gr\text{-}1^{high}$ over time during M.leprae infections. $CD11b^{+}Gr\text{-}1^{low}$ cells expressed the surface markers of M-MDSC, $Ly6C^{high}$ and $Ly6G^{low}$. In addition, $CD11b^{+}Gr\text{-}1^{low}$ cells have the nuclei of a mononuclear cell type and expressed higher levels of arginase 1 (Arg1) and inducible NO synthetase (iNOS). Furthermore, they showed a higher infection rate by M.leprae. Taken together, our results indicate that the inoculation with M.leprae induced an accumulation of $CD11b^{+}Gr\text{-}1^{low}$ at a relatively early stage, 7-month-old M.leprae-induced granulomas, and that $CD11b^{+}Gr\text{-}1^{low}$ have the characteristics of M-MDSC and may act as a reservoir for M.leprae.

Thalidomide interaction with inflammation in idiopathic pulmonary fibrosis.

Dsouza NN, Alampady V, Baby K, Maity S, Byregowda BH, Nayak Y.
Juin-2023
Inflammopharmacology.
https://pubmed.ncbi.nlm.nih.gov/36966238/

The "Thalidomide tragedy" is a landmark in the history of the pharmaceutical industry. Despite limited clinical trials, there is a continuous effort to investigate thalidomide as a drug for cancer and inflammatory diseases such as rheumatoid arthritis, lepromatous leprosy, and COVID-19. This review focuses on the possibilities of targeting inflammation by repurposing thalidomide for the treatment of idiopathic pulmonary fibrosis (IPF). Articles were searched from the Scopus database, sorted, and selected articles were reviewed. The content includes the proven mechanisms of action of thalidomide relevant to IPF. Inflammation, oxidative stress, and epigenetic mechanisms are major pathogenic factors in IPF. Transforming growth factor-β (TGF-β) is the major biomarker of IPF. Thalidomide is an effective anti-inflammatory drug in inhibiting TGF-β, interleukins (IL-6 and IL-1β), and tumour necrosis factor-α (TNF-α). Thalidomide binds cereblon, a process that is involved in the proposed mechanism in specific cancers such as breast cancer, colon cancer, multiple myeloma, and lung cancer. Cereblon is involved in activating AMP-activated protein kinase (AMPK)-TGF-β/Smad signalling, thereby attenuating fibrosis. The past few years have witnessed an improvement in the identification of biomarkers and diagnostic technologies in respiratory diseases, partly because of the COVID-19 pandemic. Hence, investment in clinical trials with a systematic plan can help repurpose thalidomide for pulmonary fibrosis.

Morsures de serpent

A retrospective analysis of epidemiology, clinical features of envenomation, and in-patient management of snakebites in a model secondary hospital of Assam, North-east India.

Kakati H, Giri S, Patra A, Taye SJ, Agarwalla D, Baruah H, Choudhary G, Kalita B, K Mukherjee A.
29-05-2023
Toxicon.
https://pubmed.ncbi.nlm.nih.gov/37257518/

Assam, a Northeastern State of India, is inhabited by several venomous snake species causing substantial morbidity and mortality. The data on the epidemiology of snakebites and their management is underreported in this region. Hence, a secondary health-based retrospective study was carried out at Demow Model Hospital, Sivasagar, Assam, to evaluate the clinical and epidemiological profile of snakebite cases reported in this

rural hospital and their management. Snakebites occurring between April 2018 to August 2022 were reviewed based on socio-demographic details of the patient, clinical symptoms, and treatment using a standard questionnaire. Out of the 1011 registered snakebite cases, 139 patients (13.7%) counted for venomous bites, among which 92 patients (66.19%) accounted for viper bites (green pit viper and Salazar's pit viper), and 30 patients (21.5%) were bitten by elapid snakes (Indian monocled Cobra, banded krait, and greater/lesser black krait). A maximum number of snakebite cases (80.5%) were reported from the interior rural villages and documented from July to September (51.3%). Elapid snake envenomed patients, except one, were successfully treated with commercial antivenom, neostigmine, and glycopyrrolate. Because commercial polyvalent antivenom against "Big Four" venomous snakes of India showed poor neutralization of pit-vipers envenomation; therefore, pit-viper bite patients were treated with repurposed drugs magnesium sulfate and glycerin compression dressing. Adverse serum reactions were reported only in 3 (11.1%) cases. The preventive measures and facilities adopted at the Demow Model Hospital significantly reduce snakebite death and morbidity; therefore, they can be s practised across various states in India as a prototype.

Acute Demyelination Following Snake Bite - An Unusual Complication.

Kalpana S, Ravi S, Muthu T.
30-05-2023
Indian J Pediatr.
https://pubmed.ncbi.nlm.nih.gov/37249832/

Compliance with national snakebite treatment guidelines in rural Sri Lankan hospitals: a cluster randomized controlled trial of a brief educational intervention.

Shahmy S, Kularatne SAM, Gawarammana IB, Rathnayake SS, Dawson AH.
27-05-2023
BMC Med Educ.
https://pubmed.ncbi.nlm.nih.gov/37245040/

Background: Snakebite is a global health problem that predominantly occurs in rural areas. In Sri Lanka, the majority of snakebite patients first present to smaller rural primary hospitals. Improving care delivered at rural hospitals has the potential to reduce morbidity and mortality from snakebites. Objective: In this study, we evaluated whether an educational intervention would increase compliance with national snakebite treatment guidelines in primary hospitals. Methods: The hospitals were randomized into educational intervention (n = 24) and control groups (n = 20). The intervention hospitals received a brief educational intervention based on Sri Lankan Medical Association (SLMA) guidelines on the management of snakebites. Control hospitals had free access to the guidelines but no additional promotion. Four outcomes were assessed: pre- and post-test knowledge at the completion of a one-day workshop of educational intervention (intervention group only); improvement in the quality of the patient's medical records; appropriateness of transfers to higher hospitals; and quality of overall management graded by a blinded expert. The data was collected over a period of 12 months. Results: All case notes of snakebite hospital admissions were reviewed. There were 1021 cases in the intervention group hospitals and 1165 cases in the control hospitals. Four hospitals in the intervention group and three hospitals in the control group did not have snakebite admissions and were excluded from the cluster analysis. The absolute quality of care was high in both groups. Post-test knowledge was improved ($p < 0.0001$) following the intervention group's educational workshop. There was no statistical difference between the two groups in terms of clinical data documentation in hospital notes (scores, $p = 0.58$) or transfer appropriateness ($p = 0.68$)-both of which were significantly different from the guidelines. Conclusion: Education of primary hospital staff improved the immediate knowledge gained but did not improve record-keeping or the appropriateness of inter-hospital patient transfer.

Prospecting Local Treatments Used in Conjunction with Antivenom Administration Following Envenomation Caused by Animals: A Systematic Review.

Carvalho ÉS, Oliveira I, Nascimento TP, da Silva Neto AV, Leal BAS, Araújo FQ, Julião BFV, Souza ARN, Abrahim AW, Macedo BBO, de Oliveira JTS, Wen FH, Pucca MB, Monteiro WM, Sachett JAG.
28-04-2023
Toxins (Basel).
https://pubmed.ncbi.nlm.nih.gov/37235348/

Envenomation caused by venomous animals may trigger significant local complications such as pain, edema, localized hemorrhage, and tissue necrosis, in addition to complications such as dermonecrosis, myonecrosis, and even amputations. This systematic review aims to evaluate scientific evidence on therapies used to target local effects caused by envenomation. The PubMed, MEDLINE, and LILACS databases were used to perform a literature search on the topic. The review was based on studies that cited procedures performed on local injuries following envenomation with the aim of being an adjuvant therapeutic strategy. The literature regarding local treatments used following envenomation reports the use of several alternative methods and/or therapies. The venomous animals found in the search were snakes (82.05%), insects (2.56%), spiders (2.56%), scorpions (2.56%), and others (jellyfish, centipede, sea urchin-10.26%). In regard to the treatments, the use of tourniquets, corticosteroids, antihistamines, and cryotherapy is questionable, as well as the use of plants and oils. Low-intensity lasers stand out as a possible therapeutic tool for these injuries. Local complications can progress to serious conditions and may result in physical disabilities and sequelae. This study compiled information on adjuvant therapeutic measures and underscores the importance of more robust scientific evidence for recommendations that act on local effects together with the antivenom.

Exploring Toxin Genes of Myanmar Russell's Viper, Daboia siamensis, through De Novo Venom Gland Transcriptomics.

Yee KT, Macrander J, Vasieva O, Rojnuckarin P.
26-04-2023
Toxins (Basel).
https://pubmed.ncbi.nlm.nih.gov/37235344/

Occupational Hazards Faced by Inland Fishers of Odisha State, India.

Prusty S, Sharma A.
Juil-2023
J Agromedicine.
https://pubmed.ncbi.nlm.nih.gov/36786390/

Onchocercose

Biting midges (Diptera: Ceratopogonidae) as putative vectors of zoonotic Onchocerca lupi (Nematoda: Onchocercidae) in northern Arizona and New Mexico, southwestern United States.

Roe CC, Holiday O, Upshaw-Bia K, Benally G, Williamson CHD, Urbanz J, Verocai GG, Ridenour CL, Nottingham R, Ford MA, Lake DP, Kennedy TA, Hepp CM, Sahl JW.
15-05-2023
Front Vet Sci.
https://pubmed.ncbi.nlm.nih.gov/37256003/

Onchocerca lupi (Rodonaja, 1967) is an understudied, vector-borne, filarioid nematode that causes ocular onchocercosis in dogs, cats, coyotes, wolves, and is also capable of infecting humans. Onchocercosis in dogs has been reported with increasing incidence worldwide. However, despite the growing number of reports describing canine *O. lupi* cases as well as zoonotic infections globally, the disease prevalence in endemic areas and vector species of this parasite remains largely unknown. Here, our study aimed to identify the occurrence of *O. lupi* infected dogs in northern Arizona, New Mexico, and Utah, United States and identify the vector of this nematode. A total of 532 skin samples from randomly selected companion animals with known geographic locations within the Navajo Reservation were collected and molecularly surveyed by PCR for the presence of *O. lupi* DNA (September 2019-June 2022) using previously published nematode primers (COI) and DNA sequencing. *O. lupi* DNA was detected in 50 (9.4%) sampled animals throughout the reservation. Using positive animal samples to target geographic locations, pointed hematophagous insect trapping was performed to identify potential *O. lupi* vectors. Out of 1,922 insects screened, 38 individual insects and 19 insect pools tested positive for the presence of *O. lupi,* all of which belong to the Diptera family. This increased surveillance of definitive host and biological vector/intermediate host is the first large scale prevalence study of *O. lupi* in companion animals in an endemic area of the United States, and identified an overall prevalence of 9.4% in companion animals as well as multiple likely biological vector and putative vector species in the southwestern United States. Furthermore, the identification of these putative vectors in close proximity to human populations coupled with multiple, local zoonotic cases highlight the One Health importance of *O. lupi*.

In vitro nematocidal potential of hydro-ethanolic and aqueous extracts of Calotropis procera (Aiton) W.T. Aiton, 1811 (Apocynaceae) and Faidherbia albida (Delile) A. Chev., 1934 (Fabacae) against Onchocerca ochengi and Caenorhabditiselegans.

Mamat A, Lame Y, Sabine Adeline FY, Yvette N, Ndode Herman ON, Arnold Roger BN, Dieudonné N.
18-05-2023
Heliyon.
https://pubmed.ncbi.nlm.nih.gov/37251817/

Onchocerciasis-associated epilepsy in Maridi, South Sudan: Modelling and exploring the impact of control measures against river blindness.

Bhattacharyya S, Vinkeles Melchers NVS, Siewe Fodjo JN, Vutha A, Coffeng LE, Logora MY, Colebunders R, Stolk WA.
25-05-2023
PLoS Negl Trop Dis.
https://pubmed.ncbi.nlm.nih.gov/37235598/

Background: Onchocerciasis, also known as "river blindness", is caused by the bite of infected female blackflies (genus Simuliidae) that transmit the parasite Onchocerca volvulus. A high onchocerciasis microfarial load increases the risk to develop epilepsy in children between the ages of 3 and 18 years. In resource-limited settings in Africa where onchocerciasis has been poorly controlled, high numbers of onchocerciasis-associated epilepsy (OAE) are reported. We use mathematical modeling to predict the impact of onchocerciasis control strategies on the incidence and prevalence of OAE. Methodology: We developed an OAE model within the well-established mathematical modelling framework ONCHOSIM. Using Latin-Hypercube Sampling (LHS), and grid search technique, we quantified transmission and disease parameters using OAE data from Maridi County, an onchocerciasis endemic area, in southern Republic of South Sudan. Using ONCHOSIM, we predicted the impact of ivermectin mass drug administration (MDA) and vector control on the epidemiology of OAE in Maridi. Principal findings: The model estimated an OAE prevalence of 4.1% in Maridi County, close to the 3.7% OAE prevalence reported in field studies. The OAE incidence is expected to rapidly decrease by >50% within the first five years of implementing annual MDA with good coverage (≥70%). With vector control at a high efficacy level (around 80% reduction of blackfly biting rates) as the sole strategy, the reduction is slower, requiring about 10 years to halve the OAE incidence. Increasing the efficacy levels of vector control, and implementing vector control simultaneously with MDA, yielded better results in preventing new cases

of OAE. **Conclusions/significances:** Our modeling study demonstrates that intensifying onchocerciasis eradication efforts could substantially reduce OAE incidence and prevalence in endemic foci. Our model may be useful for optimizing OAE control strategies.

Rage

Dog bite injuries in children seen at a tertiary care hospital in Bolivia.

Copana-Olmos R, Calderón-López ME, Jove-Veizaga A, Ochoa-Ledezma E, Gómez-Rocabado JA, Agui-Santivañez N, Ledezma-Hurtado BW, García-Delgadillo MR.
22-06-2023
Arch Argent Pediatr.
https://pubmed.ncbi.nlm.nih.gov/37261932/

Introduction. The objective of this study is to describe the characteristics of dog bite injuries in children seen at a children's hospital in Bolivia. Population and methods. This was an observational, retrospective study in patients seen between 2017 and 2021. Results. A total of 769 patients were studied. Dog bite injuries accounted for 5.6% of emergency visits and 0.8% of hospitalizations. They were more frequent in children younger than 5 years (55.1%), in whom the following were observed: greater injury severity ($p = 0.008$), history of animal provocation ($p = 0.048$), known attacking animal ($p < 0.036$), domestic accident ($p = 0.021$), greater frequency of post-exposure prophylaxis with anti-rabies serum ($p = 0.005$), and maxillofacial area as the main region involved ($p < 0.001$). There were 3 deaths due to human rabies and 1 due to hypovolemic shock. Conclusion. Dog bite injuries are a frequent cause of visit to the emergency department and hospitalization in pediatrics and have specific characteristics in children younger than 5 years.

Monoclonal antibodies for prophylaxis and therapy of respiratory syncytial virus, SARS-CoV-2, human immunodeficiency virus, rabies and bacterial infections: an update from the World Association of Infectious Diseases and Immunological Disorders and the Italian Society of Antinfective Therapy.

Esposito S, Amirthalingam G, Bassetti M, Blasi F, De Rosa FG, Halasa NB, Hung I, Osterhaus A, Tan T, Torres JP, Vena A, Principi N.
15-05-2023
Front Immunol.
https://pubmed.ncbi.nlm.nih.gov/37256125/

Rabies in a postpandemic world: resilient reservoirs, redoubtable riposte, recurrent roadblocks, and resolute recidivism.

Rupprecht CE, Mshelbwala PP, Reeves RG, Kuzmin IV.
2023
Anim Dis.
https://pubmed.ncbi.nlm.nih.gov/37252063/

Rabies virus-based labeling of layer 6 corticothalamic neurons for two-photon imaging in vivo.

Gu M, Li X, Liang S, Zhu J, Sun P, He Y, Yu H, Li R, Zhou Z, Lyu J, Li SC, Budinger E, Zhou Y, Jia H, Zhang J, Chen X.
08-04-2023
iScience.
https://pubmed.ncbi.nlm.nih.gov/37250327/

Neocortical layer 6 (L6) is less understood than other more superficial layers, largely owing to limitations of performing high-resolution investigations *in vivo*. Here, we show that labeling with the Challenge Virus Standard (CVS) rabies virus strain enables high-quality imaging of L6 neurons by conventional two-photon microscopes. CVS virus injection into the medial geniculate body can selectively label L6 neurons in the auditory cortex. Only three days after injection, dendrites and cell bodies of L6 neurons could be imaged across all cortical layers. Ca^{2+} imaging in awake mice showed that sound stimulation evokes neuronal responses from cell bodies with minimal contamination from neuropil signals. In addition, dendritic Ca^{2+} imaging revealed significant responses from spines and trunks across all layers. These results demonstrate a reliable method capable of rapid, high-quality labeling of L6 neurons that can be readily extended to other brain regions.

Safety and immunogenicity of rabies vaccine (PVRV-WIBP) in healthy Chinese aged 10-50 years old: Randomized, blinded, parallel controlled phase III clinical study.

Huang X, Liang J, Huang L, Nian X, Chen W, Zhang J, Xu X, Lin X, Wang Y, Shi J, Jia L, Li Q, Wang Q, Duan K, Li X, Ji Y, Peng F, Zhang W, Xie Z, Wang Y, Yang X.
30-05-2023
Hum Vaccin Immunother.
https://pubmed.ncbi.nlm.nih.gov/37249318/

This phase III clinical trial aimed to assess the safety and demonstrate the immunogenicity of a candidate freeze-dried purified Vero cell-based rabies vaccine (PVRV-WIBP) developed for human use. A cohort of 40 participants in stage 1 and 1956 subjects in stage 2 with an age range of 10-50 years were recruited for the phase III clinical trial. For safety analysis in stage 1, 20 participants received either 4-dose or 5-dose regimen of PVRV-WIBP. In stage 2, 1956 subjects were randomly divided into the 5-dose PVRV-WIBP, 5-dose PVRV-LNCD, and 4-dose PVRV-WIBP groups. The serum neutralizing antibody titer against rabies was determined on day 7 or 14 and day 35 or 42. Adverse reactions were recorded for more than 6 months. Most adverse reactions, which were mild and moderate in severity, occurred and resolved within 1 week after each injection in the PVRV-WIBP (4 and 5 doses) and PVRV-LNCD (5 doses) groups. All three groups achieved complete seroconversion 14 days after the initial dose and 14 days after completing the full vaccination schedule, the susceptible subjects in the PVRV-WIBP group (4-dose or 5-dose regimen) displayed higher neutralizing antibody

titers against the rabies virus compared to those in the PVRV-LNCD group (5-dose regimen). PVRV-WIBP induced non-inferior immune responses versus PVRV-LNCD as assessed by seroconversion rate. PVRV-WIBP was well tolerated and non-inferior to PVRV-LNCD in healthy individuals aged 10-50 years. The results indicated that PVRV-WIBP (both 4- and 5-dose schedules) could be an alternative to rabies post-exposure prophylaxis.

Fabrication of Pulsatile Polymeric Microparticles Encapsulating Rabies Antigen.

Graf TP, Kadasia K, Melhorn S, Kessler E, Yang H, Baryakova T, Brady S, McHugh KJ.
12-05-2023
J Vis Exp.
https://pubmed.ncbi.nlm.nih.gov/37246855/

Decline in rabies cases in international travelers during the COVID-19 pandemic.

Gautret P.
26-05-2023
Travel Med Infect Dis.
https://pubmed.ncbi.nlm.nih.gov/37245851/

Rabies Post-Exposure Prophylaxis, What the U.S. Emergency Medicine Provider Needs to Know.

Gibbons K, Dvoracek K.
27-05-2023
Acad Emerg Med.
https://pubmed.ncbi.nlm.nih.gov/37245074/

Approximately 55,000 patients per year in the United States are exposed to potentially rabid animals and receive rabies post-exposure prophylaxis (PEP) and these patients commonly present to the emergency department for wound care and PEP. Despite the number of rabies exposures seen in emergency departments each year, there appears to be a knowledge gap among healthcare providers with regard to prescribing and administering rabies PEP. The following review aims to bridge that knowledge gap by discussing the importance of obtaining a comprehensive exposure history to determine the category of the encounter, the type of animal, the location of the bite, and outside expert resources to determine whether the rabies PEP series is indicated. In addition, this article will discuss dosing, administration and schedule of the rabies vaccine and human rabies immune globulin to ensure patients are fully protected from developing rabies. Lastly, this article discusses the potential cost associated with rabies PEP and provides information on managing this barrier.

Retrospective phylogenetic analysis of rabies virus G and N genes from Serbia.

Milićević V, Glišić D, Veljović L, Maletić J, Kureljušić B.
26-05-2023
Zoonoses Public Health.
https://pubmed.ncbi.nlm.nih.gov/37243392/

Potency of Veterinary Rabies Vaccines Marketed in Sri Lanka.

Rathnadiwakara H, Gunatilake M, Servat A, Wasniewski M, Thibault JC, Cliquet F.
09-05-2023
Vaccines (Basel).
https://pubmed.ncbi.nlm.nih.gov/37243065/

Seven brands of veterinary rabies vaccines are commercially available in Sri Lanka, but there is no established procedure to test the potency of the vaccines at the local level, especially prior to their release. The aim of this study was to test the potency of these vaccines using a mouse challenge test in collaboration with the EU/WOAH/WHO Reference Laboratory for Rabies, ANSES-Nancy, France. Based on the European Pharmacopoeia, the inactivated rabies vaccines complied with the mouse potency test if the estimated potency is ≥1.0 IU in the smallest prescribed dose. Among the eight tested vaccines, four single-dose preparations (Rabisin™, Raksharab™, Nobivac™ RL, and Nobivac™ Rabies) were compliant, with potencies of 12 IU/dose, 7.2 IU/dose, 4.4 IU/dose, and 3.4 IU/dose, respectively. Three of the single-dose preparations (Canvac™ R, Defensor™ 3, and Rabies killed vaccine) were not compliant, with potency values <1.0 IU/dose. One multidose preparation (Raksharab™ multidose) had a potency of 1.3 IU/dose, even though the test was not validated. Based on these results, it appears that some rabies vaccine batches that are currently available in the local market do not comply with the mouse potency test. Testing the vaccines' potency before registration and release to the market appears to be an important step to allow good immunization to animals during pre-exposure vaccination programs.

Communication Interventions and Assessment of Drivers for Hendra Virus Vaccination Uptake.

Kropich-Grant JN, Wiley KE, Manyweathers J, Thompson KR, Brookes VJ.
04-05-2023
Vaccines (Basel).
https://pubmed.ncbi.nlm.nih.gov/37243040/

Hendra virus disease (HeVD) is an emerging zoonosis in Australia, resulting from the transmission of Hendra virus (HeV) to horses from *Pteropus* bats. Vaccine uptake for horses is low despite the high case fatality rate of HeVD in both horses and people. We reviewed evidence-based communication interventions to promote and improve HeV vaccine uptake for horses by horse owners and conducted a preliminary evaluation of potential drivers for HeV vaccine uptake using the Behavioural and Social Drivers of Vaccination (BeSD) framework developed by the World Health Organization. Six records were eligible for review following a comprehensive search and review strategy of peer-reviewed literature, but evidence-based communication interventions to promote and improve HeV vaccine uptake for horses were lacking. An evaluation of potential drivers for HeV vaccine uptake using the BeSD framework indicated that horse owners' perceptions, beliefs, social processes, and practical issues are similar to those experienced by parents making decisions about

childhood vaccines, although the overall motivation to vaccinate is lower amongst horse owners. Some aspects of HeV vaccine uptake are not accounted for in the BeSD framework (for example, alternative mitigation strategies such as covered feeding stations or the zoonotic risk of HeV). Overall, problems associated with HeV vaccine uptake appear well-documented. We, therefore, propose to move from a problems-focused to a solutions-focused approach to reduce the risk of HeV for humans and horses. Following our findings, we suggest that the BeSD framework could be modified and used to develop and evaluate communication interventions to promote and improve HeV vaccine uptake by horse owners, which could have a global application to promote vaccine uptake for other zoonotic diseases in animals, such as rabies.

Assessment of Immune Responses to Rabies Vaccination in Free-Ranging Dogs in Bengaluru, India.

Prakash Rao VC, Ramakrishnaiah S, Isloor S, Doddamane R, Lakshman D, Maralavadi MSSR, Bhat A, Chandrashekar B, Natesan K, Kondabattula G, Hegde NR.
24-04-2023
Vaccines (Basel).
https://pubmed.ncbi.nlm.nih.gov/37242992/

Comparative Evaluation of Intradermal vis-à-vis Intramuscular Pre-Exposure Prophylactic Vaccination against Rabies in Cattle.

Gopalaiah S, Appaiah KM, Isloor S, Lakshman D, Thimmaiah RP, Rao S, Gouri M, Kumar N, Govindaiah K, Bhat A, Tiwari S.
23-04-2023
Vaccines (Basel).
https://pubmed.ncbi.nlm.nih.gov/37242989/

Rabies is a progressively fatal viral disease affecting a wide variety of warm-blooded animals and human beings. With cattle being major part of Indian livestock population, rabies can result in significant financial losses. Immunization of livestock vulnerable to exposure is the best way to control rabies. The present study was undertaken to investigate the efficacy of a rabies pre-exposure prophylactic vaccine administered through different routes and to sequentially monitor the levels of rabies virus-neutralizing antibody (RVNA) titers in cattle. Thirty cattle were divided into five groups of six animals each. Group I and III animals were immunized with 1 mL and 0.2 mL of rabies vaccine through intramuscular (IM) and intradermal (ID) routes, respectively, on day 0, with a booster dose on day 21; Group II and IV animals were immunized with 1 mL and 0.2 mL of rabies vaccine, respectively, without the booster dose; unvaccinated animals served as a control (Group V). Serum samples were collected on days 0, 14, 28, and 90 to estimate RVNA titers using the rapid fluorescent focus inhibition test (RFFIT). The titers were above an adequate level (≥0.5 IU/mL) on day 14 and maintained up to 90 days in all animals administered the rabies vaccine through the IM and ID route with or without a booster dose. The study indicated that both routes of vaccination are safe and effective in providing protection against rabies. Hence, both routes can be considered for pre-exposure prophylaxis. However, the ID route proved to be more economical due to its dose-sparing effect.

Urtica dioica Agglutinin Prevents Rabies Virus Infection in a Muscle Explant Model.

Wang X, Terrie L, Wu G, Van Damme EJM, Thorrez L, Fooks AR, Banyard AC, Jochmans D, Neyts J.
28-04-2023
Pharmaceuticals (Basel).
https://pubmed.ncbi.nlm.nih.gov/37242595/

Expression Improvement of Recombinant Plasmids of the Interleukin-7 Gene in Chitosan-Derived Nanoparticles and Their Elevation of Mice Immunity.

Hou W, Zhang L, Chen J, Gu Y, Lv X, Zhang X, Li J, Liu H, Gao R.
28-04-2023
Biology (Basel).
https://pubmed.ncbi.nlm.nih.gov/37237481/

To investigate a safe and effective approach for enhancing the in vivo expression of recombinant genes and improving the systemic immunity of animals against infectious diseases, we employed the interleukin-7 (IL-7) gene from Tibetan pigs to construct a recombinant eukaryotic plasmid (VRTPIL-7). We first examined VRTPIL-7's bioactivity on porcine lymphocytes in vitro and then encapsulated it with polyethylenimine (PEI), chitosan copolymer (CS), PEG-modified galactosylated chitosan (CS-PEG-GAL) and methoxy poly (ethylene glycol) (PEG) and PEI-modified CS (CS-PEG-PEI) nanoparticles using the ionotropic gelation technique. Next, we intramuscularly or intraperitoneally injected mice with various nanoparticles containing VRTPIL-7 to evaluate their immunoregulatory effects in vivo. We observed a significant increase in neutralizing antibodies and specific IgG levels in response to the rabies vaccine in the treated mice compared to the controls. Treated mice also exhibited increased leukocytes, CD8+ and CD4+ T lymphocytes, and elevated mRNA levels of toll-like receptors (TLR1/4/6/9), IL-1, IL-2, IL-4, IL-6, IL-7, IL-23, and transforming growth factor-beta (TGF-β). Notably, the recombinant IL-7 gene encapsulated in CS-PEG-PEI induced the highest levels of immunoglobulins, CD4+ and CD8+ T cells, TLRs, and cytokines in the mice's blood, suggesting that chitosan-PEG-PEI may be a promising carrier for in vivo IL-7 gene expression and enhanced innate and adaptive immunity for the prevention of animal diseases.

Schistosomiase

Implications for selecting persistent hot spots of schistosomiasis from community- and school-based surveys in Blue Nile, North Kordofan, and Sennar States, Sudan.

Ismail HAHA, Cha S, Jin Y, Hong ST.
Mai-2023
Parasites Hosts Dis.
https://pubmed.ncbi.nlm.nih.gov/37258270/

In several schistosomiasis-endemic countries, the prevalence has remained high in some areas owing to reinfection despite repeated mass drug administration (MDA) interventions; these areas are referred to as persistent hot spots. Identifying hotspots is critical for interrupting transmission. This study aimed to determine an effective means of identifying persistent hot spots. First, we investigated the differences between Schistosoma haematobium and Schistosoma mansoni prevalence among school-aged children (SAC) estimated by a community-based survey, for which local key informants purposively selected communities, and a randomly sampled school-based survey. A total of 6,225 individuals residing in 60 villages in 8 districts of North Kordofan, Blue Nile, or Sennar States, Sudan participated in a community-based survey in March 2018. Additionally, the data of 3,959 students attending 71 schools in the same 8 districts were extracted from a nationwide school-based survey conducted in January 2017. The community-based survey identified 3 districts wherein the prevalence of S. haematobium or S. mansoni infection among SAC was significantly higher than that determined by the randomly sampled school survey (e.g., S. haematobium in the Sennar district: 10.8% vs. 1.1%, P<0.001). At the state level, the prevalence of schistosomiasis among SAC, as determined by the community-based survey, was consistently significantly higher than that determined by the school-based survey. Purposeful selection of villages or schools based on a history of MDA, latrine coverage, open defecation, and the prevalence of bloody urine improved the ability for identifying persistent hot spots.

When Parasites Stray from the Path: A curious case of Ectopic Cutaneous Schistosoma haematobium.

Siddig EE, Ahmed A.
31-05-2023
QJM.
https://pubmed.ncbi.nlm.nih.gov/37255318/

This case report highlights an unusual manifestation of schistosomiasis, where a chronic cutaneous lesion was observed much later in the disease course. The diagnosis was made after laboratory investigation of the lesion and urine analysis, revealing the presence of Schistosoma haematobium eggs. The patient had a history of swimming in freshwater during his travel to various regions in South Sudan for work. This report emphasizes the importance of a full travel history and the need for physicians to be vigilant for unusual presentations of infectious diseases. The One Health strategy is found to be useful for the prevention and control of such zoonoses in endemic countries. Further studies are needed to improve our understanding of the disease's pathology.

[Application of the "virtual-real combination" experimental teaching model in Human Parasitology teaching: a case study of comprehensive schistosome experiments].

Chen X, Zhou S, Qiu J, Chen L, Xu Z, Ji M, Guo J, Zhang R.
16-11-2022
Zhongguo Xue Xi Chong Bing Fang Zhi Za Zhi.
https://pubmed.ncbi.nlm.nih.gov/37253568/

[Intelligent identification of livestock, a source of Schistosoma japonicum infection, based on deep learning of unmanned aerial vehicle images].

Xue J, Xia S, Li Z, Wang X, Huang L, He R, Li S.
10-05-2023
Zhongguo Xue Xi Chong Bing Fang Zhi Za Zhi.
https://pubmed.ncbi.nlm.nih.gov/37253560/

Schistosome egg antigen stimulates the secretion of miR-33-carrying extracellular vesicles from macrophages to promote hepatic stellate cell activation and liver fibrosis in schistosomiasis.

Qi X, Pu Y, Chen F, Dong L, Ma Y, Wang J, Yin G, Lu D, Chen X, Zhu J, Li Y, Zhou S, Su C.
30-05-2023
PLoS Negl Trop Dis.
https://pubmed.ncbi.nlm.nih.gov/37253066/

Schistosomiasis is a serious and neglected disease with a high prevalence in tropical and subtropical countries. The primary pathology of hepatic schistosomiasis caused by Schistosoma japonicum (S. japonicum) or Schistosoma mansoni (S. mansoni) infection is egg-induced granuloma and subsequent fibrosis in the liver. Activation of hepatic stellate cells (HSCs) is the central driver of liver fibrosis. Macrophages (Mϕ), making up 30% of cells in hepatic granulomas, directly or indirectly regulate HSC activation by paracrine mechanisms, via secreting cytokines or chemokines. Currently, Mϕ-derived extracellular vesicles (EVs) are broadly involved in cell communication with adjacent cell populations. However, whether Mϕ-derived EVs could target neighboring HSCs to regulate their activation during schistosome infection remains largely unknown. Schistosome egg antigen (SEA) is considered to be the main pathogenic complex mixture involved in liver pathology. Here, we demonstrated that SEA induced Mϕ to produce abundant extracellular vesicles, which directly activated HSCs by activating their autocrine TGF-β1 signaling. Mechanistically, EVs derived from SEA-stimulated Mϕ contained increased miR-33, which were transferred into HSCs and subsequently upregulated autocrine TGF-β1 in HSCs through targeting and downregulating SOCS3 expression, thereby promoting HSC activation. Finally, we validated that EVs derived from SEA-stimulated Mϕ utilized enclosed miR-33 to promote HSC activation and liver fibrosis in S. japonicum-infected mice. Overall, our study indicates that Mϕ-derived EVs play important roles in the paracrine regulation of HSCs during the progression of hepatic schistosomiasis, representing a potential target for the prevention of liver fibrosis in hepatic schistosomiasis.

The prevalence of urogenital and intestinal schistosomiasis among school age children (6-13 years) in the Okavango Delta in Botswana.

Phaladze NA, Molefi L, Thakadu OT, Tsima O, Ngwenya BN, Molefi TL, Tshiamo WB.
30-05-2023
PLoS One.
https://pubmed.ncbi.nlm.nih.gov/37253026/

Prevalence and Associated Factors of Intestinal Parasites among Food Handlers Working in Food Service Establishments in Northwest Ethiopia, 2022.

Wondimu H, Mihret M.
18-05-2023
J Parasitol Res.
https://pubmed.ncbi.nlm.nih.gov/37252034/

Background: As in most of African countries, intestinal parasites have been widely distributed in Ethiopia and are among the 10 top causes of morbidity and mortality nationwide. Statistics for food-borne illness in various industrialized countries show that up to 60% of cases may be caused by poor food handling techniques and by contaminated food served in food service establishments. Epidemiological information on the prevalence of various intestinal parasitic infections in different regions/localities is a prerequisite to develop appropriate strategies. Objective: This study aimed to determine the magnitude of intestinal parasites among food handlers working in different food service establishments in Gondar city. Methods: A cross-sectional study was conducted with food handlers working in different food service establishments in Gondar city. Stool samples were collected from 350 food handlers and processed using the formol-ether concentration method and then microscopically examined for intestinal parasitic infections. Pre-tested and structured questionnaire was used to study the socio-demographic characteristics of food handlers. Chi-square test and *p*-value were used to assess the associations between risk factors and the parasite isolation rate. The *p*-value ≤0.05 was considered as statistically significant. Results: Of the 350 food handlers, 160 (45.71%) had parasites. Among the isolated parasites, *Ascaris lumbricoides* was found to be the most prevalent parasite 35.63%, followed by hookworm 19.38%, *Entamoeba histolytica/dispar* 16.25%, *Trichuris trichiura* 10.00%, *Strongyloides stercoralis* 8.13%, *Schistosoma mansoni* 6.88%, and *Cystoisospora belli, Hymenolepis nana*, and *Taenia* species each accounting 1.25%. Conclusion: The result of the study indicated that the magnitude of intestinal parasitosis among food handlers working at different levels of food establishments in Gondar, Ethiopia, was found to be high. Being at lower educational level and inactive role of the town's municipality are determined as a risk factor for parasitic positivity of food handlers.

Schistosomicidal, hepatoprotective and antioxidant activities of the N-acetyl-L-cysteine and/or praziquantel in experimental acute mansonic schistosomiasis.

de Lima Aires A, de Araújo HDA, Galvão AM, de Araújo SB, da Silva RL, Dos Anjos ZP, de Souza Maia MB, Souza VMO, de Azevedo Albuquerque MCP.
Juin-2023
3 Biotech.
https://pubmed.ncbi.nlm.nih.gov/37251728/

Evaluation of 43 species of Congolese medicinal plants used traditionally for the treatment of schistosomiasis leading to the isolation of an anti-schistosomal phaeophytin from Pseudolachnostylis maprouneifolia Pax.

Muya K, Kalonji M, Ilunga NW, Maseho M, Kitambala M, Kalonda M, Ndoumba K, Byanga K, Wright CW, Häberli C, Keiser J, Simbi L.
26-05-2023
J Ethnopharmacol.
https://pubmed.ncbi.nlm.nih.gov/37245710/

Ethnopharmacological relevance: Schistosomiasis (bilharzia) is an important, prevalent and neglected tropical disease for which new treatments are urgently required. In the DR Congo and other sub- and tropical countries, traditional medicines are widely used for the control of schistosomiasis. Aim of study: To evaluate 43 Congolese plant species used traditionally for the treatment of urogenital schistosomiasis against Schistosoma mansoni. Materials and methods: Methanolic extracts were screened against S. mansoni newly transformed schistosomula (NTS). Three of the most active extracts were evaluated for acute oral toxicity in guinea pigs and activity guided fractionation of the least toxic was carried out using S. mansoni NTS and adult stages. An isolated compound was identified by means of spectroscopic techniques. Results: Thirty-nine of 62 extracts killed S. mansoni NTS at 100 µg/mL and 7 extracts were active at ≥ 90% at 25 µg/mL; 3 extracts were selected for acute oral toxicity evaluation; the least toxic of these, Pseudolachnostylis maprouneifolia leaf was then subjected to activity-guided fractionation. 17^3-ethoxyphaeophorbide a (1) was isolated as an active compound with 56% activity against NTS at 50 µg/mL and 22.5% activity against adult S. mansoni at 100 µg/mL but these activities are significantly less than those of the parent fractions suggesting that other active compounds are also present and/or that synergistic interactions are taking place. Conclusion: This study has identified 39 plant extracts with activity against S. mansoni NTS lending support to their traditional use in the treatment of schistosomiasis for which new treatments are urgently needed. P. maprouneifolia leaf extract was found to have potent anti-schistosomal activity and low in vivo oral toxicity in guinea pigs; activity-guided fractionation resulted in the isolation of an active compound, 17^3-ethoxyphaeophorbide a. Phaeophorbides may merit exploration as potential anti-schistosomal agents and further work on plant species shown to have potent

activity against S. mansoni NTS in this study would be worthwhile.

Evaluation of IL-35, as a Possible Biomarker for Follow-Up after Therapy, in Chronic Human Schistosoma Infection.

Marascio N, Loria MT, Pavia G, Peronace C, Adams NJ, Campolo M, Divenuto F, Lamberti AG, Giancotti A, Barreca GS, Mazzitelli M, Trecarichi EM, Torti C, Perandin F, Bisoffi Z, Quirino A, Matera G.
17-05-2023
Vaccines (Basel).
https://pubmed.ncbi.nlm.nih.gov/37243099/

Characterization of Schistosome Sox Genes and Identification of a Flatworm Class of Sox Regulators.

Wood S, Ishida K, Hagerty JR, Karahodza A, Dennis JN, Jolly ER.
09-05-2023
Pathogens.
https://pubmed.ncbi.nlm.nih.gov/37242360/

Schistosome helminths infect over 200 million people across 78 countries and are responsible for nearly 300,000 deaths annually. However, our understanding of basic genetic pathways crucial for schistosome development is limited. The sex determining region Y-box 2 (Sox2) protein is a Sox B type transcriptional activator that is expressed prior to blastulation in mammals and is necessary for embryogenesis. Sox expression is associated with pluripotency and stem cells, neuronal differentiation, gut development, and cancer. Schistosomes express a Sox-like gene expressed in the schistosomula after infecting a mammalian host when schistosomes have about 900 cells. Here, we characterized and named this Sox-like gene *SmSOXS1*. SmSoxS1 protein is a developmentally regulated activator that localizes to the anterior and posterior ends of the schistosomula and binds to Sox-specific DNA elements. In addition to SmSoxS1, we have also identified an additional six Sox genes in schistosomes, two Sox B, one SoxC, and three Sox genes that may establish a flatworm-specific class of Sox genes with planarians. These data identify novel Sox genes in schistosomes to expand the potential functional roles for Sox2 and may provide interesting insights into early multicellular development of flatworms.

Antischistosomal effects of green and chemically synthesized silver nanoparticles: in vitro and in vivo murine model.

Hamdan BZK, Soliman MI, Taha HA, Khalil MMH, Nigm AH.
24-05-2023
Acta Trop.
https://pubmed.ncbi.nlm.nih.gov/37236335/

Oncomelania hupensis Distribution and Schistosomiasis Transmission Risk in Different Environments under Field Conditions.

Li Y, Guo S, Dang H, Zhang L, Xu J, Li S.
23-04-2023
Trop Med Infect Dis.
https://pubmed.ncbi.nlm.nih.gov/37235290/

A Bridge to Banding: Splenic Artery Embolization in Hepatosplenic Schistosomiasis.

Hassan N, Mohamed I, Rajab R, Campbell J, Zulqarnain M, Sadeddin E, Ghoz H.
24-05-2023
ACG Case Rep J.
https://pubmed.ncbi.nlm.nih.gov/37235002/

Schistosomiasis is a parasitic infection endemic to sub-Saharan Africa. The severe form of disease, caused by deposition of *Schistosoma* eggs in the portal vein, is known as hepatosplenic schistosomiasis. We present a case of a 26-year-old woman with esophageal varices in the setting of hepatosplenic schistosomiasis. This patient underwent partial splenic artery embolization to treat thrombocytopenia secondary to splenic sequestration. After embolization and improvement of cell counts, the patient was successfully able to undergo variceal band ligation.

Modelling the age-prevalence relationship in schistosomiasis: A secondary data analysis of school-aged-children in Mangochi District, Lake Malawi.

Reed AL, O'Ferrall AM, Kayuni SA, Baxter H, Stanton MC, Stothard JR, Jewell C.
03-05-2023
Parasite Epidemiol Control.
https://pubmed.ncbi.nlm.nih.gov/37234267/

Schistosomiasis is an aquatic snail borne parasitic disease, with intestinal schistosomiasis (IS) and urogenital schistosomiasis (UGS) caused by *Schistosoma mansoni* and *S. haematobium* infections, respectively. School-aged-children (SAC) are a known vulnerable group and can also suffer from co-infections. Along the shoreline of Lake Malawi a newly emerging outbreak of IS is occurring with increasing UGS co-infection rates. Age-prevalence (co)infection profiles are not fully understood. To shed light on these (co)infection trends by *Schistosoma* species and by age of child, we conducted a secondary data analysis of primary epidemiological data collected from SAC in Mangochi District, Lake Malawi, as published previously. Available diagnostic data by child, were converted into binary response infection profiles for 520 children, aged 6-15, across 12 sampled schools. Generalised additive models were then fitted to mono- and dual-infections. These were used to identify consistent population trends, finding the prevalence of IS significantly increased [p = 8.45e-4] up to 11 years of age then decreasing thereafter. A similar age-prevalence association was observed for co-infection [p = 7.81e-3]. By contrast, no clear age-infection pattern for UGS was found

[*p* = 0.114]. Peak prevalence of *Schistosoma* infection typically occurs around adolescence; however, in this newly established IS outbreak with rising prevalence of UGS co-infections, the peak appears to occur earlier, around the age of 11 years. As the outbreak of IS fulminates, further temporal analysis of the age-relationship with *Schistosoma* infection is justified. This should refer to age-prevalence models which could better reveal newly emerging transmission trends and *Schistosoma* species dynamics. Dynamical modelling of infections, alongside malacological niche mapping, should be considered to guide future primary data collection and intervention programmes.

Computational Insights into Natural Antischistosomal Metabolites as SmHDAC8 Inhibitors: Molecular Docking, ADMET Profiling, and Molecular Dynamics Simulation.

Alzain AA, Mukhtar RM, Abdelmoniem N, Elbadwi FA, Hussien A, Garelnabi EAE, Osman W, Sherif AE, Khedr AIM, Ghazawi KF, Samman WA, Ibrahim SRM, Mohamed GA, Ashour A.
15-05-2023
Metabolites.
https://pubmed.ncbi.nlm.nih.gov/37233699/

Protective human IgE responses are promoted by comparable life-cycle dependent Tegument Allergen-Like expression in Schistosoma haematobium and Schistosoma mansoni infection.

Oettle RC, Dickinson HA, Fitzsimmons CM, Sacko M, Tukahebwa EM, Chalmers IW, Wilson S.
25-05-2023
PLoS Pathog.
https://pubmed.ncbi.nlm.nih.gov/37228019/

School-based preventive chemotherapy program for schistosomiasis and soil-transmitted helminth control in Angola: 6-year impact assessment.

Bartlett AW, Mendes EP, Dahmash L, Palmeirim MS, de Almeida MC, Peliganga LB, Lufunda LMM, Direito A, Ramirez J, Mwinzi PN, Lopes S, Vaz Nery S.
17-05-2023
PLoS Negl Trop Dis.
https://pubmed.ncbi.nlm.nih.gov/37196040/

Background: A school preventive chemotherapy (PC) program for soil-transmitted helminths (STHs) and schistosomiasis has operated in Huambo, Uige and Zaire provinces, Angola, since 2013 and 2014, respectively; complemented by a school water, sanitation and hygiene (WASH) program in a subset of schools from 2016. Conducted in 2021, this is the first impact assessment of the school program for the control of schistosomiasis and STHs. Methodology/principal findings: A two-stage cluster design was used to select schools and schoolchildren for parasitological and WASH surveys. The rapid diagnostic tests (RDTs), point of care circulating cathodic antigen (POC-CCA) and Hematstix, were used to estimate Schistosoma mansoni and Schistosoma haematobium prevalence, respectively. Kato Katz was used to detect STHs, and quantify STH and S. mansoni infections. Urine filtration was used to quantify S. haematobium infections. Prevalence, infection intensity, relative prevalence reduction and egg reduction rates were calculated for schistosomiasis and STHs. Cohen's Kappa co-efficient was used to assess agreement between RDTs and microscopy. Chi-square or Fisher's exact test was used to compare WASH indicators in WASH-supported and WASH-unsupported schools. Overall, 17,880 schoolchildren (599 schools) and 6,461 schoolchildren (214 schools) participated in the schistosomiasis and STH surveys, respectively. Prevalence of any schistosomiasis in Huambo was 29.6%, Uige 35.4%, and Zaire 28.2%. Relative reduction in schistosomiasis prevalence from 2014 for Huambo was 18.8% (95% confidence interval (CI) 8.6, 29.0), Uige -92.3% (95%CI -162.2, -58.3), and Zaire -14.0% (95%CI -48.6, 20.6). Prevalence of any STH in Huambo was 16.3%, Uige 65.1%, and Zaire 28.2%. Relative reduction in STH prevalence for Huambo was -28.4% (95%CI -92.1, 35.2), Uige -10.7% (95%CI -30.2, 8.8), and Zaire -20.9% (95%CI -79.5, 37.8). A higher proportion of WASH-supported schools had improved water sources, and toilet and handwashing facilities compared to WASH-unsupported schools. Conclusions/significance: The limited impact this school program has had in controlling schistosomiasis and STHs identifies the need for a comprehensive understanding of individual, community, and environmental factors associated with transmission, and consideration for a community-wide control program.

Trachome

Reducing trachoma in women.

Jesudason T.
Juin-2023
Lancet Infect Dis.
https://pubmed.ncbi.nlm.nih.gov/37244275/

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

[High-fat intake alleviates lung injury induced by Paragonimus proliferus infection in rats through up-regulating CYP 4A1 expression in lung tissues].

Liu S, Wang Q, Wang W, Wu L, Ma Z, Wang L, Chang G, Ding J, Hua L, Chen H, Li S, Wang W.
18-04-2023
Zhongguo Xue Xi Chong Bing Fang Zhi Za Zhi.

https://pubmed.ncbi.nlm.nih.gov/37253566/

Objective: To explore the improvements of high-fat intake on lung injury induced by *Paragonimus proliferus* infection in rats, and to preliminarily explore the mechanisms underlying the role of cytochrome P450 4A1 (CYP 4A1) in the improve ments. Methods: SD rats were randomly assigned into three groups, including the normal control group (n = 10), the infection and normal diet group (n = 12) and the infection and high-fat diet group (n = 12). Rats in the normal control group were fed with normal diet and without any other treatments, and animals in the infection and normal diet group were subcutaneously injected with 8 excysted metacercariae of *P. proliferus* via the abdominal wall, followed by feeding with normal diet, while rats in the infection and high-fat diet group were subcutaneously injected with 8 excysted metacercariae of *P. proliferus* via the abdominal wall, followed by feeding with high-fat diet. All rats were sacrificed 28 weeks post-infection, and serum samples and lung specimens were collected. Following hematoxylin-eosin (HE) staining of rat lung specimens, the rat lung injury was observed under an optical microscope, and alveolitis was evaluated using semi-quantitative scoring. Serum interleukin-1β (IL-1β) and tumor necrosis factor alpha (TNF-α) levels were measured using enzyme-linked immunosorbent assay (ELISA), and the cytochrome P450 4A1 (CYP 4A1) expression was quantified in rat lung specimens at transcriptional and translational levels using quantitative real-time PCR (qPCR) and Western blotting assays. Results: Alveolar wall thickening, edema and inflammatory cell infiltration were alleviated 28 weeks post-infection with *P. proliferus* in rats in the infection and high-fat diet group relative to the infection and normal diet group, and no alveolar consolidation was seen in the infection and high-fat diet group. The semi-quantitative score of alveolitis was significantly higher in the infection and normal diet group [(2.200 ± 0.289) points] than in the normal control group [(0.300 ± 0.083) points] and the infection and high-fat diet group [(1.300 ± 0.475) points] (both P values < 0.05), and higher serum IL-1β [(151.586 ± 20.492)] pg/mL and TNF-α levels [(180.207 ± 23.379) pg/mL] were detected in the infection and normal diet group than in the normal control group [IL-1β: (103.226 ± 3.366) pg/mL; TNF-α: (144.807 ± 1.348) pg/mL] and the infection and high-fat diet group [IL-1β: (110.131 ± 12.946) pg/mL; TNF-α: (131.764 ± 27.831) pg/mL] (all P values < 0.05). In addition, lower *CYP 4A1 mRNA* (3.00 ± 0.81) and protein expression (0.40 ± 0.02) was quantified in lung specimens in the infection and normal diet group than in the normal control group [(5.03 ± 2.05) and (0.84 ± 0.14)] and the infection and high-fat diet group [(11.19 ± 3.51) and (0.68 ± 0.18)] (all P values < 0.05). Conclusions: High-fat intake may alleviate lung injuries caused by *P. proliferus* infection in rats through up-regulating CYP 4A1 expression in lung tissues at both translational and transcriptional levels.

Detection of Human Paragonimiasis by ELISA Using Recombinant Paragonimus westermani Cysteine Protease 7.

Andrade-Gomes LG, Zuniga MJ, Dolz G, Solano-Campos F.
30-05-2023
Am J Trop Med Hyg.
https://pubmed.ncbi.nlm.nih.gov/37253437/

Paragonimiasis is an important but neglected foodborne trematodiasis caused by Paragonimus mexicanus in Costa Rica. Immunological techniques for diagnosing this parasitosis in humans do not exist in Central America. The objective of the present study was to use recombinant Paragonimus westermani cysteine protease 7 to standardize an ELISA for the detection of antibodies against Paragonimus spp. Human sera positive for P. westermani, P. mexicanus, or Paragonimus spp., human sera infected with other helminths, as well as sera of healthy humans without parasitic infections, were analyzed. The sensitivity of the ELISA was 92.9%, and the specificity was 91.9%. This report is the first to describe the development of an ELISA for the diagnosis of Paragonimus spp. in Costa Rica and Central America. Using this ELISA in the health system of Costa Rica is recommended to detect infections.

Parasitological and Bacteriological Evaluation of Common Raw Fruits Collected from Two Major Markets in Iwo, Osun State, South-West Nigeria.

Oladosu OO, Olatunde DO, Olatayo AO, Atobatele B.
18-05-2023
Int J Food Sci.
https://pubmed.ncbi.nlm.nih.gov/37250492/

Brief report first report of the in vitro ovicidal activity of camel milk and its fractions on zoonotic-liver fluke (Fasciola gigantica) eggs.

Awad DAB, Eldiarby AS, Abdallah M, Hamad A, Gawad SMA.
30-05-2023
Vet Res Commun.
https://pubmed.ncbi.nlm.nih.gov/37249746/

Determination of Parasitic Contamination in Vegetables Collected from Local Markets in İzmir Province, Türkiye.

Bilgiç F, Akdur Öztürk E, Babat SÖ, Babaoğlu A, Dirim Erdoğan D, Korkmaz M.
29-05-2023
Turkiye Parazitol Derg.
https://pubmed.ncbi.nlm.nih.gov/37249114/

Objective: Fresh vegetables are an important part of a healthy and nutrient-rich diet but the consumption of raw vegetables without proper washing is the main way for transmission of parasites. This study was aimed at determining the rate of parasitic contamination in prewashed fresh vegetables sold at randomly selected 10 retail markets which is the last step to reach the consumer in İzmir, Türkiye. Methods: A total of 80 samples selected from eight types of vegetables including tomato, spinach, lettuce, rocket, mint, parsley, dill, and cucumber were examined for parasitic agents microscopically by sedimentation method after washing samples with normal

saline. Statistical analysis was performed using SPSS software version 20.0. Results: Protozoan cysts, helminth eggs, and larvae were detected in 21 (26.2%) of 80 samples from eight different vegetable species. Rhabditidiform larvae 18.7%, *Blastocystis* spp. 5%, *Toxocara* spp. 2.5%; *Ascaris* spp., *Fasciola* spp., *Entamoeba histolytica/ Entamoeba dispar* and hooked worms were found in 1.2%. Spinach and mint samples were contaminated with parasites significantly more than other fresh vegetable samples (p<0.008, odds ratio =80.0; p<0.017, odds ratio =46.6 respectively). *Cruznema* spp., a plant nematode, was found at the highest rate according to the results of culture, polymerase chain reaction and sequencing, respectively. Conclusion: In this study, the parasitic contamination was found in approximately one of the four vegetables sold in randomly selected markets in İzmir. These findings show that vegetables sold in local markets can cause parasitic infections if they are consumed without adequate washing and awareness should be raised on this issue. In addition, it was concluded that morphological examinations should be confirmed by molecular studies and sequencing as much as possible in order to avoid misdiagnosis of rhabditidiform larvae.

The First Case of Human Hepatic Fasciolosis Presented as Hepatic Pseudotumor Histopathologically Diagnosed in Romania-A Case Report.

Birlutiu V, Birlutiu RM.
17-05-2023
Healthcare (Basel).
https://pubmed.ncbi.nlm.nih.gov/37239737/

Prevalence and Risk Factors of Ovine and Caprine Fasciolosis in the Last 20 Years in China: A Systematic Review and Meta-Analysis.

Lan Z, Yu J, Zhang X, Zhang A, Deng R, Li B, Lv Q, Ma X, Gao J, Wang C.
18-05-2023
Animals (Basel).
https://pubmed.ncbi.nlm.nih.gov/37238117/

Fasciolosis is a significant zoonotic and common parasitic disease for animals and humans, creating public health concerns worldwide. This study retrieved articles related to the occurrence of *Fasciola hepatica* and *Fasciola gigantica* in sheep and goats in China by searching five databases: PubMed, ScienceDirect, the Chinese National Knowledge Infrastructure (CNKI), Wanfang Data, and the VIP Chinese Journal Database. A total of 60 valid articles were captured. The pooled prevalence of ovine and caprine fasciolosis was 26.00%. It was also found to be higher in the subgroups of Northwest China and Shaanxi Province, as well as in areas with a high altitude, rainfall of ≥800 mm, and temperature ranging between 10 °C and 20 °C. Analysis of the type of season and sampling years showed significant ($p < 0.05$) difference. In other subgroups, sheep (34.74%), hosts aged over 2 years (32.26%), females (48.33%) and free-range animals (26.83%) showed a higher disease prevalence. These results indicated that ovine and caprine fasciolosis was widely distributed, especially in Northwest China. The sampling years and the type of season are risk factors for the prevalence of ovine and caprine fasciolosis. Therefore, strategies for ovine and caprine fasciolosis control should be developed based on these epidemic risk factors, which will reduce the prevalence of fasciolosis in China.

Trypanosomes (trypanosomiase et maladie de Chagas)

Computational Prediction of Trypanosoma cruzi Epitopes Toward the Generation of an Epitope-Based Vaccine Against Chagas Disease.

Ros-Lucas A, Rioja-Soto D, Gascón J, Alonso-Padilla J.
2023
Methods Mol Biol.
https://pubmed.ncbi.nlm.nih.gov/37258934/

Chagas disease, caused by the protozoan parasite Trypanosoma cruzi, is considered a Neglected Tropical Disease. Limited investment is assigned to its study and control, even though it is one of the most prevalent parasitic infections worldwide. An innovative vaccination strategy involving an epitope-based vaccine that displays multiple immune determinants originating from different antigens could counteract the high biological complexity of the parasite and lead to a wide and protective immune response. In this chapter, we describe a computational reverse vaccinology pipeline applied to identify the most promising peptide sequences from T. cruzi proteins, prioritizing evolutionary conserved sequences, to finally select a list of T and B cell epitope candidates to be further tested in an experimental setting.

ASP-2/Trans-sialidase chimeric protein induces robust protective immunity in experimental models of Chagas' disease.

Castro JT, Brito R, Hojo-Souza NS, Azevedo B, Salazar N, Ferreira CP, Junqueira C, Fernandes AP, Vasconcellos R, Cardoso JM, Aguiar-Soares RDO, Vieira PMA, Carneiro CM, Valiate B, Toledo C, Salazar AM, Caballero O, Lannes-Vieira J, Teixeira SR, Reis AB, Gazzinelli RT.
31-05-2023
NPJ Vaccines.
https://pubmed.ncbi.nlm.nih.gov/37258518/

Immunization with the Amastigote Surface Protein-2 (ASP-2) and Trans-sialidase (TS) antigens either in the form of recombinant protein, encoded in plasmids or human adenovirus 5 (hAd5) confers robust protection against various lineages of Trypanosoma cruzi. Herein we generated a chimeric protein containing the most immunogenic regions for T and B cells from TS and ASP-2 (TRASP) and evaluated its immunogenicity in comparison with our standard protocol of heterologous prime-boost using plasmids and hAd5. Mice immunized with TRASP protein associated to Poly-ICLC (Hiltonol) were highly resistant to challenge with T. cruzi, showing a large decrease in tissue parasitism, parasitemia and no lethality.

This protection lasted for at least 3 months after the last boost of immunization, being equivalent to the protection induced by DNA/hAd5 protocol. TRASP induced high levels of T. cruzi-specific antibodies and IFNγ-producing T cells and protection was primarily mediated by $CD8^+$ T cells and IFN-γ. We also evaluated the toxicity, immunogenicity, and efficacy of TRASP and DNA/hAd5 formulations in dogs. Mild collateral effects were detected at the site of vaccine inoculation. While the chimeric protein associated with Poly-ICLC induced high levels of antibodies and $CD4^+$ T cell responses, the DNA/hAd5 induced no antibodies, but a strong $CD8^+$ T cell response. Immunization with either vaccine protected dogs against challenge with T. cruzi. Despite the similar efficacy, we conclude that moving ahead with TRASP together with Hiltonol is advantageous over the DNA/hAd5 vaccine due to pre-existing immunity to the adenovirus vector, as well as the cost-benefit for development and large-scale production.

Molecular epidemiological survey of pathogenic trypanosomes in naturally infected cattle in northern Côte d'ivoire.

Ekra JY, N'Goran EK, Mboera LEG, Gragnon BG, Assovié KRN, Mafie EM.
Mai-2023
Parasites Hosts Dis.
https://pubmed.ncbi.nlm.nih.gov/37258259/

Hallmarks of the relationship between host and Trypanosoma cruzi sulfated glycoconjugates along the course of Chagas disease.

Soprano LL, Ferrero MR, Jacobs T, Couto AS, Duschak VG.
15-05-2023
Front Cell Infect Microbiol.
https://pubmed.ncbi.nlm.nih.gov/37256110/

American Trypanosomiasis or Chagas disease (ChD), a major problem that is still endemic in large areas of Latin America, is caused by *Trypanosoma cruzi*. This agent holds a major antigen, cruzipain (Cz). Its C-terminal domain (C-T) is retained in the glycoprotein mature form and bears several post-translational modifications. Glycoproteins containing sulfated N-linked oligosaccharides have been mostly implicated in numerous specific procedures of molecular recognition. The presence of sulfated oligosaccharides was demonstrated in Cz, also in a minor abundant antigen with serine-carboxypeptidase (SCP) activity, as well as in parasite sulfatides. Sulfate-bearing glycoproteins in Trypanosomatids are targets of specific immune responses. *T. cruzi* chronically infected subjects mount specific humoral immune responses to sulfated Cz. Unexpectedly, in the absence of infection, mice immunized with C-T, but not with sulfate-depleted C-T, showed ultrastructural heart anomalous pathological effects. Moreover, the synthetic anionic sugar conjugate $GlcNAc_6SO_3$-BSA showed to mimic the N-glycan-linked sulfated epitope (sulfotope) humoral responses that natural Cz elicits. Furthermore, it has been reported that sulfotopes participate *via* the binding of sialic acid Ig-like-specific lectins (Siglecs) to sulfosialylated glycoproteins in the immunomodulation by host-parasite interaction as well as in the parasite infection process. Strikingly, recent evidence involved Cz-sulfotope-specific antibodies in the immunopathogenesis and infection processes during the experimental ChD. Remarkably, sera from chronically *T. cruzi*-infected individuals with mild disease displayed higher levels of IgG_2 antibodies specific for sulfated glycoproteins and sulfatides than those with more severe forms of the disease, evidencing that *T. cruzi* sulfotopes are antigenic independently of the sulfated glycoconjugate type. Ongoing assays indicate that antibodies specific for sulfotopes might be considered biomarkers of human cardiac ChD progression, playing a role as predictors of stability from the early mild stages of chronic ChD.

Triatoma pallidipennis (Stål, 1872) (Hemiptera: Reduviidae) and its potential for infestation in Tecozautla, Hidalgo state, Mexico.

Alejandre-Aguilar R, Antonio-Campos A, Noguez-García J, Rivas N.
Juin-2023
J Vector Ecol.
https://pubmed.ncbi.nlm.nih.gov/37255353/

Antitumor mechanisms of molecules secreted by Trypanosoma cruzi in colon and breast cancer: A review.

Sadr S, Ghiassi S, Lotfalizadeh N, Simab PA, Hajjafari A, Borji H.
29-05-2023
Anticancer Agents Med Chem.
https://pubmed.ncbi.nlm.nih.gov/37254546/

Subcellular protein localisation of Trypanosoma brucei bloodstream form-upregulated proteins maps stage-specific adaptations.

Halliday C, Dean S, Sunter JD, Wheeler RJ.
23-05-2023
Wellcome Open Res.
https://pubmed.ncbi.nlm.nih.gov/37251657/

Background: Genome-wide subcellular protein localisation in *Trypanosoma brucei,* through our TrypTag project, has comprehensively dissected the molecular organisation of this important pathogen. Powerful as this resource is , *T. brucei* has multiple developmental forms and we previously only analysed the procyclic form. This is an insect life cycle stage, leaving the mammalian bloodstream form unanalysed. The expectation is that between life stages protein localisation would not change dramatically (completely unchanged or shifting to analogous stage-specific structures). However, this has not been specifically tested. Similarly, which organelles tend to contain proteins with stage-specific expression can be predicted from known stage specific adaptations but has not been comprehensively tested. Methods: We used endogenous tagging with mNG to determine the sub-cellular localisation of the majority of proteins encoded by transcripts significantly upregulated in the bloodstream form, and performed comparison to the existing

localisation data in procyclic forms. **Results:** We have confirmed the localisation of known stage-specific proteins and identified the localisation of novel stage-specific proteins. This gave a map of which organelles tend to contain stage specific proteins: the mitochondrion for the procyclic form, and the endoplasmic reticulum, endocytic system and cell surface in the bloodstream form. **Conclusions:** This represents the first genome-wide map of life cycle stage-specific adaptation of organelle molecular machinery in *T. brucei*.

DNA damage repair proteins across the Tree of Life.

Nischwitz E, Schoonenberg VAC, Fradera-Sola A, Dejung M, Vydzhak O, Levin M, Luke B, Butter F, Scheibe M.
29-04-2023
iScience.
https://pubmed.ncbi.nlm.nih.gov/37250769/

Ultrastructural Expansion Microscopy in Three In Vitro Life Cycle Stages of Trypanosoma cruzi.

de Hernández MA, Martinez Peralta G, Vena R, Alonso VL.
12-05-2023
J Vis Exp.
https://pubmed.ncbi.nlm.nih.gov/37246875/

We describe here the application of ultrastructure expansion microscopy (U-ExM) in Trypanosoma cruzi, a technique that allows increasing the spatial resolution of a cell or tissue for microscopic imaging. This is performed by physically expanding a sample with off-the-shelf chemicals and common lab equipment. Chagas disease is a widespread and pressing public health concern caused by T. cruzi. The disease is prevalent in Latin America and has become a significant problem in non-endemic regions due to increased migration. The transmission of T. cruzi occurs through hematophagous insect vectors belonging to the Reduviidae and Hemiptera families. Following infection, T. cruzi amastigotes multiply within the mammalian host and differentiate into trypomastigotes, the non-replicative bloodstream form. In the insect vector, trypomastigotes transform into epimastigotes and proliferate through binary fission.The differentiation between the life cycle stages requires an extensive rearrangement of the cytoskeleton and can be recreated in the lab completely using different cell culture techniques. We describe here a detailed protocol for the application of U-ExM in three in vitro life cycle stages of Trypanosoma cruzi, focusing on optimization of the immunolocalization of cytoskeletal proteins. We also optimized the use of N-Hydroxysuccinimide ester (NHS), a pan-proteome label that has enabled us to mark different parasite structures.

Design, synthesis and biological evaluation of antiparasitic dinitroaniline-ether phospholipid hybrids.

Roussaki M, Magoulas GE, Fotopoulou T, Santarem N, Barrias E, Pöhner I, Luelmo S, Afroudakis P, Georgikopoulou K, Nevado PT, Eick J, Bifeld E, Corral MJ, Jiménez-Antón MD, Ellinger B, Kuzikov M, Fragiadaki I, Scoulica E, Gul S, Clos J, Prousis KC, Torrado JJ, Alunda JM, Wade RC, de Souza W, Cordeiro da Silva A, Calogeropoulou T.
19-05-2023
Bioorg Chem.
https://pubmed.ncbi.nlm.nih.gov/37244229/

A series of nine novel ether phospholipid-dinitroaniline hybrids were synthesized in an effort to deliver more potent antiparasitic agents with improved safety profile compared to miltefosine. The compounds were evaluated for their in vitro antiparasitic activity against L. infantum, L.donovani, L. amazonensis, L. major and L. tropica promastigotes, L. infantum and L. donovani intracellular amastigotes, Trypanosoma brucei brucei and against different developmental stages of Trypanosoma cruzi. The nature of the oligomethylene spacer between the dinitroaniline moiety and the phosphate group, the length of the side chain substituent on the dinitroaniline and the choline or homocholine head group were found to affect both the activity and toxicity of the hybrids. The early ADMET profile of the derivatives did not reveal major liabilities. Hybrid 3, bearing an 11-carbon oligomethylene spacer, a butyl side chain and a choline head group, was the most potent analogue of the series. It exhibited a broad spectrum antiparasitic profile against the promastigotes of New and Old World Leishmania spp., against intracellular amastigotes of two L. infantum strains and L. donovani, against T. brucei and against T. cruzi Y strain epimastigotes, intracellular amastigotes and trypomas tigotes. The early toxicity studies revealed that hybrid 3 showed a safe toxicological profile while its cytotoxicity concentration (CC_{50}) against THP-1 macrophages being >100 μM. Computational analysis of binding sites and docking indicated that the interaction of hybrid 3 with trypanosomatid α-tubulin may contribute to its mechanism of action. Furthermore, compound 3 was found to interfere with the cell cycle in T. cruzi epimastigotes, while ultrastructural studies using SEM and TEM in T. cruzi showed that compound 3 affects cellular processes that result in changes in the Golgi complex, the mitochondria and the parasite's plasma membrane. The snapshot pharmacokinetic studies showed low levels of 3 after 24 h following oral administration of 100 mg/Kg, while, its homocholine congener compound 9 presented a better pharmacokinetic profile.

Antiparasitic Activity of Plumbago auriculata Extracts and Its Naphthoquinone Plumbagin against Trypanosoma cruzi.

Peres RB, Batista MM, Bérenger ALR, Camillo FDC, Figueiredo MR, Soeiro MNC.
19-05-2023
Pharmaceuticals (Basel).
https://pubmed.ncbi.nlm.nih.gov/37242777/

Effectiveness of Nitazoxanide and Electrolyzed Oxiding Water in Treating Chagas Disease in a Canine Model.

Rodríguez-Morales O, Mendoza-Téllez EJ, Morales-Salinas E, Arce-Fonseca M.
12-05-2023
Pharmaceutics.
https://pubmed.ncbi.nlm.nih.gov/37242721/

Roles of ADP-Ribosylation during Infection Establishment by Trypanosomatidae Parasites.

Dowling J, Doig CL.
12-05-2023
Pathogens.
https://pubmed.ncbi.nlm.nih.gov/37242378/

Arylimidamides Have Potential for Chemoprophylaxis against Blood-Transmitted Chagas Disease.

Timm BL, da Gama ANS, Batista MM, Batista DDGJ, Boykin DW, De Koning HP, Correia Soeiro MN.
12-05-2023
Pathogens.
https://pubmed.ncbi.nlm.nih.gov/37242371/

Chagas disease (CD) affects over 6 million people worldwide and can be transmitted iatrogenically. Crystal violet (CV) was previously used for pathogen reduction but has harmful side-effects. In the present study, three arylimidamides (AIAs) and CV were used to sterilize mice blood samples experimentally contaminated with bloodstream trypomastigotes (BT) of *Trypanosoma cruzi*, at non hemolytic doses. All AIAs were not toxic to mouse blood cells until the highest tested concentration (96 µM). The previous treatment of BT with the AIAs impaired the infection establishment of cardiac cell cultures. In vivo assays showed that pre-incubation of mouse blood samples with the AIAs and CV (96 µM) significantly suppressed the parasitemia peak, but only the AIA DB1831 gave ≥90% animal survival, while vehicle treated samples reached 0%. Our findings support further studies regarding the potential use of AIAs for blood bank purposes.

Dipeptide Nitrile CD34 with Curcumin: A New Improved Combination Strategy to Synergistically Inhibit Rhodesain of Trypanosoma brucei rhodesiense.

Di Chio C, Previti S, Totaro N, De Luca F, Allegra A, Schirmeister T, Zappalà M, Ettari R.
09-05-2023
Int J Mol Sci.
https://pubmed.ncbi.nlm.nih.gov/37239824/

The Role of Spermidine and Its Key Metabolites in Important, Pathogenic Human Viruses and in Parasitic Infections Caused by Plasmodium falciparum and Trypanosoma brucei.

Kaiser A.
09-05-2023
Biomolecules.
https://pubmed.ncbi.nlm.nih.gov/37238673/

Seasonal Variation and Factors Affecting Trypanosoma theileri Infection in Wild Sika Deer (Ezo Sika Deer Cervus nippon yesoensis) in Eastern Hokkaido.

Hong Y, Suganuma K, Ohari Y, Kayano M, Nakazaki K, Fukumoto S, Kawazu SI, Inoue N.
22-05-202
Animals (Basel).
https://pubmed.ncbi.nlm.nih.gov/37238137/

Iron Uptake Controls Trypanosoma cruzi Metabolic Shift and Cell Proliferation.

Dick CF, Alcantara CL, Carvalho-Kelly LF, Lacerda-Abreu MA, Cunha-E-Silva NL, Meyer-Fernandes JR, Vieyra A.
22-04-2023
Antioxidants (Basel).
https://pubmed.ncbi.nlm.nih.gov/37237850/

(1) Background: Ionic transport in *Trypanosoma cruzi* is the object of intense studies. *T. cruzi* expresses a Fe-reductase (TcFR) and a Fe transporter (TcIT). We investigated the effect of Fe depletion and Fe supplementation on different structures and functions of *T. cruzi* epimastigotes in culture. (2) Methods: We investigated growth and metacyclogenesis, variations of intracellular Fe, endocytosis of transferrin, hemoglobin, and albumin by cell cytometry, structural changes of organelles by transmission electron microscopy, O_2 consumption by oximetry, mitochondrial membrane potential measuring JC-1 fluorescence at different wavelengths, intracellular ATP by bioluminescence, succinate-cytochrome c oxidoreductase following reduction of ferricytochrome c, production of H_2O_2 following oxidation of the Amplex® red probe, superoxide dismutase (SOD) activity following the reduction of nitroblue tetrazolium, expression of SOD, elements of the protein kinase A (PKA) signaling, TcFR and TcIT by quantitative PCR, PKA activity by luminescence, glyceraldehyde-3-phosphate dehydrogenase abundance and activity by Western blotting and NAD^+ reduction, and glucokinase activity recording $NADP^+$ reduction. (3) Results: Fe depletion increased oxidative stress, inhibited mitochondrial function and ATP formation, increased lipid accumulation in the reservosomes, and inhibited differentiation toward trypomastigotes, with the simultaneous metabolic shift from respiration to glycolysis. (4) Conclusion: The processes modulated for ionic Fe provide energy for the *T. cruzi* life cycle and the propagation of Chagas disease.

In Vitro Effects of Aminopyridyl Ligands Complexed to Copper(II) on the Physiology and Interaction Process of Trypanosoma cruzi.

Silva-Oliveira R, Sangenito LS, Reddy A, Velasco-Torrijos T, Santos ALS, Branquinha MH.
21-05-2023
Trop Med Infect Dis.
https://pubmed.ncbi.nlm.nih.gov/37235336/

Chagas disease is derived from the infection by the protozoan *Trypanosoma cruzi*. In many countries, benznidazole is the only drug approved for clinical use

despite several side effects and the emergence of resistant parasite strains. In this context, our group has previously pointed out that two novel aminopyridine derivatives complexed with Cu^{2+}, namely, *cis*-aquadichloro(*N*-[4-(hydroxyphenyl)methyl]-2-pyridinemethamino)copper (**3a**) and its glycosylated ligand *cis*-dichloro (*N*-{[4-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyloxy)pheny]lmethyl}-2-pyridinemethamino)copper (**3b**), are effective against *T. cruzi* trypomastigote forms. With this result in mind, the present work aimed to investigate the effects of both compounds on trypomastigotes physiology and on the interaction process with host cells. Apart from loss of plasma membrane integrity, an increased generation of reactive oxygen species (ROS) and decreased mitochondrial metabolism were observed. Pretreatment of trypomastigotes with these metallodrugs inhibited the association index with LLC-MK_2 cells in a typical dose-dependent manner. Both compounds showed low toxicity on mammalian cells (CC_{50} > 100 µM), and the IC_{50} values calculated for intracellular amastigotes were determined as 14.4 µM for **3a** and 27.1 µM for **3b**. This set of results demonstrates the potential of these aminopyridines complexed with Cu^{2+} as promising candidates for further antitrypanosomal drug development.

Chagas Disease Diagnostic Testing in Two Academic Hospitals in New Orleans, Louisiana: A Call to Action.

Proaño A, Dumonteil E, Herrera C.
15-05-2023
Trop Med Infect Dis.
https://pubmed.ncbi.nlm.nih.gov/37235325/

Geographic Distribution of the Genus Panstrongylus Berg, 1879 in the Neotropic with Emphasis on Trypanosoma cruzi Vectors.

Tineo-González E, Fermín R, Bonilla-Rivero A, Herrera L.
11-05-2023
Trop Med Infect Dis.
https://pubmed.ncbi.nlm.nih.gov/37235320/

Panstrongylus is a Neotropical taxa of 16 species, some more widespread than others, that act as vectors of Trypanosoma cruzi, the etiologic agent of Chagas disease (CD). This group is associated with mammalian reservoir niches. There are few studies of the biogeography and niche suitability of these triatomines. Using zoo-epidemiological occurrence databases, the distribution of Panstrongylus was determined based on bioclimatic modelling (DIVA GIS), parsimonious niche distribution (MAXENT), and parsimony analysis of endemic species (PAE). Through 517 records, a wide presence of P. geniculatus, P. rufotuberculatus, P. lignarius, and P. megistus was determined and recorded as frequent vectors of T. cruzi in rainforest habitats of 24-30 °C. These distributions were modeled with AUC >0.80 and <0.90, as well as with the seasonality of temperature, isothermality, and precipitation as relevant bioclimatic variables. Individual traces for each taxon in Panstrongylus-1036 records-showed widely dispersed lines for frequent vectors P. geniculatus, P. lignarius, P. rufotuberculatus, and P. megistus. Other occasional vectors showed more restricted dispersal, such as P. howardi, P. humeralis, P. lenti, P. lutzi, P. tupynambai, P. noireaiui, and P. chinai. Areas of defined environmental variation, geological change, and trans domain fluid fauna, such as the American Transition Zone and the Pacific Domain of Morrone, had the highest Panstrongylus diversity. Pan-biogeographic nodes appear to be areas of the greatest species diversity that act as corridors connecting biotopes and allowing fauna migration. Vicariance events in the geologic history of the continent need to be investigated. The geographical distribution of Panstrongylus overlapped with CD cases and Didelphis marsupialis/Dasypus novemcinctus presence, two important reservoirs in Central and South America. The information derived from the distribution of Panstrongylus provides knowledge for surveillance and vector control programs. It would increase information on the most and less relevant vector species of this zoonotic agent, for monitoring their population behavior.

Lupeol Acetate and α-Amyrin Terpenes Activity against Trypanosoma cruzi: Insights into Toxicity and Potential Mechanisms of Action.

Pardo-Rodriguez D, Cifuentes-López A, Bravo-Espejo J, Romero I, Robles J, Cuervo C, Mejía SM, Tellez J.
03-05-2023
Trop Med Infect Dis.
https://pubmed.ncbi.nlm.nih.gov/37235311/

Characterization of External Female Genitalia in Five Triatoma Laporte Species of South America (Hemiptera: Reduviidae: Triatominae).

Oliveira-Correia JPS, Gil-Santana HR, Dos Santos-Mallet JR, Galvão C.
23-04-2023
Trop Med Infect Dis.
https://pubmed.ncbi.nlm.nih.gov/37235288/

Currently, there are 158 valid species of triatomines, all of which are potential vectors of *Trypanosoma cruzi*, the etiological agent of Chagas disease. The correct taxonomic identification of triatomines is essential since each species hos a different epidemiological importance. The aim of the study is to compare five species of South American *Triatoma*. Here we present a comparative study of terminal abdominal segments in females by scanning electron microscopy (SEM) of the species *Triatoma delpontei*, *T. jurbergi*, *T. infestans* var. *melanosoma*, *T. platensis*, and *T. vandae*. The results showed diagnostic characters for the studied species. The dorsal view featured more valuable characters, with seven informative characters. Similarities were observed among *T. delpontei*, *T. infestans* var. *melanosoma*, and *T. platensis*, and between *T. jurbergi* and *T. vandae*, correlating with previous studies. Thus, female genital characters proved to be reliable and useful in the diagnosis of the *Triatoma* species studied here; additional studies, along with other sets of behavioral, morphological, and molecular data, helped to reinforce the hypotheses found here.

Detection of Trypanosoma evansi in a naturally infected cat in Indonesia using bioassay and molecular techniques.

Priyowidodo D, Sahara A, Prastowo J, Nurcahyo W, Firdausy LW.
Avr-2023
Vet World.
https://pubmed.ncbi.nlm.nih.gov/37235144/