



## **Veille scientifique**

### **Maladies tropicales négligées**

**Semaine 26**  
*26 juin au 02 juillet 2023*

Cysticercose	2
Dengue, chikungunya et maladie à virus Zika	3
Dracunculose	21
Echinococcose	22
Filariose lymphatique	25
Gale	26
Helminthiases transmises par le sol (ascaridiose, trichuriase, ankylostomiase)	27
Leishmaniose	28
Lèpre	37
Morsures de serpent	42
Mycétome	44
Onchocercose	44
Pian	45
Rage	45
Schistosomiase	48
Trachome	51
Trématodoses d'origine alimentaire (clonorchiose, opisthorchiase, fasciolase et paragonimose)	52
Trypanosomes (trypanosomiase et maladie de Chagas)	54
Ulcère de Buruli	59

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## Cysticercose

### Development and Laboratory Evaluation of a Simple, Field-Applicable Coproantigen Enzyme-Linked Immunosorbent Assay for Diagnosis of Taeniasis in Northern Peru.

Castillo Y, Wardle MT, Gamboa R, Elizalde M, Vilchez P, Rodriguez S, Gilman RH, Gonzalez AE, O'Neal SE, Garcia HH.

27-06-2023

*J Clin Microbiol.*

<https://pubmed.ncbi.nlm.nih.gov/37367233/>

Coproantigen detection by enzyme-linked immunosorbent assay (coAg ELISA) is a vital tool for detecting and treating cases of *Taenia solium* taeniasis. However, the assay's procedures require costly materials and sophisticated equipment, which are typically inaccessible in rural settings where the disease is endemic. To overcome these barriers, we developed and evaluated a field-applicable coAg ELISA. The field coAg ELISA was developed and evaluated across four phases using known positive and negative stool samples collected from northern Peru. Phase I focused on field assay development, phase II on a small-scale performance evaluation, phase III on a large-scale evaluation, and phase IV on the use and reliability of a colorimetric scale card. All samples were processed using the field and standard assay procedures and compared using signal-to-noise ratios, correlation tests, performance characteristics, and agreement statistics where appropriate. The field coAg ELISA using reagents stored at -20°C and commercially available water and milk powder, and relying on spontaneous separation of the supernatant, had performance comparable to the standard assay. The field coAg ELISA was strongly correlated with the standard in both the small- and large-scale laboratory evaluation ( $r = 0.99$  and  $r = 0.98$ , respectively). Finally, the field assay had an almost perfect agreement between independent readers ( $\kappa = 0.975$ ) and between each reader and the spectrophotometer. The field coAg ELISA demonstrated performance comparable to the standard, providing a low-cost alternative to the standard assay for identifying cases of intestinal taeniasis in a low-resource setting.

### Parasitic Eye Diseases: Nuances in Rapid Identification and Advanced Microscopy.

Das D, Rehman O, Bhattacharjee K, Bhattacharjee H, Jyoti Barman M, Choudhury A, Deka A, Islam S.

26-06-2023

*Ocul Immunol Inflamm.*

<https://pubmed.ncbi.nlm.nih.gov/37364062/>

**Aim:** To study parasitic eye diseases in a tertiary institute of North-east India by live examination of parasites, rapid staining, and scanning electron microscopy (SEM). **Methods:** A 12-year retrospective analysis was performed and all patients diagnosed with ocular parasitic diseases were identified. Examination under a compound microscope, fluorescein staining, and scanning electron

microscopy were done. **Results:** A total of 160 ocular parasitosis cases were identified. The cases for which rapid staining and SEM studies were done included Cysticercosis ( $n = 18$ , 11.25%), Hydatidosis ( $n = 5$ , 3.13%), Dirofilariasis ( $n = 5$ , 3.13%), Thelaziasis ( $n = 3$ , 1.87%), and Gnathostomiasis ( $n = 2$ , 1.25%). Live examination was performed in 11 cases (6.63%) and 8 cases (4.82%) underwent scanning electron microscopy. **Conclusion:** Fluorescein staining for identification of parasites and SEM study helped in detailing microscopic and ultrastructural findings.

### An institutional experience of hydatidosis and cysticercosis in Nepal: a retrospective chart review.

Sharma N, Tiwari SB, Gaire P, Manandhar U, Bohara S, Nepal G.

17-05-2023

*Ann Med Surg (Lond).*

<https://pubmed.ncbi.nlm.nih.gov/37363564/>

This study aimed to investigate the demographic characteristics, anatomical distribution, and histopathological features of hydatidosis and cysticercosis in a Nepalese population presenting to a tertiary care hospital. The study also aimed to provide a better understanding of the clinical and pathological aspects of these diseases in the local context. **Methods:** This retrospective study analyzed all cases of hydatidosis and cysticercosis reported in the Department of Pathology at Tribhuvan University Teaching Hospital between January 2013 and December 2019. Demographic, clinical, radiological, and histopathological data were collected and analyzed from hospital charts. **Results:** During the 7-year study period, the authors identified 112 cases of hydatid cysts and 26 cases of cysticercosis. The mean age of patients with hydatidosis was 33.86 years (range: 5-74 years), while the mean age of patients with cysticercosis was 25.39 years (range: 4-63 years). Females were more commonly affected with hydatidosis (68, 61.7%) than males (44, 39.3%), resulting in a male-to-female ratio of 0.6:1. In contrast, there was no significant sex difference in cysticercosis cases, with 14 (53.85%) males and 12 (46.15%) females affected. The most commonly affected site for hydatid cysts was the lung (47 cases, 42%), followed by the liver (41 cases, 36.6%). The study identified three cases of neurocysticercosis. The average diameter of hydatid cysts and cysticercosis was 8.7 cm and 1.7 cm, respectively. **Conclusion:** In conclusion, our study provides important insights into the clinical and pathological features of hydatidosis and cysticercosis in a Nepalese population. These zoonotic diseases pose a significant health burden, particularly among the poor and marginalized populations. Our findings highlight the need to integrate prevention and control measures into the healthcare system to decrease the overall burden of these diseases.

### Seroprevalence of porcine cysticercosis in traditional farms in South-Eastern Côte d'Ivoire.

Koffi KE, Soumahoro MK, N'Dri KB, Nowakowski M, Guédé CM, Boka OM, Melki J, Touré OA, Djaman J, Bellalou J, N'Goran KE, Jambou R.  
02-06-2023

*Parasite Epidemiol Control.*

<https://pubmed.ncbi.nlm.nih.gov/37361928/>

### **Triplex ELISA for Assessing Durability of *Taenia solium* Seropositivity after Neurocysticercosis Cure.**

Tang NL, Nash TE, Corda M, Nutman TB, O'Connell EM.  
Juil-2023

*Emerg Infect Dis.*

<https://pubmed.ncbi.nlm.nih.gov/37347506/>

Neurocysticercosis prevalence estimates often are based on serosurveys. However, assessments of *Taenia solium* seropositivity durability in patients with various neurocysticercosis types are lacking. We optimized a triplex serologic ELISA by using synthetic GP50, T24H, and Ts18var3 antigens for *T. solium*. We used that assay to test sequential serologic responses over several years after neurocysticercosis cure in 46 patients, 9 each with parenchymal or ventricular neurocysticercosis and 28 with subarachnoid disease. Triplex results were concordant with 98% of positive and 100% of negative enzyme-linked immunoelectrotransfer blots. Eight years after neurocysticercosis cure, 11.1% of patients with parenchymal, 47.3% with subarachnoid, and 41.7% with ventricular disease were still seropositive. Median time to seroreversion after cure in this cohort in a *T. solium* nonendemic area was 2 years for parenchymal disease, 4 years for ventricular disease, and 8 years for subarachnoid disease. Our findings can inform epidemiologic models that rely on serosurveys to estimate disease burden.

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## **Dengue, chikungunya et maladie à virus Zika**

### **Stealth invaders: unraveling the mystery of neurotropic viruses and their elusive presence in cerebrospinal fluid - a comprehensive review.**

Srichawla BS, Kipkorir V, Manan MR, Dhali A, Diebel S, Sawant T, Zia S, Carrion-Alvarez D, Suteja RC, Nurani K, Găman MA.

27-04-2023

*Ann Med Surg (Lond).*

<https://pubmed.ncbi.nlm.nih.gov/37363567/>

Neurotropic viruses are a threat to human populations due to ongoing zoonosis. A wide array of neurological manifestations can occur most often including parkinsonism, encephalitis/encephalopathy, flaccid myelitis, and Guillain-Barré syndrome. Neuroinvasion occurs through: transneural transmission, blood brain barrier (BBB) dysfunction, and 'trojan horse' mechanism or infected immune cell trafficking into the central nervous system (CNS). Transneural transmission occurs through virus mediated hijacking of intracellular transport proteins allowing retrograde viral transport. BBB dysfunction

occurs through cytokine storm increasing membrane permissibility. Increased chemokine expression allows leukocyte trafficking to the BBB. Virally infected leukocytes may successfully pass through the BBB allowing the pathogen to infect microglia and other CNS cell types. We define cerebrospinal fluid (CSF) nondetection as a virus' ability to evade direct CSF detection but still causing significant neurological symptoms and disease. Mechanisms of CSF nondetection include: transneuronal propagation through trans-synaptic transmission, and synaptic microfusion, as well as intrathecal antibody synthesis and virus neutralization. Direct virus detection in CSF is associated with an increased neurological disease burden. However, the lack of CSF detection does not exclude CNS involvement due to possible neuroevasive mechanisms.

### **Dreadful infectious disease outbreaks threaten flood-ravaged pakistan: short communication.**

Shaikh OA, Rahim M, Essarani M, Nadeem S, Ochani S, Hasibuzzaman MA, Ullah K.

03-05-2023

*Ann Med Surg (Lond).*

<https://pubmed.ncbi.nlm.nih.gov/37363565/>

### **A short communication of 2022 dengue outbreak in Bangladesh: a continuous public health threat.**

Islam MA, Hemo MK, Marzan AA, Arman MS, Hasan MN, Haque MA, Bhattacharya P.

12-04-2023

*Ann Med Surg (Lond).*

<https://pubmed.ncbi.nlm.nih.gov/37363468/>

Dengue virus infection, a highly prominent health concern, has caused many health complications, positive cases, and deaths in Bangladesh in previous years. However, the prevalence of this infection and fatality rates in 2022 has shattered all prior records. The dengue virus vector, mosquitoes, found a high prevalence of infection due to the weather's favorable conditions for breeding in the months of June and July. While there is presently no particular vaccination for dengue infection, awareness of its epidemiology, pathogenesis, signs, and symptoms may aid in the development of improved diagnostic and treatment strategies. The government should also improve the infrastructure of cities to make prevent mosquito breeding and the spread of dengue infection.

### ***Aedes aegypti* and *Aedes albopictus* (Diptera: Culicidae) ecology, biology, behaviour, and implications on arbovirus transmission in Thailand: Review.**

Ahebwa A, Hii J, Neoh KB, Chareonviriyaphap T.

30-04-2023

*One Health.*

<https://pubmed.ncbi.nlm.nih.gov/37363263/>

### **The pathology of co-infection with Usutu virus and Plasmodium spp. in naturally infected Eurasian blackbirds (*Turdus merula*).**

**Agliani G, Giglia G, de Bruin E, van Mastrigt T, Blom R, Sikkema RS, Kik M, Koopmans MPG, Gröne A, Van den Brand JMA.**

01-04-2023

*One Health.*

<https://pubmed.ncbi.nlm.nih.gov/37363251/>

Usutu virus (USUV) is a mosquito-borne zoonotic flavivirus causing mortality in Eurasian blackbirds (*Turdus merula*) in Europe. In dead blackbirds, avian malaria co-infection due to mosquito-borne hemsporidians (e.g., *Plasmodium* spp.) has been reported. In humans, a similar co-infection of a flavivirus, Dengue virus, and *Plasmodium* spp. is causing increased severity of clinical disease. Currently, the effects of co-infection of arboviruses and hemsporidians in blackbirds remain unclear. This study investigates the rate of USUV and *Plasmodium* spp. co-infection in found-dead blackbirds ( $n = 203$ ) from 2016 to 2020 in the Netherlands. Presence of *Plasmodium* spp. was evaluated by cytology (43/203; 21,2%), histopathology (94/186; 50,5%) and qPCR (179/203; 88,1%). The severity of histological lesions in USUV and *Plasmodium* spp. co-infected dead blackbirds (121/203; 59,6%) were compared with those in *Plasmodium* spp. single-infected cases. Additionally, since no knowledge is present on the infection rate on live birds and mosquitoes in the Netherlands, a small group of live blackbirds ( $n = 12$ ) and selected in the field-collected mosquito pools ( $n = 96$ ) in 2020 were tested for the presence of *Plasmodium* spp. The latter was detected in the tested live blackbirds by qPCR (8/10; 80%), and cytology (3/11; 27,3%) and in the mosquito pools by qPCR (18/96; 18,7%). For this study, co-infection between USUV and *Plasmodium* spp. was observed only in the dead blackbirds. The high *Plasmodium* spp. presence, associated with lower lesions score, in single infected found dead birds suggest a predominantly smaller pathogenic role as single agent. On the other hand, the higher histological lesion scores observed in USUV and *Plasmodium* spp. co-infected birds suggests a major pathogenic role for the virus or an increased severity of the lesions due to a possible interplay of the two agents.

### **A clinical perspective of chitosan nanoparticles for infectious disease management.**

**Dilnawaz F, Acharya S, Kanungo A.**

05-04-2023

*Polym Bull (Berl).*

<https://pubmed.ncbi.nlm.nih.gov/37362954/>

Infectious diseases and their effective management are still a challenge in this modern era of medicine. Diseases, such as the SARS-CoV-2, Ebola virus, and Zika virus, still put human civilization at peril. Existing drug banks, which include antivirals, antibacterial, and small-molecule drugs, are the most advocated method for treatment, although effective but they still flounder in many instances. This calls for finding more effective alternatives for tackling the

menace of infectious diseases. Nanoformulations are progressively being implemented for clinical translation and are being considered a new paradigm against infectious diseases. Natural polymers like chitosan are preferred to design nanoparticles owing to their biocompatibility, biodegradation, and long shelf-life. The chitosan nanoparticles (CNPs) being highly adaptive delivers contemporary prevention for infectious diseases. Currently, they are being used as antibacterial, drug, and vaccine delivery vehicles, and wound-dressing materials, for infectious disease treatment. Although the recruitment of CNPs in clinical trials associated with infectious diseases is minimal, this may increase shortly due to the sudden emergence of unknown pathogens like SARS-CoV-2, thus turning them into a panacea for the management of microorganisms. This review particularly focuses on the all-around application of CNPs along with their recent clinical applications in infectious disease management.

### **Strategies in the optimization of DNA hybridization conditions and its role in electrochemical detection of dengue virus (DENV) using response surface methodology (RSM).**

**Abdul Rashid JI, Yusof NA, Abdullah J, Shomiad Shueb RH.**

16-06-2023

*RSC Adv.*

<https://pubmed.ncbi.nlm.nih.gov/37362605/>

### **Maternal Zika Virus Infection in the First Trimester and Fetal Stigmata in the Third Trimester.**

**Singh D, Kaur L.**

31-01-2023

*Indian J Radiol Imaging.*

<https://pubmed.ncbi.nlm.nih.gov/37362378/>

Zika is a flavivirus that is transmitted primarily by the bite of an infected Aedes mosquito. It can also be transmitted by blood transfusion, sexual contact, and from an infected mother to the unborn baby. Zika virus infection is of particular concern in pregnancy as transplacental transmission of the virus has the potential to cause significant fetal morbidity. Ultrasonography plays a pivotal role in the fetal surveillance of a pregnant woman infected with Zika. There have been outbreaks of Zika virus infection in various parts of India, the most recent occurring in Kanpur in November 2021. We report a case of a primigravida who had Zika virus infection during the first trimester of pregnancy but the fetus presented with the sequelae of infection in the third trimester. This report highlights the sonographic red flags for fetal Zika infection and the importance of serial monitoring in pregnant women exposed to Zika virus.

### **Early infectious diseases identification based on complex probabilistic hesitant fuzzy N-soft information.**

**Ashraf S, Kousar M, Hameed MS.**

16-05-2023

*Soft comput.*

<https://pubmed.ncbi.nlm.nih.gov/37362277/>

This paper aims to assess and deal with the challenges experienced by medical professionals caring for infectious diseases. In Pakistan, public health is still a serious concern and the main contributor to morbidity and mortality is infectious diseases. The major issue is a resemblance in the clinical symptoms of infectious diseases such as tuberculosis, hepatitis, COVID-19, dengue, and malaria. Early detection of infectious disease is crucial in order to start treatment with counseling and medication. This can only be done if several infections with similar clinical traits can be diagnosed depending on several criteria, including the availability of various kits, the ability to carry out diagnostic procedures, money, and technical staff. But woefully Pakistan's economy is badly battered due to several circumstances. Therefore, we are unable to provide patients with enough diagnostic testing kits and broadly accessible therapy choices, which makes diagnosis more difficult and create hesitancy with fuzziness and randomness. For this purpose, we introduced the new concept of the complex probabilistic hesitant fuzzy N-soft set. We defined its fundamental operations (like restricted and extended union, restricted and extended intersection, weak, top and bottom weak complements, as well as soft max-AND or soft min-OR) with examples. We also discussed their many properties with their proofs and theorems. Furthermore, we developed the algorithms for decision-making where doctors use the complex probabilistic hesitant fuzzy N-soft information to identify a particular disease. Furthermore, we explained numerical illustration of two case studies. Moreover, a sensitive and comparative analysis is discussed. In the last, we conclude the whole study.

### **The buzz in the field: the interaction between viruses, mosquitoes, and metabolism.**

**Ratnayake OC, Chotiwan N, Saavedra-Rodriguez K, Perera R.**

26-04-2023

*Front Cell Infect Microbiol.*

<https://pubmed.ncbi.nlm.nih.gov/37360524/>

### **A novel approach for rapid and sensitive detection of Zika virus utilizing silver nanoislands as SERS platform.**

**Tripathi MN, Jangir P, Aakriti, Rai S, Gangwar M, Nath G, Saxena PS, Srivastava A.**

19-06-2023

*Spectrochim Acta A Mol Biomol Spectrosc.*

<https://pubmed.ncbi.nlm.nih.gov/37356391/>

To control the spread of the disease, the Zika virus (ZIKV), a flavivirus infection spread by mosquitoes and common in across the world, needs to be accurately and promptly diagnosed. This endeavour gets challenging when early-stage illnesses have low viral loads. As a result, we have created a biosensor based on surface-enhanced Raman scattering (SERS) for the quick, accurate, and timely diagnosis of the Zika virus. In this study, a glass coverslip was coated with silver nanoislands, which were then

utilized as the surface for creating the sensing platform. Silver nanoislands exhibit strong plasmonic activity and good conductive characteristics. It enhances the Raman signals as a result and gives the SERS platform an appropriate surface. The created platform has been applied to Zika virus detection. With a limit of detection (LOD) of 0.11 ng/mL, the constructed sensor exhibits a linear range from 5 ng/mL to 1000 ng/mL. Hence, even at the nanogram scale, this technique may be a major improvement over clinical diagnosis approaches for making proper, precise, and accurate Zika virus detection.

### **Multiobjective optimization to assess dengue control costs using a climate-dependent epidemiological model.**

**de Vasconcelos ASV, de Lima JS, Cardoso RTN.**

24-06-2023

*Sci Rep.*

<https://pubmed.ncbi.nlm.nih.gov/37355697/>

Arboviruses, diseases transmitted by arthropods, have become a significant challenge for public health managers. The World Health Organization highlights dengue as responsible for millions of infections worldwide annually. As there is no specific treatment for the disease and no free-of-charge vaccine for mass use in Brazil, the best option is the measures to combat the vector, the *Aedes aegypti* mosquito. Therefore, we proposed an epidemiological model dependent on temperature, precipitation, and humidity, considering symptomatic and asymptomatic dengue infections. Through computer simulations, we aimed to minimize the amount of insecticides and the social cost demanded to treat patients. We proposed a case study in which our model is fitted with real data from symptomatic dengue-infected humans in an epidemic year in a Brazilian city. Our multiobjective optimization model considers an additional control using larvicide, adulticide, and ultra-low volume spraying. The work's main contribution is studying the monetary cost of the actions to combat the vector demand versus the hospital cost per confirmed infected, comparing approaches with and without additional control. Results showed that the additional vector control measures are cheaper than the hospital treatment without the vector control would be.

### **FEN1-aided recombinase polymerase amplification (FARPA) for one-pot and multiplex detection of nucleic acids with an ultra-high specificity and sensitivity.**

**Ma Y, Wu H, Chen S, Xie C, Hu J, Qi X, Ma X, Chu Y, Shan J, Lu Y, Cui L, Zou B, Zhou G.**

13-06-2023

*Biosens Bioelectron.*

<https://pubmed.ncbi.nlm.nih.gov/37354713/>

### **Interventions against Aedes/dengue at the household level: a systematic review and meta-analysis.**

**Montenegro-Quiñonez CA, Louis VR, Horstick O, Velayudhan R, Dambach P, Runge-Ranzinger S.**

21-06-2023



### Development of virus-like particles with inbuilt immunostimulatory properties as vaccine candidates.

Collett S, Earnest L, Carrera Montoya J, Edeling MA, Yap A, Wong CY, Christiansen D, Roberts J, Mumford J, Lecouturier V, Pavot V, Marco S, Loi JK, Simmons C, Gulab SA, Mackenzie JM, Elbourne A, Ramsland PA, Cameron G, Hans D, Godfrey DI, Torresi J.

07-06-2023

*Front Microbiol.*

<https://pubmed.ncbi.nlm.nih.gov/37350788/>

The development of virus-like particle (VLP) based vaccines for human papillomavirus, hepatitis B and hepatitis E viruses represented a breakthrough in vaccine development. However, for dengue and COVID-19, technical complications, such as an incomplete understanding of the requirements for protective immunity, but also limitations in processes to manufacture VLP vaccines for enveloped viruses to large scale, have hampered VLP vaccine development. Selecting the right adjuvant is also an important consideration to ensure that a VLP vaccine induces protective antibody and T cell responses. For diseases like COVID-19 and dengue fever caused by RNA viruses that exist as families of viral variants with the potential to escape vaccine-induced immunity, the development of more efficacious vaccines is also necessary. Here, we describe the development and characterisation of novel VLP vaccine candidates using SARS-CoV-2 and dengue virus (DENV), containing the major viral structural proteins, as prototypes for a novel approach to produce VLP vaccines. The VLPs were characterised by Western immunoblot, enzyme immunoassay, electron and atomic force microscopy, and *in vitro* and *in vivo* immunogenicity studies. Microscopy techniques showed proteins self-assemble to form VLPs authentic to native viruses. The inclusion of the glycolipid adjuvant,  $\alpha$ -galactosylceramide ( $\alpha$ -GalCer) in the vaccine formulation led to high levels of natural killer T (NKT) cell stimulation *in vitro*, and strong antibody and memory CD8<sup>+</sup> T cell responses *in vivo*, demonstrated with SARS-CoV-2, hepatitis C virus (HCV) and DEN VLPs. This study shows our unique vaccine formulation presents a promising, and much needed, new vaccine platform in the fight against infections caused by enveloped RNA viruses.

### Singapore's 5 decades of dengue prevention and control-Implications for global dengue control.

Ho SH, Lim JT, Ong J, Hapuarachchi HC, Sim S, Ng LC.

22-06-2023

*PLoS Negl Trop Dis.*

<https://pubmed.ncbi.nlm.nih.gov/37347767/>

### Safety and immunogenicity of a single-shot live-attenuated chikungunya vaccine: a double-blind, multicentre, randomised, placebo-controlled, phase 3 trial.

Schneider M, Narciso-Abraham M, Hadl S, McMahon R, Toepfer S, Fuchs U, Hochreiter R, Bitzer A, Kosulin K, Larcher-Senn J, Mader R, Dubischar K, Zoihs O, Jaramillo JC, Eder-Lingelbach S, Buerger V, Wressnigg N.

24-06-2023

*Lancet.*

<https://pubmed.ncbi.nlm.nih.gov/37321235/>

**Background:** VLA1553 is a live-attenuated vaccine candidate for active immunisation and prevention of disease caused by chikungunya virus. We report safety and immunogenicity data up to day 180 after vaccination with VLA1553. **Methods:** This double-blind, multicentre, randomised, phase 3 trial was done in 43 professional vaccine trial sites in the USA. Eligible participants were healthy volunteers aged 18 years and older. Patients were excluded if they had history of chikungunya virus infection or immune-mediated or chronic arthritis or arthralgia, known or suspected defect of the immune system, any inactivated vaccine received within 2 weeks before vaccination with VLA1553, or any live vaccine received within 4 weeks before vaccination with VLA1553. Participants were randomised (3:1) to receive VLA1553 or placebo. The primary endpoint was the proportion of baseline negative participants with a seroprotective chikungunya virus antibody level defined as 50% plaque reduction in a micro plaque reduction neutralisation test ( $\mu$ PRNT) with a  $\mu$ PRNT<sub>50</sub> titre of at least 150, 28 days after vaccination. The safety analysis included all individuals who received vaccination. Immunogenicity analyses were done in a subset of participants at 12 pre-selected study sites. These participants were required to have no major protocol deviations to be included in the per-protocol population for immunogenicity analyses. This trial is registered at ClinicalTrials.gov, [NCT04546724](https://clinicaltrials.gov/ct2/show/study/NCT04546724). **Findings:** Between Sept 17, 2020 and April 10, 2021, 6100 people were screened for eligibility. 1972 people were excluded and 4128 participants were enrolled and randomised (3093 to VLA1553 and 1035 to placebo). 358 participants in the VLA1553 group and 133 participants in the placebo group discontinued before trial end. The per-protocol population for immunogenicity analysis comprised 362 participants (266 in the VLA1553 group and 96 in the placebo group). After a single vaccination, VLA1553 induced seroprotective chikungunya virus neutralising antibody levels in 263 (98.9%) of 266 participants in the VLA1553 group (95% CI 96.7-99.8;  $p < 0.0001$ ) 28 days post-vaccination, independent of age. VLA1553 was generally safe with an adverse event profile similar to other licensed vaccines and equally well tolerated in younger and older adults. Serious adverse events were reported in 46 (1.5%) of 3082 participants exposed to VLA1553 and eight (0.8%) of 1033 participants in the placebo arm. Only two serious adverse events were considered related to VLA1553 treatment (one mild myalgia and one syndrome of inappropriate antidiuretic hormone secretion). Both participants recovered fully. **Interpretation:** The strong immune response and the generation of seroprotective titres in almost all vaccinated participants suggests that VLA1553 is an excellent candidate for the prevention of disease caused by chikungunya virus.

### Live-attenuated Chikungunya vaccine: a possible new era.

Stephenson KE.

24-06-2023

*Lancet*.

<https://pubmed.ncbi.nlm.nih.gov/37321234/>

### Susceptibility of *Aedes albopictus*, *Ae. aegypti* and human populations to Ross River virus in Kuala Lumpur, Malaysia.

Fu JYL, Chua CL, Abu Bakar AS, Vythilingam I, Wan Sulaiman WY, Alphey L, Chan YF, Sam IC.

12-06-2023

*PLoS Negl Trop Dis*.

<https://pubmed.ncbi.nlm.nih.gov/37307291/>

### Oviposition Preferences of *Aedes aegypti* in Msambweni, Kwale County, Kenya.

Musunzaji PS, Ndenga BA, Mzee S, Abubakar LU, Kitron UD, Labeaud AD, Mutuku FM.

01-06-2023

*J Am Mosq Control Assoc*.

<https://pubmed.ncbi.nlm.nih.gov/37270926/>

*Aedes aegypti* is the primary vector of dengue fever virus (DENV) worldwide. Infusions made from organic materials have been shown to act as oviposition attractants for *Ae. aegypti*; however, studies on locally suitable infusion materials are lacking. The current study assessed the suitability of 4 locally available materials as oviposition infusions for use in surveillance and control of *Ae. aegypti* in Kwale County, Kenya. Oviposition infusion preferences were assessed in laboratory, semifield, and field conditions, using 4 infusions made from banana, grass, neem, and coconut. In addition, ovitrapping in wall, grass, bush, and banana microhabitats was done in 10 houses each in urban and rural coastal households to determine suitable oviposition microhabitats. Overall, the highest oviposition responses were observed for banana infusion, followed by neem and grass infusions, which were comparable. Coconut infusion resulted in the lowest oviposition response. Although female *Ae. aegypti* did not show preference for any microhabitat, the oviposition activity across all the microhabitats was highly enhanced by use of the organic infusions. Banana, neem, and grass infusions could be used to attract gravid mosquitoes to oviposition sites laced with insecticide to kill eggs. Additionally, banana plantings could be important targets for integrated vector control programs.

### 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.

15-06-2023

*Bioorg Med Chem*.

<https://pubmed.ncbi.nlm.nih.gov/37253304/>

### Climate change and vector-borne diseases: a multi-omics approach of

### temperature-induced changes in the mosquito.

Bellone R, Lechat P, Mousson L, Gilbert V, Piorkowski G, Bohers C, Merits A, Kornobis E, Reveillaud J, Paupy C, Vazeille M, Martinet JP, Madec Y, De Lamballerie X, Dauga C, Failloux AB.

23-06-2023

*J Travel Med*.

<https://pubmed.ncbi.nlm.nih.gov/37171132/>

**Background:** Climate change and globalization contribute to the expansion of mosquito vectors and their associated pathogens. Long spared, temperate regions have had to deal with the emergence of arboviruses traditionally confined to tropical regions. Chikungunya virus (CHIKV) was reported for the first time in Europe in 2007, causing a localized outbreak in Italy, which then recurred repeatedly over the years in other European localities. This raises the question of climate effects, particularly temperature, on the dynamics of vector-borne viruses. The objective of this study is to improve the understanding of the molecular mechanisms set up in the vector in response to temperature. **Methods:** We combine three complementary approaches by examining *Aedes albopictus* mosquito gene expression (transcriptomics), bacterial flora (metagenomics) and CHIKV evolutionary dynamics (genomics) induced by viral infection and temperature changes. **Results:** We show that temperature alters profoundly mosquito gene expression, bacterial microbiome and viral population diversity. We observe that (i) CHIKV infection upregulated most genes (mainly in immune and stress-related pathways) at 20°C but not at 28°C, (ii) CHIKV infection significantly increased the abundance of Enterobacteriaceae *Serratia marcescens* at 28°C and (iii) CHIKV evolutionary dynamics were different according to temperature. **Conclusion:** The substantial changes detected in the vectorial system (the vector and its bacterial microbiota, and the arbovirus) lead to temperature-specific adjustments to reach the ultimate goal of arbovirus transmission; at 20°C and 28°C, the Asian tiger mosquito *Ae. albopictus* was able to transmit CHIKV at the same efficiency. Therefore, CHIKV is likely to continue its expansion in the northern regions and could become a public health problem in more countries than those already affected in Europe.

### Soluble NS1 Antagonizes IgG- and IgA-Mediated Monocytic Phagocytosis of DENV Infected Cells.

Waldran MJ, Wegman AD, Bahr LE, Roy NH, Currier JR, Waickman AT.

28-06-2023

*J Infect Dis*.

<https://pubmed.ncbi.nlm.nih.gov/37103221/>

Dengue virus (DENV) is endemic in >100 countries, infecting an estimated 400 million individuals every year. Infection with DENV raises an antibody response primarily targeting viral structural proteins. However, DENV encodes several immunogenic nonstructural (NS) proteins, one of which, NS1, is expressed on the membrane of DENV-infected cells. IgG and IgA isotype antibodies that bind NS1 are abundant in serum following

DENV infection. Our study aimed to determine if NS1-binding IgG and IgA isotype antibodies contribute to the clearance of DENV-infected cells by antibody-mediated cellular phagocytosis. We observed that both IgG and IgA isotype antibodies can facilitate monocytic uptake of DENV NS1-expressing cells in an FcγRI- and FcαRI-dependent fashion. Interestingly, this process was antagonized by the presence of soluble NS1, suggesting that the production of soluble NS1 by infected cells may serve as immunological chaff, antagonizing opsonization and clearance of DENV-infected cells.

### Flaviviruses and the Traveler: Around the World and to Your Stage. A Review of West Nile, Yellow Fever, Dengue, and Zika Viruses for the Practicing Pathologist.

Hale GL.

Juin-2023

*Mod Pathol.*

<https://pubmed.ncbi.nlm.nih.gov/37059228/>

### Production and Characterization of Two Specific ZIKV Antigens Based on Bioinformatic Analysis and Serological Screening.

Ribeiro Mota Souza R, Campos GS, Hughes Carvalho R, Brandão Peixoto I, Santos Galante R, Santana Moreira L, Beutinger Marchioro S, José Meyer Nascimento R, Sardi SI.

Nov-2023

*Immunol Invest.*

<https://pubmed.ncbi.nlm.nih.gov/37036441/>

**Background:** The high structural similarity between the Zika virus (ZIKV) and other flaviviruses, such as Dengue Virus (DENV), complicates the identification of the infecting virus due to the occurrence of cross-reactions in serological assays. This phenomenon has increased the demand for more specific antigens for immunodiagnostic applications. **Methods:** The present work aimed to identify specific regions of ZIKV and produce unique antigens through computational methods, molecular and microbiological techniques. **Results:** Based on the computational analysis we successfully expressed two recombinant proteins derived from specific regions of the ZIKV. Through serological assays using characterized sera, we observed that the region 146-182 of ZIKV's E protein, expressed in tandem, was not reactive despite the predictive sensitivity and specificity observed by computer analyses. On the other hand, the non-denatured fraction 220-352 of ZIKV's NS1 showed greater specificity to IgG+ sera of ZIKV by dot blot and western blot, which highlights its properties as a possible tool in the diagnosis of ZIKV. **Conclusion:** These findings demonstrate that ZIKV NS1 fraction 220-352 is a potential tool that may be applied in the development of serological diagnosis. We also provided data that suggest the non-applicability of the region 146-182 of ZIKV's protein E in serological assays despite previous indications about its potential based on computational analysis.

### Detection of DENV-2 and ZIKV coinfection in southeastern Brazil by serum and urine testing.

da Conceição PJP, de Carvalho LR, de Godoy BLV, Nogueira ML, Terzian ACB, de Godoy MF, Calmon MF, Bittar C, Rahal P.

Juin-2023

*Med Microbiol Immunol.*

<https://pubmed.ncbi.nlm.nih.gov/37029306/>

### Paper-based electrochemical biosensors for the diagnosis of viral diseases.

Ataide VN, Pradela-Filho LA, Ameku WA, Negahdary M, Oliveira TG, Santos BG, Paixão TRLC, Angnes L.

27-06-2023

*Mikrochim Acta.*

<https://pubmed.ncbi.nlm.nih.gov/37368054/>

Paper-based electrochemical analytical devices (ePADs) have gained significant interest as promising analytical units in recent years because they can be fabricated in simple ways, are low-cost, portable, and disposable platforms that can be applied in various fields. In this sense, paper-based electrochemical biosensors are attractive analytical devices since they can promote diagnose several diseases and potentially allow decentralized analysis. Electrochemical biosensors are versatile, as the measured signal can be improved by using mainly molecular technologies and nanomaterials to attach biomolecules, resulting in an increase in their sensitivity and selectivity. Additionally, they can be implemented in microfluidic devices that drive and control the flow without external pumping and store reagents, and improve the mass transport of analytes, increasing sensor sensitivity. In this review, we focus on the recent developments in electrochemical paper-based devices for viruses' detection, including COVID-19, Dengue, Zika, Hepatitis, Ebola, AIDS, and Influenza, among others, which have caused impacts on people's health, especially in places with scarce resources. Also, we discuss the advantages and disadvantages of the main electrode's fabrication methods, device designs, and biomolecule immobilization strategies. Finally, the perspectives and challenges that need to be overcome to further advance paper-based electrochemical biosensors' applications are critically presented.

### Angiotensin II and dengue.

Mosquera-Sulbaran JA, Pedreañez A, Hernandez-Fonseca JP, Hernandez-Fonseca H.

27-06-2023

*Arch Virol.*

<https://pubmed.ncbi.nlm.nih.gov/37368044/>

### Aedes aegypti, Ae. albopictus and Culex quinquefasciatus Adults Found Coexisting in Urban and Semiurban Dwellings of Southern Chiapas, Mexico.

Lopez-Solis AD, Solis-Santoyo F, Saavedra-Rodriguez K, Sanchez-Guillen D, Castillo-Vera A, Gonzalez-Gomez R, Rodriguez AD, Penilla-Navarro P.



17-06-2023

*Insects.*

<https://pubmed.ncbi.nlm.nih.gov/37367381/>

Tapachula, Mexico, a tropical city, is an endemic area for dengue, in addition to several outbreaks in the last decade with chikungunya and Zika. As part of the migratory corridor from Central to North America and the risks of scattered infectious diseases that this implies, the identification and distribution of potential disease vectors in and around residential areas are essential in terms of entomological surveillance for the prevention of disease outbreaks. The identification of mosquito species of medical importance coexisting in houses and cemeteries in Tapachula and two semiurban sites in southern Chiapas was investigated. Adult mosquitoes were collected from May to December 2018, resting inside and outside houses and in the tombstones and fallen tree leaves in cemeteries. A total of 10,883 mosquitoes belonging to three vector species were collected across 20 sites; 6738 were from neighborhood houses, of which 55.4% were *Culex quinquefasciatus*, 41.6% *Aedes aegypti*, and 2.9% *Ae. albopictus*. *Aedes aegypti* was the most common mosquito resting inside houses (56.7%), while *Ae. albopictus* and *Cx. quinquefasciatus* were mostly found resting outside houses (75.7%). In the cemeteries, *Cx. quinquefasciatus* (60.8%) and *Ae. albopictus* (37.3%) were the most abundant, while *Ae. aegypti* (1.9%) was the least abundant. This is the first report to identify adults of three major disease vector species coexisting in the domestic environment of urban and semiurban sites and *Ae. albopictus* adult resting inside of urban houses in Mexico. It would be opportune to consider comprehensive strategies that can be applied in this region to control the three species at the same time and avoid outbreaks of the diseases they transmit.

### **Genetic Differentiation of *Aedes aegypti* (Diptera: Culicidae) in Areas with High Rates of Infestation in Mid-North Region of Brazil.**

Rodrigues LF, Sousa AA, Mendes Júnior WP, Cardoso E Silva AC, Nascimento MHSD, Barros MC, Sampaio I, Fraga EDC.

06-06-2023

*Insects.*

<https://pubmed.ncbi.nlm.nih.gov/37367345/>

*Aedes aegypti* is the principal vector of the arboviruses-yellow fever, dengue virus, chikungunya, and Zika virus. Given the epidemiological importance of this mosquito, its capacity to adapt to different habitats, and its resistance to many types of control measures, systematic research into the genetic variability of the populations of this mosquito is one of the most important steps toward a better understanding of its population structure and vector competence. In this context, the present study verified the presence of distinct genetic lineages of *Ae. aegypti* in areas with high infestation rates, based on the analysis of microsatellite markers. The samples were collected in nine municipalities with high building infestation rates in the Mid-North region of Brazil. Six microsatellite loci were genotyped in the 138 samples, producing a total of 32 alleles, varying from one to nine

alleles per locus in each of the different populations. The AMOVA revealed greater within-population genetic differentiation with high fixation rates. The general analysis of population structure, based on a Bayesian approach, revealed  $K = 2$ , with two *Ae. aegypti* lineages that were highly differentiated genetically. These data on the connectivity of the populations and the genetic isolation of the lineages provide important insights for the development of innovative strategies for the control of the populations of this important disease vector.

### **Experimental Dengue Virus Type 4 Infection Increases the Expression of MicroRNAs-15/16, Triggering a Caspase-Induced Apoptosis Pathway.**

Casseb SMM, Melo KFL, Carvalho CAM, Santos CRD, Franco ECS, Vasconcelos PFDC.

26-05-2023

*Curr Issues Mol Biol.*

<https://pubmed.ncbi.nlm.nih.gov/37367040/>

### **Molecularly Imprinted Polymer-Based Electrochemical Sensors for the Diagnosis of Infectious Diseases.**

Pilvenyte G, Ratautaite V, Boguzaite R, Ramanavicius S, Chen CF, Viter R, Ramanavicius A.

05-06-2023

*Biosensors (Basel).*

<https://pubmed.ncbi.nlm.nih.gov/37366985/>

### **Dengue hemorrhagic fever with bleeding and fluid overload in a patient with active lupus nephritis: a case report of diagnostic and therapeutic challenges.**

Vidanapathirana M, Atukorala I.

26-06-2023

*BMC Infect Dis.*

<https://pubmed.ncbi.nlm.nih.gov/37365496/>

### **Prevalence and Predictors of COVID-19 Long-Term Symptoms: A Cohort Study from the Amazon Basin.**

Silva KM, Freitas DCA, Medeiros SS, Miranda LVA, Carmo JBM, Silva RG, Becker LL, Abreu ES, Buranello L, Souza MSM, Nadruz W, Fernandes-Silva MM, Maguire JH, Toledo-Cornell C, Silvestre OM.

26-06-2023

*Am J Trop Med Hyg.*

<https://pubmed.ncbi.nlm.nih.gov/37364863/>

It remains unclear whether a previous history of tropical infectious diseases and a second SARS-CoV-2 infection may influence the likelihood of later symptoms. In this prospective cohort study, individuals infected with SARS-CoV-2 were followed up by telephone shortly after diagnosis of COVID-19 and again 12 months later. Poisson regression was used to identify the predictors of the highest number of symptoms in the post-COVID-19 syndrome. A total of 1,371 patients with COVID-19, with a mean age of  $39.7 \pm 11.7$  years and 50% female, were followed for 12 months. Reinfection was found in 32

(2.3%) participants, and 806 (58.8%) individuals reported a previous history of dengue, malaria, Zika, chikungunya, leprosy, and visceral leishmaniasis. Eight hundred seventy-seven (63.9%) participants reported late symptoms related to COVID-19. After adjusting for multiple factors, female sex, non-White race, number of acute-phase symptoms, body mass index, and reinfection were independent predictors of higher number of symptoms in post-COVID-19 syndrome. Female sex, non-White race, number of acute-phase symptoms, body mass index, and reinfection, but not previous endemic tropical diseases, were associated with long-term symptoms.

### Prevalence, Characteristics, and Outcomes Associated with Acute Kidney Injury among Adult Patients with Severe Dengue in Mainland China.

**Wang C, Hong W, Ou Z, Yang H, Zhao L, Zhang Z, Zhang F.**  
26-06-2023

*Am J Trop Med Hyg.*

<https://pubmed.ncbi.nlm.nih.gov/37364862/>

### Boophilin D1, a Kunitz type protease inhibitor, as a source of inhibitors for the ZIKA virus NS2B-NS3 protease.

**Manzato VM, Di Santo C, Torquato RJS, Coelho C, Gallo G, Hardy L, Würtele M, Tanaka AS.**

24-06-2023

*Biochimie.*

<https://pubmed.ncbi.nlm.nih.gov/37364769/>

Arboviruses are a global concern for a multitude of reasons, including their increased incidence and human mortality. Vectors associated with arboviruses include the mosquito *Aedes* sp., which is responsible for transmitting the Zika virus. Flaviviruses, like the Zika virus, present only one chymotrypsin-like serine protease (NS3) in their genome. Together with host enzymes, the NS2B co-factor NS3 protease complex are essential for the viral replication cycle by virus polyprotein processing. To search for Zika virus NS2B-NS3 protease (ZIKV<sub>Pro</sub>) inhibitors, a phage display library was constructed using the Boophilin domain 1 (BoophD1), a thrombin inhibitor from the Kunitz family. A BoophilinD1 library mutated at positions P1-P4' was constructed, presenting a titer of  $2.9 \times 10^6$  (cfu), and screened utilizing purified ZIKV<sub>Pro</sub>. The results demonstrated at the P1-P4' positions the occurrence of 47% RALHA sequence (mut 12) and 11.8% RASWA sequence (mut14), SMRPT, or KALIP (wt) sequence. BoophD1-wt and mutants 12 and 14 were expressed and purified. The purified BoophD1 wt, mut 12 and 14, presented  $K_i$  values for ZIKV<sub>Pro</sub> of 0.103, 0.116, and 0.101  $\mu$ M, respectively. The BoophD1 mutant inhibitors inhibit the Dengue virus 2 protease (DENV2) with  $K_i$  values of 0.298, 0.271, and 0.379  $\mu$ M, respectively. In conclusion, BoophD1 mut 12 and 14 selected for ZIKV<sub>Pro</sub> demonstrated inhibitory activity like BoophD1-wt, suggesting that these are the strongest Zika inhibitors present in the BoophD1 mutated phage display library. Furthermore, BoophD1 mutants selected for ZIKV<sub>Pro</sub> inhibit both Zika and Dengue 2 proteases making them potential pan-flavivirus inhibitors.

### Design, synthesis, antiviral evaluation, and In silico studies of acrylamides targeting nsP2 from Chikungunya virus.

**Souza BG, Choudhary S, Vilela GG, Passos GFS, Costa CACB, Freitas JD, Coelho GL, Brandão JA, Anderson L, Bassi ÊJ, Araújo-Júnior JX, Tomar S, Silva-Júnior EFD.**

19-06-2023

*Eur J Med Chem.*

<https://pubmed.ncbi.nlm.nih.gov/37364511/>

The Togaviridae family comprises several New- and Old-World Alphaviruses that have been responsible for thousands of human illnesses, including the RNA arbovirus Chikungunya virus (CHIKV). Firstly, it was reported in Tanzania in 1952 but rapidly it spread to several countries from Europe, Asia, and the Americas. Since then, CHIKV has been circulating in diverse countries around the world, leading to increased morbidity rates. Currently, there are no FDA-approved drugs or licensed vaccines to specifically treat CHIKV infections. Thus, there is a lack of alternatives to fight against this viral disease, making it an unmet need. Structurally, CHIKV is composed of five structural proteins (E3, E2, E1, C, and 6k) and four non-structural proteins (nsP1-4), in which nsP2 represents an attractive antiviral target for designing novel inhibitors since it has an essential role in the virus replication and transcription. Herein, we used a rational drug design strategy to select some acrylamide derivatives to be synthesized and evaluated against CHIKV nsP2 and also screened on CHIKV-infected cells. Thus, two regions of modifications were considered for these types of inhibitors, based on a previous study of our group, generating 1560 possible inhibitors. Then, the 24 most promising ones were synthesized and screened by using a FRET-based enzymatic assay protocol targeting CHIKV nsP2, identifying LQM330, 333, 336, and 338 as the most potent inhibitors, with  $K_i$  values of  $48.6 \pm 2.8$ ,  $92.3 \pm 1.4$ ,  $2.3 \pm 1.5$ , and  $181.8 \pm 2.5$   $\mu$ M, respectively. Still, their  $K_m$  and  $V_{max}$  kinetic parameters were also determined, along with their competitive binding modes of CHIKV nsP2 inhibition. Then, ITC analyses revealed  $K_D$  values of 127, 159, 198, and 218  $\mu$ M for LQM330, 333, 336, and 338, respectively. Also, their  $\Delta H$ ,  $\Delta S$ , and  $\Delta G$  physicochemical parameters were determined. MD simulations demonstrated that these inhibitors present a stable binding mode with nsP2, interacting with important residues of this protease, according to docking analyzes. Moreover, MM/PBSA calculations displayed that van der Waals interactions are mainly responsible for stabilizing the inhibitor-nsP2 complex, and their binding energies corroborated with their  $K_i$  values, having  $-198.7 \pm 15.68$ ,  $-124.8 \pm 17.27$ ,  $-247.4 \pm 23.78$ , and  $-100.6 \pm 19.21$  kcal/mol for LQM330, 333, 336, and 338, respectively. Since Sindbis (SINV) nsP2 is similar to CHIKV nsP2, these best inhibitors were screened against SINV-infected cells, and it was verified that LQM330 presented the best result, with an  $EC_{50}$  value of  $0.95 \pm 0.09$   $\mu$ M. Even at 50  $\mu$ M concentration, LQM338 was found to be cytotoxic on Vero cells after 48 h. Then, LQM330, 333, and 336 were evaluated against CHIKV-infected cells in antiviral assays, in which LQM330 was found to be the most promising antiviral candidate in this study, exhibiting an  $EC_{50}$  value of  $5.2 \pm 0.52$   $\mu$ M and SI of 31.78. The intracellular flow cytometry demonstrated that

LQM330 is able to reduce the CHIKV cytopathogenic effect on cells, and also reduce the percentage of CHIKV-positive cells from  $66.1\% \pm 7.05$  to  $35.8\% \pm 5.78$  at 50  $\mu\text{M}$  concentration. Finally, qPCR studies demonstrated that LQM330 was capable of reducing the number of viral RNA copies/ $\mu\text{L}$ , suggesting that CHIKV nsP2 is targeted by this inhibitor as its mechanism of action.

### **A Habitat Model for Disease Vector *Aedes aegypti* in the Tampa Bay Area, FloridaA.**

**Uelmen JA, Mapes CD, Prasauskas A, Boohene C, Burns L, Stuck J, Carney RM.**

01-06-2023

*J Am Mosq Control Assoc.*

<https://pubmed.ncbi.nlm.nih.gov/37364184/>

### **Curcumin interferes with chitin synthesis in *Aedes aegypti*: a computational and experimental investigation.**

**Rao P, Ninama J, Dudhat M, Goswami D, Rawal RM.**

26-06-2023

*Mol Divers.*

<https://pubmed.ncbi.nlm.nih.gov/37358753/>

Throughout history, vector-borne diseases have consistently posed significant challenges to human health. Among the strategies for vector control, chemical insecticides have seen widespread use since their inception. Nevertheless, their effectiveness is continually undermined by the steady growth of insecticide resistance within these vector populations. As such, the demand for more robust, efficient, and cost-effective natural insecticides has become increasingly pressing. One promising avenue of research focuses on chitin, a crucial structural component of mosquitoes' exoskeletons and other insects. Chitin not only provides protection and rigidity but also lends flexibility to the insect body. It undergoes substantial transformations during insect molting, a process known as ecdysis. Crucially, the production of chitin is facilitated by an enzyme known as chitin synthase, making it an attractive target for potential novel insecticides. Our recent study delved into the impacts of curcumin, a natural derivative of turmeric, on chitin synthesis and larval development in *Aedes aegypti*, a mosquito species known to transmit dengue and yellow fever. Our findings demonstrate that even sub-lethal amounts of curcumin can significantly reduce overall chitin content and disrupt the cuticle development in the 4th instar larvae of *Aedes aegypti*. Further to this, we utilized computational analyses to investigate how curcumin interacts with chitin synthase. Techniques such as molecular docking, pharmacophore feature mapping, and molecular dynamics (MD) simulations helped to illustrate that curcumin binds to the same site as polyoxin D, a recognized inhibitor of chitin synthase. These findings point to curcumin's potential as a natural, bioactive larvicide that targets chitin synthase in mosquitoes and potentially other insects.

### **Reemergence of Dengue Virus Serotype 3, Brazil, 2023.**

**Naveca FG, Santiago GA, Maito RM, Ribeiro Meneses CA, do Nascimento VA, de Souza VC, do Nascimento FO, Silva D, Mejía M, Gonçalves L, de Figueiredo RMP, Ribeiro Cruz AC, Diniz Nunes BT, Presibella MM, Quallio Marques NF, Riediger IN, de Mendonça MCL, de Bruycker-Nogueira F, Sequeira PC, de Filippis AMB, Resende P, Campos T, Wallau GL, Gräf T, Delatorre E, Kopp E, Morrison A, Muñoz-Jordán JL, Bello G.**

Juill-2023

*Emerg Infect Dis.*

<https://pubmed.ncbi.nlm.nih.gov/37347884/>

### **Long non-coding RNAs regulate *Aedes aegypti* vector competence for Zika virus and reproduction.**

**Belavilas-Trovas A, Tastsoglou S, Dong S, Kefi M, Tavadia M, Mathiopoulou KD, Dimopoulos G.**

15-06-2023

*PLoS Pathog.*

<https://pubmed.ncbi.nlm.nih.gov/37319296/>

Long non-coding RNAs (lncRNAs) play critical regulatory roles in various cellular and metabolic processes in mosquitoes and all other organisms studied thus far. In particular, their involvement in essential processes such as reproduction makes them potential targets for the development of novel pest control approaches. However, their function in mosquito biology remains largely unexplored. To elucidate the role of lncRNAs in mosquitoes' reproduction and vector competence for arboviruses, we have implemented a computational and experimental pipeline to mine, screen, and characterize lncRNAs related to these two biological processes. Through analysis of publicly available Zika virus (ZIKV) infection-regulated *Aedes aegypti* transcriptomes, at least six lncRNAs were identified as being significantly upregulated in response to infection in various mosquito tissues. The roles of these ZIKV-regulated lncRNAs (designated Zinc1, Zinc2, Zinc3, Zinc9, Zinc10 and Zinc22), were further investigated by dsRNA-mediated silencing studies. Our results show that silencing of Zinc1, Zinc2, and Zinc22 renders mosquitoes significantly less permissive to ZIKV infection, while silencing of Zinc22 also reduces fecundity, indicating a potential role for Zinc22 in trade-offs between vector competence and reproduction. We also found that silencing of Zinc9 significantly increases fecundity but has no effect on ZIKV infection, suggesting that Zinc9 may be a negative regulator of oviposition. Our work demonstrates that some lncRNAs play host factor roles by facilitating viral infection in mosquitoes. We also show that lncRNAs can influence both mosquito reproduction and permissiveness to virus infection, two biological systems with important roles in mosquito vectorial capacity.

### **Shared Molecular Signatures Across Zika Virus Infection and Multiple Sclerosis Highlight AP-1 Transcription Factor as a Potential Player in Post-ZIKV MS-Like Phenotypes.**

**da Silva EV, Fontes-Dantas FL, Dantas TV, Dutra A, Nascimento OJM, Alves-Leon SV.**

**Aug-2023**

*Mol Neurobiol.*

<https://pubmed.ncbi.nlm.nih.gov/37046138/>

Zika virus (ZIKV) is an arbovirus of the Flaviviridae genus that has rapidly disseminated from across the Pacific to the Americas. Robust evidence has indicated a crucial role of ZIKV in congenital virus syndrome, including neonatal microcephaly. Moreover, emerging evidence suggests an association between ZIKV infection and the development of an extensive spectrum of central nervous system inflammatory demyelinating diseases (CNS ID), such as multiple sclerosis-like clinical phenotypes. However, the underlying mechanisms of host-pathogen neuro-immune interactions remain to be elucidated. This study aimed to identify common transcriptional signatures between multiple sclerosis (MS) and ZIKV infection to generate molecular interaction networks, thereby leading to the identification of deregulated processes and pathways, which could give an insight of these underlying molecular mechanisms. Our investigation included publicly available transcriptomic data from MS patients in either relapse or remission (RR-MS) and datasets of subjects acutely infected by ZIKV for both immune peripheral cells and central nervous system cells. The protein-protein interaction (PPI) analysis showed upregulated AP-1 transcription factors (JUN and FOS) among the top hub and bottleneck genes in RR-MS and ZIKV data. Gene enrichment analysis retrieved a remarkable presence of ontologies and pathways linked to oxidative stress responses, immune cell function, inflammation, interleukin signaling, cell division, and transcriptional regulation commonly enriched in both scenarios. Considering the recent findings concerning AP-1 function in immunological tolerance breakdown, regulation of inflammation, and its function as an oxidative stress sensor, we postulate that the ZIKV trigger may contribute as a boost for the activation of such AP-1-regulated mechanisms that could favor the development of MS-like phenotypes following ZIKV infection in a genetically susceptible individual.

### **Spectrum of Disorders associated with Tetany.**

**Santra G.**

**Mar-2023**

*J Assoc Physicians India.*

<https://pubmed.ncbi.nlm.nih.gov/37354510/>

**Introduction:** Awareness regarding the etiological spectrum of tetany is poor among physicians. Because of poor awareness, tetany is underdiagnosed and undertreated. **Materials and methods:** Databases like PubMed, PubMed Central, Scopus, and Google Scholar are searched to identify peer-reviewed articles on tetany. Case reports, case series, and original articles are analyzed to identify different causes of tetany prevalent in the community. Different causes found are analyzed and tabulated, and finally, a flowchart is made on the approach for diagnosing different underlying pathologies of tetany. **Results:** Both metabolic and respiratory alkalosis are important causes of tetany because of reduced ionized

calcium levels. Gitelman syndrome (GS) is associated with metabolic alkalosis, hypokalemia, hypomagnesemia and hypocalciuria, and frequently causes normocalcemic tetany. Recurrent vomiting and primary hyperaldosteronism also cause tetany due to metabolic alkalosis. Hyperventilation syndrome (HVS) leads to respiratory alkalosis and is a frequent cause of tetany. Hyperventilation-induced tetany is also seen after spinal anesthesia and in respiratory disorders like asthma. Vitamin D deficiency (VDD), primary hypoparathyroidism, and pseudohypoparathyroidism (PHP) (1a, 1b, and 2) cause hypocalcemic tetany. Hypomagnesemia causes hypocalcemia and tetany due to peripheral parathyroid hormone resistance and impaired parathyroid hormone secretion. Drugs causing tetany include bisphosphonates, denosumab, cisplatin, antiepileptics, aminoglycosides, diuretics, etc. Tetany is also seen in acute pancreatitis, dengue, falciparum malaria, hyperemesis gravidarum, tumor lysis syndrome (TLS), massive blood transfusion, etc. Conclusion: The spectrum of disorders associated with tetany is diverse. Awareness of different causes will help early and proper diagnosis of tetany.

### **Hirudin versus citrate as an anticoagulant for ROTEM platelet whole blood impedance aggregometry in thrombocytopenic patients.**

**Wickramasinghe W, Alvitigala BY, Perera T, Karunanayake P, Jayasinghe S, Rajapakse S, Weerasingha P, Wijewickrama A, Arya R, Goerlinger K, Gooneratne LV.**

**Dec-2023**

*Platelets.*

<https://pubmed.ncbi.nlm.nih.gov/37370234/>

### **Travel-Related Diagnoses Among U.S. Nonmigrant Travelers or Migrants Presenting to U.S. GeoSentinel Sites - GeoSentinel Network, 2012-2021.**

**Brown AB, Miller C, Hamer DH, Kozarsky P, Libman M, Huits R, Rizwan A, Emetulu H, Waggoner J, Chen LH, Leung DT, Bourque D, Connor BA, Licitra C, Angelo KM.**

**30-06-2023**

*MMWR Surveill Summ.*

<https://pubmed.ncbi.nlm.nih.gov/37368820/>

**Problem/condition:** During 2012-2021, the volume of international travel reached record highs and lows. This period also was marked by the emergence or large outbreaks of multiple infectious diseases (e.g., Zika virus, yellow fever, and COVID-19). Over time, the growing ease and increased frequency of travel has resulted in the unprecedented global spread of infectious diseases. Detecting infectious diseases and other diagnoses among travelers can serve as sentinel surveillance for new or emerging pathogens and provide information to improve case identification, clinical management, and public health prevention and response. **Reporting period:** 2012-2021. **Description of system:** Established in 1995, the GeoSentinel Network (GeoSentinel), a collaboration between CDC and the International Society of Travel Medicine, is a global, clinical-care-based surveillance and research network of travel and tropical medicine sites that

monitors infectious diseases and other adverse health events that affect international travelers. GeoSentinel comprises 71 sites in 29 countries where clinicians diagnose illnesses and collect demographic, clinical, and travel-related information about diseases and illnesses acquired during travel using a standardized report form. Data are collected electronically via a secure CDC database, and daily reports are generated for assistance in detecting sentinel events (i.e., unusual patterns or clusters of disease). GeoSentinel sites collaborate to report disease or population-specific findings through retrospective database analyses and the collection of supplemental data to fill specific knowledge gaps. GeoSentinel also serves as a communications network by using internal notifications, ProMed alerts, and peer-reviewed publications to alert clinicians and public health professionals about global outbreaks and events that might affect travelers. This report summarizes data from 20 U.S. GeoSentinel sites and reports on the detection of three worldwide events that demonstrate GeoSentinel's notification capability.

**Results:** During 2012-2021, data were collected by all GeoSentinel sites on approximately 200,000 patients who had approximately 244,000 confirmed or probable travel-related diagnoses. Twenty GeoSentinel sites from the United States contributed records during the 10-year surveillance period, submitting data on 18,336 patients, of which 17,389 lived in the United States and were evaluated by a clinician at a U.S. site after travel. Of those patients, 7,530 (43.3%) were recent migrants to the United States, and 9,859 (56.7%) were returning nonmigrant travelers. Among the recent migrants to the United States, the median age was 28.5 years (range = <19 years to 93 years); 47.3% were female, and 6.0% were U.S. citizens. A majority (89.8%) were seen as outpatients, and among 4,672 migrants with information available, 4,148 (88.8%) did not receive pretravel health information. Of 13,986 diagnoses among migrants, the most frequent were vitamin D deficiency (20.2%), Blastocystis (10.9%), and latent tuberculosis (10.3%). Malaria was diagnosed in 54 (<1%) migrants. Of the 26 migrants diagnosed with malaria for whom pretravel information was known, 88.5% did not receive pretravel health information. Before November 16, 2018, patients' reasons for travel, exposure country, and exposure region were not linked to an individual diagnosis. Thus, results of these data from January 1, 2012, to November 15, 2018 (early period), and from November 16, 2018, to December 31, 2021 (later period), are reported separately. During the early and later periods, the most frequent regions of exposure were Sub-Saharan Africa (22.7% and 26.2%, respectively), the Caribbean (21.3% and 8.4%, respectively), Central America (13.4% and 27.6%, respectively), and South East Asia (13.1% and 16.9%, respectively). Migrants with diagnosed malaria were most frequently exposed in Sub-Saharan Africa (89.3% and 100%, respectively). Among nonmigrant travelers returning to the United States, the median age was 37 years (range = <19 years to 96 years); 55.7% were female, 75.3% were born in the United States, and 89.4% were U.S. citizens. A majority (90.6%) were seen as outpatients, and of 8,967 nonmigrant travelers with available information, 5,878 (65.6%) did not receive pretravel health information. Of 11,987 diagnoses, the most frequent were related to the gastrointestinal system

(5,173; 43.2%). The most frequent diagnoses among nonmigrant travelers were acute diarrhea (16.9%), viral syndrome (4.9%), and irritable bowel syndrome (4.1%). Malaria was diagnosed in 421 (3.5%) nonmigrant travelers. During the early (January 1, 2012, to November 15, 2018) and later (November 16, 2018, to December 31, 2021) periods, the most frequent reasons for travel among nonmigrant travelers were tourism (44.8% and 53.6%, respectively), travelers visiting friends and relatives (VFRs) (22.0% and 21.4%, respectively), business (13.4% and 12.3%, respectively), and missionary or humanitarian aid (13.1% and 6.2%, respectively). The most frequent regions of exposure for any diagnosis among nonmigrant travelers during the early and later period were Central America (19.2% and 17.3%, respectively), Sub-Saharan Africa (17.7% and 25.5%, respectively), the Caribbean (13.0% and 10.9%, respectively), and South East Asia (10.4% and 11.2%, respectively). Nonmigrant travelers who had malaria diagnosed were most frequently exposed in Sub-Saharan Africa (88.6% and 95.9% during the early and later period, respectively) and VFRs (70.3% and 57.9%, respectively). Among VFRs with malaria, a majority did not receive pretravel health information (70.2% and 83.3%, respectively) or take malaria chemoprophylaxis (88.3% and 100%, respectively).

**Interpretation:** Among ill U.S. travelers evaluated at U.S. GeoSentinel sites after travel, the majority were nonmigrant travelers who most frequently received a gastrointestinal disease diagnosis, implying that persons from the United States traveling internationally might be exposed to contaminated food and water. Migrants most frequently received diagnoses of conditions such as vitamin D deficiency and latent tuberculosis, which might result from adverse circumstances before and during migration (e.g., malnutrition and food insecurity, limited access to adequate sanitation and hygiene, and crowded housing.). Malaria was diagnosed in both migrants and nonmigrant travelers, and only a limited number reported taking malaria chemoprophylaxis, which might be attributed to both barriers to acquiring pretravel health care (especially for VFRs) and lack of prevention practices (e.g., insect repellent use) during travel. The number of ill travelers evaluated by U.S. GeoSentinel sites after travel decreased in 2020 and 2021 compared with previous years because of the COVID-19 pandemic and associated travel restrictions. GeoSentinel detected limited cases of COVID-19 and did not detect any sentinel cases early in the pandemic because of the lack of global diagnostic testing capacity.

**Public health action:** The findings in this report describe the scope of health-related conditions that migrants and returning nonmigrant travelers to the United States acquired, illustrating risk for acquiring illnesses during travel. In addition, certain travelers do not seek pretravel health care, even when traveling to areas in which high-risk, preventable diseases are endemic. Health care professionals can aid international travelers by providing evaluations and destination-specific advice. Health care professionals should both foster trust and enhance pretravel prevention messaging for VFRs, a group known to have a higher incidence of serious diseases after travel (e.g., malaria and enteric fever). Health care professionals should continue to advocate for medical care in underserved populations (e.g., VFRs and



migrants) to prevent disease progression, reactivation, and potential spread to and within vulnerable populations. Because both travel and infectious diseases evolve, public health professionals should explore ways to enhance the detection of emerging diseases that might not be captured by current surveillance systems that are not site based.

### **Emergence of a New Strain of DENV-2 in South America: Introduction of the Cosmopolitan Genotype through the Brazilian-Peruvian Border.**

**Amorim MT, Hernández LHA, Naveca FG, Essashika Prazeres IT, Wanzeller ALM, Silva EVPD, Casseb LMN, Silva FSD, da Silva SP, Nunes BTD, Cruz ACR.**

17-06-2023

*Trop Med Infect Dis.*

<https://pubmed.ncbi.nlm.nih.gov/37368743/>

Dengue virus 2 (DENV-2) seriously contributes to dengue-related mortality. It includes five nonsylvatic genotypes, with cosmopolitan being the most widespread with a significant contribution to the total number of DENV-2 cases globally. In South America, the cosmopolitan genotype was first recorded in 2019 in Madre de Dios, Peru, and then in Goiás (Midwest Brazil) in November 2021. In this study, we tested 163 human serum samples from Acre (Northern Brazil) collected during a DENV outbreak between 2020 and 2021 for all DENV genotypes by RT-qPCR. Of the 163 samples, 139 were positive for DENV-2, and 5 were positive for DENV-1. Five DENV-2-positive samples from early 2021 were sequenced, and the sequences clustered with the three other DENV-2 cosmopolitan genotype sequences already recorded on the continent. These results create a geographical link, suggesting the possible route of introduction of the DENV-2 cosmopolitan genotype into Brazil through the border with Peru, from which it may have dispersed to Midwest Brazil.

### **Epidemiology and Economic Burden of Chikungunya: A Systematic Literature Review.**

**Costa LB, Barreto FKA, Barreto MCA, Santos THPD, Andrade MMO, Farias LABG, Freitas ARR, Martinez MJ, Cavalcanti LPG.**

31-05-2023

*Trop Med Infect Dis.*

<https://pubmed.ncbi.nlm.nih.gov/37368719/>

Chikungunya (CHIK) is a re-emerging viral infection endemic in tropical and subtropical areas. While the typical clinical presentation is an acute febrile syndrome, long-term articular complications and even death can occur. This review characterizes the global epidemiological and economic burden of chikungunya. The search included studies published from 2007 to 2022 in MEDLINE, Embase, LILACS, and SciELO for a thorough evaluation of the literature. Rayyan software was used for data analysis, and data were summarized descriptively and reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Seventy-six publications were included. Chikungunya is widely distributed in the tropics, including Africa, Asia, South

America, and Oceania/the Pacific Islands, and co-circulates with other simultaneous arboviruses such as DENV, ZIKV, and YFV. Chikungunya infection can lead to chronic articular manifestations with a significant impact on the quality of life in the long term. In addition, it generates absenteeism and economic and social losses and can cause fatal infections in vulnerable populations, mainly in high-risk patients with co-morbidities and at the extremes of age. Reported costs associated with CHIKV diseases are substantial and vary by region, age group, and public/private delivery of healthcare services. The chikungunya disease burden includes chronicity, severe infections, increased hospitalization risks, and associated mortality. The disease can impact the economy in several spheres, significantly affecting the health system and national economies. Understanding and measuring the full impact of this re-emerging disease is essential.

### **Novel Essential Oils Blend as a Repellent and Toxic Agent against Disease-Transmitting Mosquitoes.**

**Kamaraj C, Satish Kumar RC, Al-Ghanim KA, Nicoletti M, Sathiyamoorthy V, Sarvesh S, Ragavendran C, Govindarajan M.**

08-06-2023

*Toxics.*

<https://pubmed.ncbi.nlm.nih.gov/37368617/>

### **Clinical-epidemiological characteristics of deaths due to dengue during an outbreak in northern Peru.**

**Luque N, Cilloniz C, Pons MJ, Donaires F, Albornoz R, Mendocilla-Risco M, Espinoza M.**

Jan-Mar 2023

*Rev Peru Med Exp Salud Publica.*

<https://pubmed.ncbi.nlm.nih.gov/37377238/>

Motivation for the study. To describe the characteristics of patients who died from severe dengue fever during the 2017 El Niño in Piura. Main findings. Mortality from severe dengue was higher in adult women. First contact with healthcare took place mostly in higher level hospitals. Admission to a specialized unit was late for severe dengue cases. Implications. Control of dengue fever involves several aspects, such as, access to health, prevention, water availability, vector control and education; therefore, it is important to strengthen public health policies in this regard. In order to achieve this goal, local and central government sectors must be involved.

### **Antiviral Activity of Catechin against Dengue Virus Infection.**

**Yi B, Chew BXZ, Chen H, Lee RCH, Fong YD, Chin WX, Mok CK, Chu JJH.**

15-06-2023

*Viruses.*

<https://pubmed.ncbi.nlm.nih.gov/37376676/>

### **An Update on Current Antiviral Strategies to Combat Human Cytomegalovirus Infection.**

**Panda K, Parashar D, Viswanathan R.**

12-06-2023

Viruses.

<https://pubmed.ncbi.nlm.nih.gov/37376657/>

### **Detection of Zika Virus in *Aedes aegypti* and *Aedes albopictus* Mosquitoes Collected in Urban Forest Fragments in the Brazilian Amazon.**

**Gomes EO, Sacchetto L, Teixeira M, Chaves BA, Hendy A, Mendonça C, Guimarães I, Linhares R, Brito D, Valério D, Cordeiro JSM, Neto AVS, Sampaio VS, Scarpassa VM, Buenemann M, Vasilakis N, Baia-da-Silva DC, Nogueira ML, Mourão MPG, Lacerda MVG.**

12-06-2023

Viruses.

<https://pubmed.ncbi.nlm.nih.gov/37376655/>

Zika virus (ZIKV) is an RNA flavivirus (*Flaviviridae* family) endemic in tropical and subtropical regions that is transmitted to humans by *Aedes (Stegomyia)* species mosquitoes. The two main urban vectors of ZIKV are *Aedes aegypti* and *Aedes albopictus*, which can be found throughout Brazil. This study investigated ZIKV infection in mosquito species sampled from urban forest fragments in Manaus (Brazilian Amazon). A total of 905 non-engorged female *Ae. aegypti* (22 specimens) and *Ae. albopictus* (883 specimens) were collected using BG-Sentinel traps, entomological hand nets, and Prokopack aspirators during the rainy and dry seasons between 2018 and 2021. All pools were macerated and used to inoculate C6/36 culture cells. Overall, 3/20 (15%) *Ae. aegypti* and 5/241 (2%) *Ae. albopictus* pools screened using RT-qPCR were positive for ZIKV. No supernatants from *Ae. aegypti* were positive for ZIKV (0%), and 15 out of 241 (6.2%) *Ae. albopictus* pools were positive. In this study, we provide the first-ever evidence of *Ae. albopictus* naturally infected with ZIKV in the Amazon region.

### **Novel Mode of nanoLuciferase Packaging in SARS-CoV-2 Virions and VLPs Provides Versatile Reporters for Virus Production.**

**Gullberg RC, Frydman J.**

07-06-2023

Viruses.

<https://pubmed.ncbi.nlm.nih.gov/37376634/>

### **Maternal Th17 Profile after Zika Virus Infection Is Involved in Congenital Zika Syndrome Development in Children.**

**Fialho EMS, Veras EM, Jesus CM, Gomes LN, Khouri R, Sousa PS, Ribeiro MRC, Batista RFL, Costa LC, Nascimento FRF, Silva AAM, Soeiro-Pereira PV.**

04-06-2023

Viruses.

<https://pubmed.ncbi.nlm.nih.gov/37376620/>

Brazil is one of the countries that experienced an epidemic of microcephaly and other congenital manifestations related to maternal Zika virus infection which can result in Congenital Zika Syndrome (CZS). Since the Zika virus can

modulate the immune system, studying mothers' and children's immune profiles become essential to better understanding CZS development. Therefore, we investigated the lymphocyte population profile of children who developed CZS and their mothers' immune response in this study. The study groups were formed from the Plaque Reduction Neutralization Test (PRNT) (CZS+ group) result. To evaluate the lymphocyte population profile, we performed phenotyping of peripheral lymphocytes and quantification of serum cytokine levels. The immunophenotyping and cytokine profile was correlated between CZS+ children and their mothers. Both groups exhibited increased interleukin-17 levels and a reduction in the subpopulation of CD4+ T lymphocytes. In contrast, the maternal group showed a reduction in the population of B lymphocytes. Thus, the development of CZS is related to the presence of an inflammatory immune profile in children and their mothers characterized by Th17 activation.

### **Gut Bacterial Diversity of Field and Laboratory-Reared *Aedes albopictus* Populations of Rio de Janeiro, Brazil.**

**Baltar JMC, Pavan MG, Corrêa-Antônio J, Couto-Lima D, Maciel-de-Freitas R, David MR.**

31-05-2023

Viruses.

<https://pubmed.ncbi.nlm.nih.gov/37376609/>

**Background:** The mosquito microbiota impacts different parameters in host biology, such as development, metabolism, immune response and vector competence to pathogens. As the environment is an important source of acquisition of host associate microbes, we described the microbiota and the vector competence to Zika virus (ZIKV) of *Aedes albopictus* from three areas with distinct landscapes. **Methods:** Adult females were collected during two different seasons, while eggs were used to rear F1 colonies. Midgut bacterial communities were described in field and F1 mosquitoes as well as in insects from a laboratory colony (>30 generations, LAB) using 16S rRNA gene sequencing. F1 mosquitoes were infected with ZIKV to determine virus infection rates (IRs) and dissemination rates (DRs). Collection season significantly affected the bacterial microbiota diversity and composition, e.g., diversity levels decreased from the wet to the dry season. Field-collected and LAB mosquitoes' microbiota had similar diversity levels, which were higher compared to F1 mosquitoes. However, the gut microbiota composition of field mosquitoes was distinct from that of laboratory-reared mosquitoes (LAB and F1), regardless of the collection season and location. A possible negative correlation was detected between Acetobacteraceae and *Wolbachia*, with the former dominating the gut microbiota of F1 *Ae. albopictus*, while the latter was absent/undetectable. Furthermore, we detected significant differences in infection and dissemination rates (but not in the viral load) between the mosquito populations, but it does not seem to be related to gut microbiota composition, as it was similar between F1 mosquitoes regardless of their population. **Conclusions:** Our results indicate that the environment and the

collection season play a significant role in shaping mosquitoes' bacterial microbiota.

### **Does Intra-Uterine Exposure to the Zika Virus Increase Risks of Cognitive Delay at Preschool Ages? Findings from a Zika-Exposed Cohort from Grenada, West Indies.**

Fernandes M, Evans R, Cheng M, Landon B, Noël T, Macpherson C, Cudjoe N, Burgen KS, Waechter R, LaBeaud AD, Blackmon K.

30-05-2023

Viruses.

<https://pubmed.ncbi.nlm.nih.gov/37376590/>

### **Retrospective Spatio-Temporal Dynamics of Dengue Virus 1, 2 and 4 in Paraguay.**

Vazquez C, Alcantara LCJ, Fonseca V, Lima M, Xavier J, Adelino T, Fritsch H, Castro E, de Oliveira C, Schuab G, Lima ARJ, Villalba S, Gomez de la Fuente A, Rojas A, Cantero C, Fleitas F, Aquino C, Ojeda A, Sequera G, Torales J, Barrios J, Elias MC, Iani FCM, Ortega MJ, Gamarra ML, Montoya R, Rodrigues ES, Kashima S, Sampaio SC, Coluchi N, Leite J, Gresh L, Franco L, Lourenço J, Rico JM, Bispo de Filippis AM, Giovanetti M.

30-05-2023

Viruses.

<https://pubmed.ncbi.nlm.nih.gov/37376575/>

### **Review on Main Arboviruses Circulating on French Guiana, An Ultra-Peripheral European Region in South America.**

Bonifay T, Le Turnier P, Epelboin Y, Carvalho L, De Thoisy B, Djossou F, Duchemin JB, Dussart P, Enfissi A, Lavergne A, Mutricy R, Nacher M, Rabier S, Talaga S, Talarmin A, Rousset D, Epelboin L.

29-05-2023

Viruses.

<https://pubmed.ncbi.nlm.nih.gov/37376570/>

French Guiana (FG), a French overseas territory in South America, is susceptible to tropical diseases, including arboviruses. The tropical climate supports the proliferation and establishment of vectors, making it difficult to control transmission. In the last ten years, FG has experienced large outbreaks of imported arboviruses such as *Chikungunya* and *Zika*, as well as endemic arboviruses such as dengue, *Yellow fever*, and *Oropouche* virus. Epidemiological surveillance is challenging due to the differing distributions and behaviors of vectors. This article aims to summarize the current knowledge of these arboviruses in FG and discuss the challenges of arbovirus emergence and reemergence. Effective control measures are hampered by the nonspecific clinical presentation of these diseases, as well as the *Aedes aegypti* mosquito's resistance to insecticides. Despite the high seroprevalence of certain viruses, the possibility of new epidemics cannot be ruled out. Therefore, active epidemiological surveillance is needed to identify potential outbreaks, and an adequate sentinel surveillance system and broad

virological diagnostic panel are being developed in FG to improve disease management.

### **Zika Virus Induces Degradation of the Numb Protein Required through Embryonic Neurogenesis.**

He J, Yang L, Chang P, Yang S, Wang Y, Lin S, Tang Q, Zhang Y.

27-05-2023

Viruses.

<https://pubmed.ncbi.nlm.nih.gov/37376558/>

### **ZIKV Strains Elicit Different Inflammatory and Anti-Viral Responses in Microglia Cells.**

Oliveira FBC, Freire VPASS, Coelho SVA, Meuren LM, Palmeira JDF, Cardoso AL, Neves FAR, Ribeiro BM, Argañaraz GA, Arruda LB, Argañaraz ER.

26-05-2023

Viruses.

<https://pubmed.ncbi.nlm.nih.gov/37376550/>

In recent years, the Zika Virus (ZIKV) has caused pandemic outbreaks associated with a high rate of congenital ZIKV syndrome (CZS). Although all strains associated with worldwide outbreaks derive from the Asian lineage, the reasons for their enhanced spread and severity are not fully understood. In this study, we conducted a comparative analysis of miRNAs (miRNA-155/146a/124) and their cellular targets (SOCS1/3, SHP1, TRAF6, IRAK1), as well as pro- and anti-inflammatory and anti-viral cytokines (IL-6, TNF- $\alpha$ , IFN- $\gamma$ , IL-10, and IFN- $\beta$ ) and peroxisome proliferator-activated receptor  $\gamma$  (PPAR- $\gamma$ ) expression in BV2 microglia cells infected with ZIKV strains derived from African and Asian lineages (ZIKV<sub>MR766</sub> and ZIKV<sub>PE243</sub>). BV2 cells were susceptible to both ZIKV strains, and showed discrete levels of viral replication, with delayed release of viral particles without inducing significant cytopathogenic effects. However, the ZIKV<sub>MR766</sub> strain showed higher infectivity and replicative capacity, inducing a higher expression of microglial activation markers than the ZIKV<sub>PE243</sub> strain. Moreover, infection with the ZIKV<sub>MR766</sub> strain promoted both a higher inflammatory response and a lower expression of anti-viral factors compared to the ZIKV<sub>PE243</sub> strain. Remarkably, the ZIKV<sub>PE243</sub> strain induced significantly higher levels of the anti-inflammatory nuclear receptor-PPAR- $\gamma$ . These findings improve our understanding of ZIKV-mediated modulation of inflammatory and anti-viral innate immune responses and open a new avenue to explore underlying mechanisms involved in the pathogenesis of ZIKV-associated diseases.

### **Analyses of Early ZIKV Genomes Are Consistent with Viral Spread from Northeast Brazil to the Americas.**

de Moraes L, Portilho MM, Vrancken B, Van den Broeck F, Santos LA, Cucco M, Tauro LB, Kikuti M, Silva MMO, Campos GS, Reis MG, Barral A, Barral-Netto M, Boaventura VS, Vandamme AM, Theys K, Lemey P, Ribeiro GS, Khouri R.

25-05-2023

#### Viruses.

<https://pubmed.ncbi.nlm.nih.gov/37376536/>

The Americas, particularly Brazil, were greatly impacted by the widespread Zika virus (ZIKV) outbreak in 2015 and 2016. Efforts were made to implement genomic surveillance of ZIKV as part of the public health responses. The accuracy of spatiotemporal reconstructions of the epidemic spread relies on the unbiased sampling of the transmission process. In the early stages of the outbreak, we recruited patients exhibiting clinical symptoms of arbovirus-like infection from Salvador and Campo Formoso, Bahia, in Northeast Brazil. Between May 2015 and June 2016, we identified 21 cases of acute ZIKV infection and subsequently recovered 14 near full-length sequences using the amplicon tiling multiplex approach with nanopore sequencing. We performed a time-calibrated discrete phylogeographic analysis to trace the spread and migration history of the ZIKV. Our phylogenetic analysis supports a consistent relationship between ZIKV migration from Northeast to Southeast Brazil and its subsequent dissemination beyond Brazil. Additionally, our analysis provides insights into the migration of ZIKV from Brazil to Haiti and the role Brazil played in the spread of ZIKV to other countries, such as Singapore, the USA, and the Dominican Republic. The data generated by this study enhances our understanding of ZIKV dynamics and supports the existing knowledge, which can aid in future surveillance efforts against the virus.

#### **An Overview of Indian Biomedical Research on the Chikungunya Virus with Particular Reference to Its Vaccine, an Unmet Medical Need.**

**Varikkodan MM, Kunnathodi F, Azmi S, Wu TY.**

15-06-2023

*Vaccines (Basel).*

<https://pubmed.ncbi.nlm.nih.gov/37376491/>

#### **Estimating the Impact of Consecutive Blood Meals on Vector Competence of *Aedes albopictus* for Chikungunya Virus.**

**Veronesi E, Paslaru A, Ettlin J, Ravasi D, Flacio E, Tanadini M, Guidi V.**

20-06-2023

*Pathogens.*

<https://pubmed.ncbi.nlm.nih.gov/37375539/>

The continuous expansion of *Aedes albopictus* in Europe and the increases in autochthonous arboviruses transmissions in the region urge a better understanding of the virus transmission dynamic. Recent work described enhanced chikungunya virus (CHIKV) dissemination in *Aedes aegypti* mosquitoes exposed to a virus-free blood meal three days after their infection with CHIKV. Our study investigated the impact of a second blood meal on the vector competence of *Ae. albopictus* from southern Switzerland infected with CHIKV. Seven-day-old *Ae. albopictus* females were exposed to CHIKV-spiked blood and incubated at constant (27 °C) and fluctuating (14-28 °C) temperatures. Four days post-infection (dpi), some of these females were re-fed with a non-infectious blood meal. Virus infectivity, dissemination, transmission rate,

and efficiency were investigated at seven and ten dpi. No enhanced dissemination rate was observed among females fed a second time; however, re-fed females have shown higher transmission efficiency than those fed only once after seven days post-infection and incubated under a fluctuating temperature regime. Vector competence for CHIKV was confirmed in *Ae. albopictus* from southern Switzerland. We did not observe an increase in dissemination rates among mosquitoes fed a second time (second blood meal), regardless of the temperature regime.

#### **PICTUREE-Aedes: A Web Application for Dengue Data Visualization and Case Prediction.**

**Yi C, Vajdi A, Ferdousi T, Cohnstaedt LW, Scoglio C.**

29-06-2023

*Pathogens.*

<https://pubmed.ncbi.nlm.nih.gov/37375461/>

#### **Joint influence of architectural and spatiotemporal factors on the presence of *Aedes aegypti* in urban environments.**

**Liao JR, Tu WC, Chiu MC, Kuo MH, Cheng HC, Chan CC, Dai SM.**

29-06-2023

*Pest Manag Sci.*

<https://pubmed.ncbi.nlm.nih.gov/37384574/>

#### **Evaluation of the immunogenicity and efficacy of an rVSV vaccine against Zika virus infection in macaca nemestrina.**

**Tisoncik-Go J, Voss KM, Lewis TB, Muruato AE, Kuller L, Finn EE, Betancourt D, Wangari S, Ahrens J, Iwayama N, Grant RF, Murnane RD, Edlefsen PT, Fuller DH, Barber GN, Gale M Jr, O'Connor MA.**

2023

*Front Virol.*

<https://pubmed.ncbi.nlm.nih.gov/37383986/>

Zika virus (ZIKV) is a mosquito-borne flavivirus that causes an acute febrile illness. ZIKV can be transmitted between sexual partners and from mother to fetus. Infection is strongly associated with neurologic complications in adults, including Guillain-Barré syndrome and myelitis, and congenital ZIKV infection can result in fetal injury and congenital Zika syndrome (CZS). Development of an effective vaccine is imperative to protect against ZIKV vertical transmission and CZS. Recombinant Vesicular Stomatitis virus (rVSV) is a highly effective and safe vector for the delivery of foreign immunogens for vaccine purposes. Here, we evaluate an rVSV vaccine expressing the full length pre-membrane (prM) and ZIKV envelope (E) proteins (VSV-ZprME), shown to be immunogenic in murine models of ZIKV infection, for its capacity to induce immune responses in nonhuman primates. Moreover, we assess the efficacy of the rVSVΔM-ZprME vaccine in the protection of pigtail macaques against ZIKV infection. Administration of the rVSVΔM-ZprME vaccine was safe, but it did not induce robust anti-ZIKV T-cell responses, IgM or IgG antibodies, or neutralizing antibodies in most animals. Post ZIKV challenge, animals that received the



rVSVΔM control vaccine lacking ZIKV antigen had higher levels of plasma viremia compared to animals that received the rVSVΔM-ZprME vaccine. Anti-ZIKV neutralizing Ab titers were detected in a single animal that received the rVSVΔM-ZprME vaccine that was associated with reduced plasma viremia. The overall suboptimal ZIKV-specific cellular and humoral responses post-immunization indicates the rVSVΔM-ZprME vaccine did not elicit an immune response in this pilot study. However, recall antibody response to the rVSVΔM-ZprME vaccine indicates it may be immunogenic and further developments to the vaccine construct could enhance its potential as a vaccine candidate in a nonhuman primate pre-clinical model.

### Exploring the strategies for upgrading the rural unqualified health practitioners in West Bengal, India: A knowledge, attitude and practices assessment-based approach.

**Debsarma D.**

11-11-2022

*Health Policy Open.*

<https://pubmed.ncbi.nlm.nih.gov/37383573/>

**Introduction:** Rural Unqualified Health Practitioners (RUHPs) are more common in the village health system in India and other developing countries. They only provides primary care to patients with diarrhea, cough, malaria, dengue, ARI/pneumonia, skin diseases, etc. As they are unqualified so their quality of health practices is substandard and inappropriate to practices. **Objective and contribution:** The intention of this work was to assess the Knowledge, Attitude, and Practices (KAP) of diseases among RUHPs and proposing a blueprint of potential intervention strategies for improving their knowledge and practice.

**Materials and methods:** The study has used a cross-sectional primary data and adopted quantitative approach. For assessment purpose, a composite KAP Score was constructed for two diseases (malaria and dengue). **Results:** The study observed that the KAP Score amongst the RUHPs are on average (about 50%) in most of the individual variables and composite scores for malaria and dengue in West Bengal, India. Their KAP score increased with age, level of education, working experiences, type of practitioners, using android mobile, work satisfaction, organization membership, attending RMP/Government workshop, heard WHO/IMC treatment protocol. **Conclusion:** The study suggested multistage interventions includes targeting young practitioners, allopathic and homeopathic quack, launching ubiquitous app-based medical-learning, and government-sponsored workshop should be significant interventions to improve the level of knowledge, change positive attitudes, and adhere to standard health practice.

**[Analysis of the impact of health management measures for entry personnel on imported Dengue fever in Guangdong Province, 2020-2022].**

**Tan XH, Deng AP, Zhang YT, Luo M, Deng H, Yang YW, Duan JH, Peng ZQ, Zhang M.**

10-06-2023

*Zhonghua Liu Xing Bing Xue Za Zhi.*

<https://pubmed.ncbi.nlm.nih.gov/37380419/>

**Objective:** To explore the impact of health management measures for entry personnel (entry management measures) against COVID-19 on the epidemiological characteristics of imported Dengue fever in Guangdong Province from 2020 to 2022. **Methods:** Data of imported Dengue fever from January 1, 2016 to August 31, 2022, mosquito density surveillance from 2016 to 2021, and international airline passengers and Dengue fever annual reported cases from 2011 to 2021 in Guangdong were collected. Comparative analysis was conducted to explore changes in the epidemic characteristics of imported Dengue fever before the implementation of entry management measures (from January 1, 2016 to March 20, 2020) and after the implementation (from March 21, 2020 to August 31, 2022). **Results:** From March 21, 2020, to August 31, 2022, a total of 52 cases of imported Dengue fever cases were reported, with an imported risk intensity of 0.12, which were lower than those before implementation of entry management measures (1 828, 5.29). No significant differences were found in the characteristics of imported cases before and after implementation of entry management measures, including seasonality, sex, age, career, and imported countries (all  $P>0.05$ ). 59.62% (31/52) of cases were found at the centralized isolation sites and 38.46% (20/52) at the entry ports. However, before implementation of entry management measures, 95.08% (1 738/1 828) of cases were found in hospitals. Among 51 cases who had provided entry dates, 82.35% (42/51) and 98.04% (50/51) of cases were found within seven days and fourteen days after entry, slightly higher than before implementation [(72.69%(362/498) and 97.59% (486/498)]. There was significant difference between the monthly mean values of *Aedes mosquito* larval density (Bretto index) from 2020 to 2021 and those from 2016 to 2019 ( $Z=2.83$ ,  $P=0.005$ ). There is a strong positive correlation between the annual international airline passengers volume in Guangdong from 2011 to 2021 and the annual imported Dengue fever cases ( $r=0.94$ ,  $P<0.001$ ), and a positive correlation also existed between the international passenger volume and the annual indigenous Dengue fever cases ( $r=0.72$ ,  $P=0.013$ ). **Conclusions:** In Guangdong, the entry management measures of centralized isolation for fourteen days after entry from abroad had been implemented, and most imported Dengue fever cases were found within fourteen days after entry. The risk of local transmission caused by imported cases has reduced significantly.

**The effects of allosteric and competitive inhibitors on ZIKV protease conformational dynamics explored through smFRET, nanoDSF, DSF, and <sup>19</sup>F NMR.**

**Maus H, Hammerschmidt SJ, Hinze G, Barthels F, Pérez Carrillo VH, Hellmich UA, Basché T, Schirmeister T.**

21-06-2023



### Computational workflow for investigating highly variable genes in single-cell RNA-seq across multiple time points and cell types.

Arora JK, Opasawatchai A, Teichmann SA, Matangkasombut P, Charoensawan V.

27-06-2023

STAR Protoc.

<https://pubmed.ncbi.nlm.nih.gov/37379219/>

Here, we present a computational approach for investigating highly variable genes (HVGs) associated with biological pathways of interest, across multiple time points and cell types in single-cell RNA-sequencing (scRNA-seq) data. Using public dengue virus and COVID-19 datasets, we describe steps for using the framework to characterize the dynamic expression levels of HVGs related to common and cell-type-specific biological pathways over multiple immune cell types. For complete details on the use and execution of this protocol, please refer to Arora et al.<sup>1</sup>.

### Posterior Reversible Leucoencephalopathy Syndrome: Case Series, Comments, and Diagnostic Dilemma.

Chaudhuri J, Basu S, Roy MK, Chakravarty A.

28-06-2023

Curr Neurol Neurosci Rep.

<https://pubmed.ncbi.nlm.nih.gov/37378723/>

### Identification of an Arylnaphthalene Lignan Derivative as an Inhibitor against Dengue Virus Serotypes 1 to 4 (DENV-1 to -4) Using a Newly Developed DENV-3 Infectious Clone and Replicon.

Hu M, Li WF, Wu T, Yang Y, Chen G, Chen T, Liu Y, Mei Y, Wu D, Wei Y, Luo T, Zhang HJ, Li YP.

28-06-2023

Microbiol Spectr.

<https://pubmed.ncbi.nlm.nih.gov/37378517/>

Dengue virus (DENV) is the most widespread arbovirus, causing symptoms ranging from dengue fever to severe dengue, including hemorrhagic fever and shock syndrome. Four serotypes of DENV (DENV-1 to -4) can infect humans; however, no anti-DENV drug is available. To facilitate the study of antivirals and viral pathogenesis, here we developed an infectious clone and a subgenomic replicon of DENV-3 strains for anti-DENV drug discovery by screening a synthetic compound library. The viral cDNA was amplified from a serum sample from a DENV-3-infected individual during the 2019 epidemic; however, fragments containing the prM-E-partial NS1 region could not be cloned until a DENV-3 consensus sequence with 19 synonymous substitutions was introduced to reduce putative Escherichia coli promoter activity. Transfection of the resulting cDNA clone, plasmid DV3syn, released an infectious virus titer of  $2.2 \times 10^2$  focus-forming units (FFU)/mL. Through serial passages, four adaptive

mutations (4M) were identified, and addition of 4M generated recombinant DV3syn\_4M, which produced viral titers ranging from  $1.5 \times 10^4$  to  $6.7 \times 10^4$  FFU/mL and remained genetically stable in transformant bacteria. Additionally, we constructed a DENV-3 subgenomic replicon and screened an aryl naphthalene lignan library, from which C169-P1 was identified as exhibiting inhibitory effects on viral replicon. A time-of-drug addition assay revealed that C169-P1 also impeded the internalization process of cell entry. Furthermore, we demonstrated that C169-P1 inhibited the infectivity of DV3syn\_4M, as well as DENV-1, DENV-2, and DENV-4, in a dose-dependent manner. This study provides an infectious clone and a replicon for the study of DENV-3 and a candidate compound for future development against DENV-1 to -4 infections. **IMPORTANCE** Dengue virus (DENV) is the most prevalent mosquito-transmitted virus, and there is no anti-dengue drug. Reverse genetic systems representative of different serotype viruses are invaluable tools for the study of viral pathogenesis and antiviral drugs. Here, we developed an efficient infectious clone of a clinical DENV-3 genotype III isolate. We successfully overcame the instability of flavivirus genome-length cDNA in transformant bacteria, an unsolved issue for construction of cDNA clones of flaviviruses, and adapted this clone to efficiently produce infectious viruses following plasmid transfection of cell culture. Moreover, we constructed a DENV-3 subgenomic replicon and screened a compound library. An aryl naphthalene lignan, C169-P1, was identified as an inhibitor of virus replication and cell entry. Finally, we demonstrated that C169-P1 exhibited a broad-spectrum antiviral effect against the infections with DENV-1 to -4. The reverse genetic systems and the compound candidate described here facilitate the study of DENV and related RNA viruses.

### Expression of anti-chikungunya single-domain antibodies in transgenic Aedes aegypti reduces vector competence for chikungunya virus and Mayaro virus.

Webb EM, Compton A, Rai P, Chuong C, Paulson SL, Tu Z, Weger-Lucarelli J.

12-06-2023

Front Microbiol.

<https://pubmed.ncbi.nlm.nih.gov/37378291/>

Chikungunya virus (CHIKV) and Mayaro virus (MAYV) are closely related alphaviruses that cause acute febrile illness accompanied by an incapacitating polyarthralgia that can persist for years following initial infection. In conjunction with sporadic outbreaks throughout the sub-tropical regions of the Americas, increased global travel to CHIKV- and MAYV-endemic areas has resulted in imported cases of MAYV, as well as imported cases and autochthonous transmission of CHIKV, within the United States and Europe. With increasing prevalence of CHIKV worldwide and MAYV throughout the Americas within the last decade, a heavy focus has been placed on control and prevention programs. To date, the most effective means of controlling the spread of these viruses is through mosquito control programs. However, current programs have limitations in their effectiveness; therefore, novel approaches are necessary to control the spread of these

crippling pathogens and lessen their disease burden. We have previously identified and characterized an anti-CHIKV single-domain antibody (sdAb) that potently neutralizes several alphaviruses including Ross River virus and Mayaro virus. Given the close antigenic relationship between MAYV and CHIKV, we formulated a single defense strategy to combat both emerging arboviruses: we generated transgenic *Aedes aegypti* mosquitoes that express two camelid-derived anti-CHIKV sdAbs. Following an infectious bloodmeal, we observed significant reduction in CHIKV and MAYV replication and transmission potential in sdAb-expressing transgenic compared to wild-type mosquitoes; thus, this strategy provides a novel approach to controlling and preventing outbreaks of these pathogens that reduce quality of life throughout the tropical regions of the world.

### **Zika virus-like particles (VLPs) produced in insect cells.**

de Mello RG, Bernardino TC, Guardalini LGO, Astray RM, Antoniazzi MM, Jared SGS, Núñez EGF, Jorge SAC.

12-06-2023

*Front Pharmacol.*

<https://pubmed.ncbi.nlm.nih.gov/37377933/>

### **The Dengue Prevalence and Mortality Rate Surpass COVID-19 in Bangladesh: Possible Strategies to Fight Against a Double-Punch Attack.**

Shayla TA, Paul M, Sayma NJ, Suhee FI, Islam MR.

23-06-2023

*Clin Pathol.*

<https://pubmed.ncbi.nlm.nih.gov/37377618/>

### **Insecticide resistance levels and associated mechanisms in three *Aedes aegypti* populations from Venezuela.**

Rubio-Palis Y, Dzuris N, Sandi C, Vizcaino-Cabarrus RL, Corredor-Medina C, González JA, Lenhart AE.

23-06-2023

*Mem Inst Oswaldo Cruz.*

<https://pubmed.ncbi.nlm.nih.gov/37377253/>

### **The CD133 and CD34 cell types in human umbilical cord blood have the capacity to produce infectious dengue virus particles.**

Vats A, Ho TC, Puc I, Chang CH, Perng GC, Chen PL.

29-06-2023

*Sci Rep.*

<https://pubmed.ncbi.nlm.nih.gov/37386042/>

Although dengue virus (DENV) can establish infections in hematopoietic stem progenitor cells (HSPCs), there is little information on dengue virus persistent infection in CD34+ and CD133+ cell surface glycoproteins of hematopoietic stem cells (HSCs). CD34 and CD133 also function as cell-cell adhesion factors, which are present in umbilical cord blood (UCB). In this study, we sought to establish a persistent infection model of DENV infection in UCB using a prolonged period of infection lasting 30 days. Post-infection, the results exhibited a productive and non-

productive phase of DENV production. Using a plaque assay, Western blot, and confocal microscopy, we demonstrated that CD133 and CD34 cells are target cells for DENV infection. Moreover, we showed that DENV particles can be recovered from the non-productive phase of DENV-infected CD34 and CD133 cells after co-incubation with Vero cells. We concluded that CD133 and CD34 retain their capacity to produce the infectious virus due to proliferation and their ability to repopulate, as deduced from a BrdU proliferation assay and flow cytometry analysis using t-distributed stochastic neighbor embedding. In summary, the platform to co-culture infected primitive HSCs from their non-productive phase onto Vero cells will give new insights into understanding the DENV dynamics in cell-to-cell transmission and reactivation of the virus.

### **Introduction of chikungunya virus in coastal northeast Brazil.**

Postigo-Hidalgo I, Jo WK, Pedroso C, Brites C, Drexler JF.

26-06-2023

*Lancet Microbe.*

<https://pubmed.ncbi.nlm.nih.gov/37385284/>

### **Dengue Outbreak Response during COVID-19 Pandemic, Key Largo, Florida, USA, 2020.**

Rowe D, McDermott C, Veliz Y, Kerr A, Whiteside M, Coss M, Huff C, Leal A, Kopp E, LaCrue A, Heberlein LA, Adams LE, Santiago GA, Munoz-Jordan JL, Paz-Bailey G, Morrison AM; Florida Department of Health Dengue Investigation Team1.

29-06-2023

*Emerg Infect Dis.*

<https://pubmed.ncbi.nlm.nih.gov/37385262/>

### **[Preparing for Pandemics].**

Yan X, Barbero F, Wunderlich R.

Juin-2023

*Anesthesiol Intensivmed Notfallmed Schmerzther.*

<https://pubmed.ncbi.nlm.nih.gov/37385241/>

The current COVID-19 pandemic has contributed to millions of deaths globally and it is estimated that the hit to the global economy could reach more than twelve trillion US-dollars. Disease outbreaks have often pushed weak health systems to a breaking point, as witnessed during cholera, Ebola and Zika virus upsurges. The preparation of a plan involves the analysis of a scenario divided into the disaster cycle's four phases: preparation, response, recovery, and mitigation. Several levels of planning are recognised according to the goals to be reached: strategic plans are directed to define the organisational context and overall aims, operational plans with putting the strategy into place, tactical plans explain how resources will be allocated and managed, as well as provide essential instructions to the responders. The hospital surge capacity relies on the reorganisation of resources according to four categories: system, staff, stuff (supplies), and space. Each of these components needs to be analysed, implemented, and tested during the preparation phase to reduce the occurrence of a critical

overrun of the response capabilities, as this will trigger the recourse of contingency plans. The response to pandemics must be associated with public health and social measures, as well as with initiatives to support the psychophysical health of healthcare workers.

### **The oral repellent - science fiction or common sense? Insects, vector-borne diseases, failing strategies, and a bold proposition.**

**Bauer IL.**

28-06-2023

*Trop Dis Travel Med Vaccines.*

<https://pubmed.ncbi.nlm.nih.gov/37381000/>

Over the last decades, unimaginable amounts of money have gone into research and development of vector control measures, repellents, treatment, and vaccines for vector borne diseases. Technological progress and scientific breakthroughs allowed for ever more sophisticated and futuristic strategies. Yet, each year, millions of people still die or suffer from potentially serious consequences of malaria or dengue to more recent infections, such as Zika or Chikungunya, or of debilitating consequences of neglected tropical diseases. This does not seem value for money. In addition, all current vector control strategies and personal protection methods have shortcomings, some serious, that are either destructive to non-target species or unsatisfactory in their effectiveness. On the other hand, the rapid decline in insect populations and their predators reflects decades-long aggressive and indiscriminate vector control. This major disruption of biodiversity has an impact on human life not anticipated by the well-meaning killing of invertebrates. The objective of this paper is to re-examine current control methods, their effectiveness, their impact on biodiversity, human and animal health, and to call for scientific courage in the pursuit of fresh ideas. This paper brings together topics that are usually presented in isolation, thereby missing important links that offer potential solutions to long-standing problems in global health. First, it serves as a reminder of the importance of insects to human life and discusses the few that play a role in transmitting disease. Next, it examines critically the many currently employed vector control strategies and personal protection methods. Finally, based on new insights into insect chemosensation and attractants, this perspective makes a case for revisiting a previously abandoned idea, the oral repellent, and its use via currently successful methods of mass-application. The call is out for focused research to provide a powerful tool for public health, tropical medicine, and travel medicine.

### **The Interpretation of Arterial Blood Gas During the Apneic Phase of a Patient With Obstructive Sleep Apnea: A Case Report.**

**Sahoo A.**

18-06-2023

*Cureus.*

<https://pubmed.ncbi.nlm.nih.gov/37378244/>

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## **Dracunculose**

### **Orbitrap Mass Spectrometry-Based Profiling of Secondary Metabolites in Two Unexplored Eminium Species and Bioactivity Potential.**

**Babacan EY, Zheleva-Dimitrova D, Gevrenova R, Bouyahya A, Balos MM, Cakilcioglu U, Sinan KI, Zengin G.**

08-06-2023

*Plants (Basel).*

<https://pubmed.ncbi.nlm.nih.gov/37375878/>

### **Insight into Nephrotoxicity and Processing Mechanism of *Arisaema erubescens* (Wall.) Schott by Metabolomics and Network Analysis.**

**Wang M, Yang N, Wu X, Zou T, Zheng J, Zhu H, Zhao C, Wang J.**

19-06-2023

*Drug Des Devel Ther.*

<https://pubmed.ncbi.nlm.nih.gov/37360574/>

**Background:** *Arisaematis* Rhizome (AR) has been used as a damp-drying, phlegm-resolving, wind-expelling, pain-alleviating, and swelling-relieving drug for thousands of years. However, the toxicity limits its clinical applications. Therefore, AR is usually processed (Paozhi in Chinese) prior to clinical use. In this study, the integration of ultra-high performance liquid chromatography-quadrupole/time-of-flight mass spectrometry-based metabolomics and network analysis was adopted to investigate the metabolic shifts induced by AR and explore the processing mechanism. **Materials and methods:** Extracts of crude and processed AR products (1g/kg) were intragastrically administered to rats once daily for four consecutive weeks. The renal function was evaluated by blood urea nitrogen, creatinine, interleukin-1 beta (IL-1 $\beta$ ) and tumor necrosis factor-alpha (TNF- $\alpha$ ), malondialdehyde (MDA), super oxide dismutase (SOD), the ratio of glutathione/glutathione disulfide (GSH/GSSH), glutathione peroxidase (GSH-Px) and histopathological examination. Furthermore, the chemical composition of AR was clarified by ultra-high performance liquid chromatography-quadrupole/time-of-flight mass spectrometry, after which the integration of metabolomics and network analysis was adopted to investigate the metabolic shifts induced by AR and explore the processing mechanism. **Results:** Crude AR caused renal damage by stimulating inflammation and oxidative stress, as confirmed by the increased production of IL-1 $\beta$ , TNF- $\alpha$  and MDA, and decreased levels of SOD, GSH/GSSH and GSH-Px. Processing with ginger juice, alumen and bile juice alleviated the damage to kidney. Metabolomics results showed that a total of 35 potential biomarkers enriched in amino acid metabolism, glycerophospholipid metabolism, fatty acid-related pathways, etc. were deduced to be responsible for the nephrotoxicity of AR and the toxicity-reducing effect of processing. **Conclusion:** This work provided theoretical and data support for the in-depth study of the processing mechanism, showing that processing reduces AR nephrotoxicity through multiple metabolic pathways.

### **Trophic transfer of microplastics from producer (*Lemna minuta*) to primary consumer (*Cataclysta lemnata*) in a freshwater food chain.**

**Mariani F, Di Lernia D, Venditti I, Pelella E, Muzzi M, Di Giulio A, Ceschin S.**

15-09-2023

*Sci Total Environ.*

<https://pubmed.ncbi.nlm.nih.gov/37247734/>

Contamination by microplastics (0.1 µm-5 mm plastic fragments) is currently one of the major threats to the conservation of aquatic and terrestrial ecosystems worldwide. Growing awareness on this issue has led to an increase in studies on the effects of microplastics on freshwater organisms, although there are still few investigations on possible transfer of this contaminant along water trophic chains from producers to primary consumers. In this study, aquatic herbivorous larvae of the moth *Cataclysta lemnata* were fed on microplastic-free (control) and contaminated (MPs treatment) *Lemna minuta* fronds. For treatments, *Lemna* fronds were grown in mineral water enriched with fluorescent microparticles of poly(styrene-co-methyl methacrylate) (MPs, 100 mg/L) and then fed to the larvae as a food source. Microplastics effects on larvae were tested at 0, 7, 14 and 21 days of exposure, corresponding to sensitive phases of the insect life cycle. Contaminant impact was assessed based on some parameters such as viability, larva body size/weight, feeding alterations and regularity of the insect life cycle. Using scanning electron and fluorescence microscopy, the presence of microplastics in the larvae was verified. The finding of fluorescent microplastics in both the intestinal lumen and excrement samples showed that larvae ingested contaminated *Lemna* fronds. In addition, larvae fed contaminated fronds were strongly affected by the presence of microplastic contaminant over time, showing high mortality (90 %) and total inability to complete the life cycle after 21 days by failing to reach the winged adult phase. In control tests, survival rates were higher than in treatments, and 50 % of the larvae managed to pupate and emerge as moths, reaching the adult phase. The results show that there was a trophic transfer of microplastics from producer to primary consumer along a freshwater food chain, generating negative effects on the life cycle of this aquatic herbivore.

### **EDTA as a legacy soil chelutant: a comparative study to a more environmentally sensitive alternative for metal removal by *Pistia stratiotes* L.**

**Lebrun M, Száková J, Drábek O, Tejnecký V, Hough RL, Beesley L, Wang H, Trakal L.**

Juin-2023

*Environ Sci Pollut Res Int.*

<https://pubmed.ncbi.nlm.nih.gov/37202639/>

### **Complete Genome Sequence Resource of *Pectobacterium colocasium* Strain F1-1 that Causes Soft Rot Disease of Taro.**

**Huang CJ, Wu TL, Zheng PX, Ou JY, Ting CL, Lin YC.**

Juin-2023

*Plant Dis.*

<https://pubmed.ncbi.nlm.nih.gov/36451306/>

*Pectobacterium colocasium* is a recently named, narrow-host-range phytopathogenic bacterium causing soft rot of taro (*Colocasium esculenta*). It is found on the Chinese mainland and the island of Taiwan. Taro is a domesticated crop with a long history of cultivation in Taiwan and the Pacific islands. However, not much was known about *Pectobacterium* spp. from taro, especially from the islands in the Pacific. Herein, we report a high-quality, completely annotated genome sequence of *P. colocasium* strain F1-1. The 4,816,345 bp genome, which was assembled with Illumina and Nanopore reads with 217× and 311× coverage, respectively, consists of one chromosome and no plasmid. This completely circularized genome will aid future studies in comparative genomics, evolution, and pathogenicity of *P. colocasium*. This genome resource will also be helpful for developing strategies to control *P. colocasium* in taro.[Formula: see text] Copyright © 2023 The Author(s). This is an open access article distributed under the CC BY-NC-ND 4.0 International license.

### **Smartphone-Based DIY Home Microsurgical Training with 3D Printed Microvascular Clamps and Japanese Noodles.**

**Ng ZY, Honeyman C, Lellouch AG, Pandya A, Papavasiliou T.**

2023

*Eur Surg Res.*

<https://pubmed.ncbi.nlm.nih.gov/34915484/>

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## **Echinococcoses**

### **Dogs as a source for the spreading of enteric parasites including zoonotic ones in Giza Province, Egypt.**

**Khalifa MM, Fouad EA, Kamel NO, Auda HM, El-Bahy MM, Ramadan RM.**

22-06-2023

*Res Vet Sci.*

<https://pubmed.ncbi.nlm.nih.gov/37379694/>

To investigate the impact of domestic and stray dogs on the transmission of zoonotic and other parasites to humans in contact with them, fecal samples were collected from 80 domestic dogs that presented at a clinic with health disturbances and 220 randomly selected stray dogs housed in shelters. The parasitological examination of these samples revealed infection by six zoonotic and four non-zoonotic parasites in varying percentages. The zoonotic parasites included *Ancylostoma caninum*, *Toxocara canis*, *Dipylidium caninum*, *Echinococcus granulosus*, *Cryptosporidium* species, and *Giardia* cysts and trophozoites. The other parasites included *Toxascaris leonina*, *Trichuris vulpis*, *Taenia* species eggs, and *Isospora canis* oocysts. The infection rate was higher in stray dogs (60%) than in domestic dogs (40%). Infected dogs in both groups were generally unhealthy, with poor body condition recorded in 13.8% of domestic dogs and 63.6% of stray dogs. The infection rate was higher (92%) among



shelter workers than among domestic dog owners (66.7%). *Giardia* assemblages A and D from dogs and assemblage A from humans, as well as two isolates of *Cryptosporidium canis* (*C. canis*), one from dogs and the other from humans, were submitted in the GenBank with the accession numbers OQ870443, OQ870444, and OQ919265 for *Giardia* and OQ917532 & OQ915519 for *C. canis* of dogs & human, respectively. In conclusion, domestic and stray dogs play an essential role in transmitting zoonotic parasites to humans in contact with them, and regular deworming and strict hygienic measures are recommended to minimize their impact on human health.

### [Laparoscopic partial resection of spleen in a 15-year-old girl].

**Ushakov KV, Askerov RF, Chundokova MA, Zalikhin DV, Dondup OM.**  
2023

*Khirurgiia (Mosk).*

<https://pubmed.ncbi.nlm.nih.gov/37379412/>

### Giant Echinococcosis of the Liver with Suppuration: A Case Report and Review of the Literature.

**Kosmidis CS, Papadopoulos K, Mystakidou CM, Sevva C, Koulouris C, Varsamis N, Mantalovas S, Lagopoulos V, Magra V, Theodorou V, Ouzouni S, Iason Katsios N, Axi P, Sapalidis K, Kesisoglou I.**

02-06-2023

*Medicina (Kaunas).*

<https://pubmed.ncbi.nlm.nih.gov/37379694/>

To investigate the impact of domestic and stray dogs on the transmission of zoonotic and other parasites to humans in contact with them, fecal samples were collected from 80 domestic dogs that presented at a clinic with health disturbances and 220 randomly selected stray dogs housed in shelters. The parasitological examination of these samples revealed infection by six zoonotic and four non-zoonotic parasites in varying percentages. The zoonotic parasites included *Ancylostoma caninum*, *Toxocara canis*, *Dipylidium caninum*, *Echinococcus granulosus*, *Cryptosporidium* species, and *Giardia* cysts and trophozoites. The other parasites included *Toxascaris leonina*, *Trichuris vulpis*, *Taenia* species eggs, and *Isospora canis* oocysts. The infection rate was higher in stray dogs (60%) than in domestic dogs (40%). Infected dogs in both groups were generally unhealthy, with poor body condition recorded in 13.8% of domestic dogs and 63.6% of stray dogs. The infection rate was higher (92%) among shelter workers than among domestic dog owners (66.7%). *Giardia* assemblages A and D from dogs and assemblage A from humans, as well as two isolates of *Cryptosporidium canis* (*C. canis*), one from dogs and the other from humans, were submitted in the GenBank with the accession numbers OQ870443, OQ870444, and OQ919265 for *Giardia* and OQ917532 & OQ915519 for *C. canis* of dogs & human, respectively. In conclusion, domestic and stray dogs play an essential role in transmitting zoonotic parasites to humans in contact with them, and regular deworming and strict hygienic

measures are recommended to minimize their impact on human health.

### Emergence of *Echinococcus multilocularis* in Central Continental Croatia: A Human Case Series and Update on Prevalence in Foxes.

**Balen Topić M, Papić N, Višković K, Sviben M, Filipec Kanižaj T, Jadrijević S, Jurković D, Beck R.**

16-06-2023

*Life (Basel).*

<https://pubmed.ncbi.nlm.nih.gov/37374184/>

Human alveolar echinococcosis (HAE), caused by the metacestode stage of *Echinococcus multilocularis*, has emerged in many European countries over the last two decades. Here, we report the first data on the new HAE focus with increasing incidence in central Croatia, describe its clinical presentation and outcomes in diagnosed patients, and provide an update on the prevalence and geographic distribution of *Echinococcus multilocularis* in red foxes. After the initial case in 2017 from the eastern state border, from 2019 to 2022, five new autochthonous HAE cases were diagnosed, all concentrated in the Bjelovar-Bilogora County (the county incidence in 2019 and 2021: 0.98/10<sup>5</sup>, in 2022: 2.94/10<sup>5</sup>/year; prevalence for 2019-2022: 4.91/10<sup>5</sup>). The age range among four female and two male patients was 37-67 years. The patients' liver lesions varied in size from 3.1 to 15.5 cm (classification range: P2N0M0-P4N1M0), and one patient had dissemination to the lungs. While there were no fatalities, postoperative complications in one patient resulted in liver transplantation. In 2018, the overall prevalence of red foxes was 11.24% (28/249). A new focus on HAE has emerged in central continental Croatia, with the highest regional incidence in Europe. Screening projects among residents and the implementation of veterinary preventive measures following the One Health approach are warranted.

### Effectiveness Evaluation of Viti's vinifera Leaf Extract on the Viability of *Echinococcus* Eggs and *Protoscolices* In Vitro.

**Mares MM, Al-Quraishy S, Murshed M.**

18-06-2023

*Vet Sci.*

<https://pubmed.ncbi.nlm.nih.gov/37368786/>

### Green Synthesis, Characterization, and Antiparasitic Effects of Gold Nanoparticles against *Echinococcus granulosus* *Protoscoleces*.

**Raziani Y, Shakib P, Rashidipour M, Cheraghipour K, Ghasemian Yadegari J, Mahmoudvand H.**

09-06-2023

*Trop Med Infect Dis.*

<https://pubmed.ncbi.nlm.nih.gov/37368731/>

Echinococcosis, or hydatidosis, is one of the most important zoonotic diseases, which is initiated by the larval stage in the clasts of *Echinococcus granulosus*. For



the treatment of hydatidosis, surgery is still the preferred method and the first line of treatment for symptomatic patients. Unfortunately, most of the scolical agents that are injected inside cysts during hydatid cyst surgery have side effects, including leaking out of the cyst and adverse effects on the living tissue of the host, such as necrosis of liver cells, which limits their use. This work was carried out to study the lethal effect of green synthesized gold nanoparticles (Au-NCs) against hydatid cyst protoscoleces. Au-NCs were green synthesized using the *Saturja khuzestanica* extract. Au-NCs were characterized by UV-visible absorbance assay, electron microscopy analysis, X-ray diffraction (XRD), and Fourier transform infrared (FTIR) spectroscopy. Scolical properties of Au-NCs (1-5 mg/mL) were studied against protoscoleces for 10-60 min. The effect of Au-NCs on the expression level of the caspase-3 gene as well as the ultrastructural examination was studied by real-time PCR and scanning electron microscopy (SEM). The cytotoxicity of Au-NCs on hepatocellular carcinoma (HepG<sub>2</sub>) and normal embryonic kidney (HEK293) cell lines was also studied by the cell viability assay. The obtained Au-NCs are cubes and have an average size of 20-30 nm. The highest scolical efficacy was observed at 5 mg/mL with 100% mortality after 20 min of treatment for hydatid cyst protoscoleces. In ex vivo, Au-NCs required more incubation time, indicating more protoscolical effects. Au-NCs markedly upregulated the gene level of caspase-3 in protoscoleces; whereas they changed the ultra-structure of protoscoleces by weakening and disintegrating the cell wall, wrinkles, and protrusions due to the formation of blebs. We showed the effective in vitro and ex vivo scolical effects of Au-NCs against hydatid cyst protoscoleces by provoking the apoptosis process of caspase-3 activation and changing the ultrastructure of protoscoleces with no significant cytotoxicity against human normal cells. However, additional studies should be conducted to determine the possible harmful side effects and accurate efficacy.

### **Propofol Induces the Expression of Nrf2 and HO-1 in *Echinococcus granulosus* via the JNK and p38 Pathway In Vitro.**

**Luo G, Ma B, Jiang Y, Lv H.**

03-06-2023

*Trop Med Infect Dis.*

<https://pubmed.ncbi.nlm.nih.gov/37368724/>

### **Effect of Temperature and Ionic Substitutions on the Tegumental Potentials of Protoscoleces of *Echinococcus granulosus*.**

**Carabajal MPA, Fernández Salom MJ, Olivera S, Cantiello HF.**

02-06-2023

*Trop Med Infect Dis.*

<https://pubmed.ncbi.nlm.nih.gov/37368721/>

### **Vertebromedullary hydatidosis: a case report.**

**Haouas MY, Jihri A, Makhchoune M, Limi J, Lakhdar A.**

12-04-2023

*Ann Med Surg (Lond).*

<https://pubmed.ncbi.nlm.nih.gov/37363601/>

The contamination of humans with the larval form of the tapeworm *Echinococcus granulosus* results in the parasitic disease known as hydatidosis. Even though hydatid disease is widespread in Maghreb nations, bone hydatidosis is still uncommon. **Case presentation:** This article presents the case of a 12-year-old child with no particular pathological antecedent, who presents a spinal cord compression syndrome evolving gradually for 2 weeks whose objective clinical examination found a 2/5 paraparesis with a sharp pyramidal syndrome and subxiphoid sensory level. Medullary MRI has objectified an aspect of hydatid cysts at the level of D8 D9 and D10 compressing the spinal cord. **Clinical discussion:** Management was surgical by decompression by laminectomy of stage D8, D9, and D10 under general anesthesia and put on albendazole, the diagnosis was confirmed by histopathological examination, the evolution was marked by a partial recovery of deficit. **Conclusions:** Clinical symptomatology is vague with a gradually inescapable movement towards spinal or root pressure.

### **Bilateral hydatid cyst of the breast: a case report and review of the literature.**

**Al Sharei A, Abu-Jeyyab M, Al-Khalaileh M, Al-Awabdeh M, Al-Asbahi H, Al-Dwairy S, Al-Share M.**

20-04-2023

*Ann Med Surg (Lond).*

<https://pubmed.ncbi.nlm.nih.gov/37363452/>

### **Interaction between tissue-dwelling helminth and the gut microbiota drives mucosal immunoregulation.**

**Wang Y, Guo A, Zou Y, Mu W, Zhang S, Shi Z, Liu Z, Cai X, Zhu XQ, Wang S.**

24-06-2023

*NPJ Biofilms Microbiomes.*

<https://pubmed.ncbi.nlm.nih.gov/37355675/>

Tissue-dwelling helminths affect billions of people around the world. They are potent manipulators of the host immune system, prominently by promoting regulatory T cells (Tregs) and are generally associated with a modified host gut microbiome. However, the role of the gut microbiota in the immunomodulatory processes for these non-intestinal parasites is still unclear. In the present study, we used an extra-intestinal cestode helminth model-larval *Echinococcus multilocularis* to explore the tripartite partnership (host-helminth-bacteria) in the context of regulating colonic Tregs in Balb/c mice. We showed that larval *E. multilocularis* infection in the peritoneal cavity attenuated colitis in Balb/c mice and induced a significant expansion of colonic Foxp3<sup>+</sup> Treg populations. Fecal microbiota depletion and transplantation experiments showed that the gut microbiota contributed to increasing Tregs after the helminth infection. Shotgun metagenomic and metabolic analyses revealed that the gut microbiome structure after infection was significantly shifted with a remarkable increase of *Lactobacillus reuteri* and that the microbial metabolic capability was reprogrammed to produce more

Treg cell regulator-short-chain fatty acids in feces. Furthermore, we also prove that the *L. reuteri* strain elevated in infected mice was sufficient to promote the colonic Treg frequency and its growth was potentially associated with T cell-dependent immunity in larval *E. multilocularis* infection. Collectively, these findings indicate that the extraintestinal helminth drives expansions of host colonic Tregs through the gut microbes. This study suggests that the gut microbiome serves as a critical component of anti-inflammation effects even for a therapy based on an extraintestinal helminth.

### **The mouse model of chronic asthma: Airway remodelling and disease exacerbation by somatic antigen of *Echinococcus granulosus*.**

Ghabdian S, Parandeh Shirvan S, Maleki M, Borji H.  
Juil-2023  
*Parasite Immunol.*  
<https://pubmed.ncbi.nlm.nih.gov/37292031/>

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## **Filariose lymphatique**

### **Assessing the cost-effectiveness of integrated case management of Neglected Tropical Diseases in Liberia.**

Godwin-Akpan TG, Diaconu K, Edmiston M, Smith JS Jr, Sosu F, Weiland S, Kollie KK.  
29-06-2023  
*BMC Health Serv Res.*  
<https://pubmed.ncbi.nlm.nih.gov/37386431/>

### **Stage-Dependent Increase of Systemic Immune Activation and CCR5<sup>+</sup>CD4<sup>+</sup> T Cells in Filarial Driven Lymphedema in Ghana and Tanzania.**

Rahamani AA, Horn S, Ritter M, Feichtner A, Osei-Mensah J, Serwaa Opoku V, Batsa Debrah L, Marandu TF, Haule A, Mhidze J, Ngenya A, Demetrius M, Klarmann-Schulz U, Hoelscher M, Geldmacher C, Hoerauf A, Kalinga A, Debrah AY, Kroidl I.  
07-06-2023  
*Pathogens.*  
<https://pubmed.ncbi.nlm.nih.gov/37375499/>

Chronic lymphedema caused by infection of *Wuchereria bancrofti* is a disfiguring disease that leads to physical disability, stigmatization, and reduced quality of life. The edematous changes occur mainly on the lower extremities and can progress over time due to secondary bacterial infections. In this study, we characterized participants with filarial lymphedema from Ghana and Tanzania as having low (stage 1-2), intermediate (stage 3-4), or advanced (stage 5-7) lymphedema to determine CD4<sup>+</sup> T cell activation patterns and markers associated with immune cell exhaustion. A flow cytometry-based analysis of peripheral whole blood revealed different T cell phenotypes within participants with different stages of filarial lymphedema. In detail, increased frequencies of CD4<sup>+</sup>HLA-DR<sup>+</sup>CD38<sup>+</sup> T cells were associated with higher stages of filarial lymphedema in patients from Ghana and

Tanzania. In addition, significantly increased frequencies of CCR5<sup>+</sup>CD4<sup>+</sup> T cells were seen in Ghanaian participants with advanced LE stages, which was not observed in the Tanzanian cohort. The frequencies of CD8<sup>+</sup>PD-1<sup>+</sup> T cells were augmented in individuals with higher stage lymphedema in both countries. These findings show distinct activation and exhaustion patterns in lymphedema patients but reveal that immunological findings differ between West and East African countries.

### **Assessing Boron-Pleuromutilin AN11251 for the Development of Antibacterial Agents.**

Han MJ, Pan M, Xiao G, Yuan Y, Chen S, Zou Z.  
08-06-2023  
*Molecules.*  
<https://pubmed.ncbi.nlm.nih.gov/37375183/>

### **"Our interventions are still here to support communities during the pandemic": Resuming mass drug administration for neglected tropical diseases after COVID-19 implementation delays.**

Itaye T, Matendechero SH, Mbonigaba JB, Gebretsadik FS, Molefi TL, Baayenda G, Ruberanziza E, Kollie KK, Zilabumba J, Dembele M, Deribe K, Adrien EM, Polo MR; Kikundi African NTD Program Managers Community of Practice.  
26-06-2023  
*PLoS Negl Trop Dis.*  
<https://pubmed.ncbi.nlm.nih.gov/37363911/>

The COVID-19 pandemic disrupted essential health services, including those provided by national neglected tropical disease (NTD) programs. Most mass drug administration (MDA) programs were postponed for 6-12 months following World Health Organization guidance released in April 2020 to temporarily halt NTD programs and launch necessary COVID-19 precautions. While NTD-endemic countries have since resumed MDA activities, it is critical to understand implementers' perspectives on the key challenges and opportunities for program relaunch, as these insights are critical for maximizing gains towards disease control and elimination during public health emergencies. Using data from using online surveys and focus group discussions, this mixed-methods study sought perspectives from Ministry of Health NTD Program Managers and implementing partners from non-governmental organizations working in sub-Saharan Africa. Data analysis revealed that findings converged around several main themes: disruptions for MDA programs included resource shortages due to prioritization of pandemic response, challenges adhering to COVID-19 safety protocols, and community hesitancy due to coronavirus transmission fears. Identified solutions for restarting MDA programs focused on adapting intervention delivery and packaging to minimize disease transmission, embracing technology to optimize intervention planning and delivery, and identifying opportunities to promote program integration between pandemic response strategies and NTD campaign delivery.

Findings identifies key challenges due to disruptions to NTD program delivery and provide strategic recommendations for endemic countries to build resilient programs that can continue to perform during and beyond global pandemics.

### **Pharmacokinetics, feasibility and safety of co-administering azithromycin, albendazole, and ivermectin during mass drug administration: A review.**

**McPherson S, Solomon AW, Seife F, Solomon H, Gebre T, Mabey DCW, Marks M.**

14-06-2023

*PLoS Negl Trop Dis.*

<https://pubmed.ncbi.nlm.nih.gov/37315102/>

**Introduction:** Traditionally, health ministries implement mass drug administration programmes for each neglected tropical disease (NTD) as separate and distinct campaigns. Many NTDs have overlapping endemicity suggesting co-administration might improve programme reach and efficiency, helping accelerate progress towards 2030 targets. Safety data are required to support a recommendation to undertake co-administration.

**Methodology:** We aimed to compile and summarize existing data on co-administration of ivermectin, albendazole and azithromycin, including both data on pharmacokinetic interactions and data from previous experimental and observational studies conducted in NTD-endemic populations. We searched PubMed, Google Scholar, research and conference abstracts, gray literature, and national policy documents. We limited the publication language to English and used a search period from January 1st, 1995 through October 1st, 2022. Search terms were: azithromycin and ivermectin and albendazole, mass drug administration co-administration trials, integrated mass drug administration, mass drug administration safety, pharmacokinetic dynamics, and azithromycin and ivermectin and albendazole. We excluded papers if they did not include data on co-administration of azithromycin and both albendazole and ivermectin, or azithromycin with either albendazole or ivermectin alone. **Results:** We identified a total of 58 potentially relevant studies. Of these we identified 7 studies relevant to the research question and which met our inclusion criteria. Three papers analyzed pharmacokinetic and pharmacodynamic interactions. No study found evidence of clinically significant drug-drug interactions likely to impact safety or efficacy. Two papers and a conference presentation reported data on the safety of combinations of at least two of the drugs. A field study in Mali suggested the rates of adverse events were similar with combined or separate administration, but was underpowered. A further field study in Papua New Guinea used all three drugs as part of a four-drug regimen also including diethylcarbamazine; in this setting, co-administration appeared safe but there were issues with the consistency in how adverse events were recorded. **Conclusion:** There are relatively limited data on the safety profile of co-administering ivermectin, albendazole and azithromycin as an integrated regimen for NTDs. Despite the limited amount of data, available evidence suggests that such a strategy is safe with an absence of clinically

important drug-drug interactions, no serious adverse events reported and little evidence for an increase in mild adverse events. Integrated MDA may be a viable strategy for national NTD programmes.

### **Evaluating the availability and quality of services for lymphatic filariasis morbidity in Ghana.**

**Edmiston M, Atinbire S, Mensah EO, Mensah E, Alomatu B, Asemanyi Mensah K, Palmer S.**

12-06-2023

*PLoS Negl Trop Dis.*

<https://pubmed.ncbi.nlm.nih.gov/37307289/>

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## **Gale**

### **Scabies in Spain: Trends in Public Interest and Ectoparasiticide Use.**

**Fernández Campo Á, Navarro Fernández Í, Arcos González P.**

23-06-2023

*Actas Dermosifiliogr.*

<https://pubmed.ncbi.nlm.nih.gov/37356548/>

Scabies is an ectoparasitic dermatosis caused by the *Sarcoptes scabiei* var. *hominis* mite, which lives and reproduces in humans. Its incidence in Spain has increased in recent years. The aim of this study was to complement existing evidence on the increasing number of scabies cases in our country by analyzing changes in ectoparasiticide prescriptions and Internet searches for scabies infestations measured by Google Trends. We also examined correlations between these 2 variables. Our results show that public interest in scabies has increased in recent years and is positively and significantly correlated with an increasing use of ectoparasiticides. We believe that Google Trends should be considered as a complementary tool for monitoring real-time trends in scabies infestations in Spain.

### **Comment on "Epidemic Scabies: New Treatment Challenges in an Ancient Disease".**

**Suárez-Amor Ó, Monteagudo B, Cabanillas M.**

23-06-2023

*Actas Dermosifiliogr.*

<https://pubmed.ncbi.nlm.nih.gov/37356544/>

### **Detection of a knockdown mutation in the voltage-sensitive sodium channel associated with permethrin tolerance in *Sarcoptes scabiei* var. *hominis* mites.**

**Riebenbauer K, Purkhauser K, Walochnik J, Urban N, Weber PB, Stamm T, Handisurya A.**

25-06-2023

*J Eur Acad Dermatol Venereol.*

<https://pubmed.ncbi.nlm.nih.gov/37356045/>

**Background:** Increasing evidence has sparked a debate on the loss of sensitivity of scabies mites to conventional

permethrin therapy. Mutations in the voltage-sensitive sodium channels (VSSC) were associated with knockdown resistance (kdr) in many arthropods, but have never been identified in *Sarcoptes scabiei* var. *hominis* mites. **Objectives:** To identify factors contributing to therapy failure. **Methods:** 67 mites were collected from 64 scabies-infested patients in Vienna, Austria, of whom 85.9% were refractory to prior permethrin-based treatments, and genotyped for the presence of nucleotide polymorphisms in domain II of the VSSC, known to be associated with kdr. Information regarding previous antiscabietic therapies, decontamination procedures and possible re-infestations by contacts as well as the response to re-imposed therapies were obtained. **Results:** Sequence alignment comparisons revealed previously unidentified mutations in the coding region of domain II of the VSSC. A novel A1663T transversion was detected in 97.0% of the mites, resulting in a non-synonymous substitution from methionine to leucine, M918L, a mutation known to confer kdr in other arthropods. In addition, a synonymous G1659A transition was identified in one mite, which otherwise showed a nucleotide sequence identical to the wild-type reference. No major inconsistencies were observed within the previous therapeutic and decontamination procedures, which could have accounted for the observed non-responsiveness to permethrin-based therapies. Subsequent cure of infestation was achieved in 65.6% of the participants, predominantly by combination therapies with topical permethrin and systemic ivermectin. However, in 14.6% of the cured cases, permethrin monotherapy sufficed for eradication of scabies, albeit in some cases prolonged exposure was necessary. **Conclusions:** The kdr-associated M918L mutation in the VSSC gene has now emerged in *S. scabiei* var. *hominis* mites. Hence, loss of sensitivity to permethrin due to kdr-type resistance may be more prevalent than anticipated and may be decisive for the therapy responsiveness of scabies-infested patients.

### Pharmacokinetics of ivermectin metabolites and their activity against *Anopheles stephensi* mosquitoes.

Kern C, Müller P, Chaccour C, Liechti ME, Hamann F, Duthaler U.

24-06-2023

*Malar J.*

<https://pubmed.ncbi.nlm.nih.gov/37355605/>

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

**No impact of helminth coinfection in patients with smear positive tuberculosis on immunoglobulin levels using a novel method measuring *Mycobacterium tuberculosis*-specific antibodies.**

Pushpamithran G, Skoglund C, Olsson F, Méndez-Aranda M, Schön T, Segelmark M, Stendahl O, Gilman RH, Blomgran R.

29-06-2023

*Allergy Asthma Clin Immunol.*

<https://pubmed.ncbi.nlm.nih.gov/37386541/>

Helminth/tuberculosis (TB)-coinfection can reduce cell-mediated immunity against *Mycobacterium tuberculosis* (Mtb) and increase disease severity, although the effects are highly helminth species dependent. Mtb have long been ranked as the number one single infectious agent claiming the most lives. The only licensed vaccine for TB (BCG) offers highly variable protection against TB, and almost no protection against transmission of Mtb. In recent few years the identification of naturally occurring antibodies in humans that are protective during Mtb infection has reignited the interest in adaptive humoral immunity against TB and its possible implementation in novel TB vaccine design. The effects of helminth/TB coinfection on the humoral response against Mtb during active pulmonary TB are however still unclear, and specifically the effect by globally prevalent helminth species such as *Ascaris lumbricoides*, *Strongyloides stercoralis*, *Ancylostoma duodenale*, *Trichuris trichiura*. Plasma samples from smear positive TB patients were used to measure both total and Mtb-specific antibody responses in a Peruvian endemic setting where these helminths are dominating. Mtb-specific antibodies were detected by a novel approach coating ELISA-plates with a Mtb cell-membrane fraction (CDC1551) that contains a broad range of Mtb surface proteins. Compared to controls without helminths or TB, helminth/TB coinfecting patients had high levels of Mtb-specific IgG (including an IgG1 and IgG2 subclass response) and IgM, which were similarly increased in TB patients without helminth infection. These data, indicate that helminth/TB coinfecting have a sustained humoral response against Mtb at the level of active TB only. More studies on the species-specific impact of helminths on the adaptive humoral response against Mtb using a larger sample size, and in relation to TB disease severity, are needed.

### Intestinal helminth infections and associated risk factors among adults in the Lao People's Democratic Republic.

Phonekeo S, Kounnavong S, Vonglokhom M, Siengsounthone L, Homsana A, Gummin S, Vounatsu P, Nittiyanant P, Worawichawong S, Aekplakorn W, Odermatt P, Sayasone S.

30-06-2023

*Infect Dis Poverty.*

<https://pubmed.ncbi.nlm.nih.gov/37386528/>

**Background:** Helminthiases are highly endemic in Southeast Asia, including the Lao People's Democratic Republic (Lao PDR). This study aimed to assess the current intestinal helminth infections and the associated risk factors among adults across the Lao PDR. **Methods:** A cross-sectional survey was conducted in 165 villages across 17 provinces and the Vientiane Capital, Lao PDR. A multi-stage sampling method was employed to select the adult study participants ( $\geq 18$  years). Data collection included (1) interview of the study participants, (2)



physical measurements, and (3) a five gram of stool sample from each study participant was collected and preserved in 10% formalin solution for intestinal helminth detection using formalin-ether concentration technique (FECT). Descriptive analysis was used to describe the socio-demographic characteristics of study participants and the prevalence of intestinal helminth infections. Logistic regressions were applied to test the association between intestinal helminth infection and individual risk factors. A P-value below 0.05 was considered statistically significant. **Results:** A total of 2800 study participants were enrolled. Their average age was 46.0 years; 57.8% were female. Overall, 30.9%, 8.6% and 1.5% of study participants were infected with one, two, or three different intestinal helminth species, respectively. Among the study participants 21.6% were infected with hookworm, 18.8% with *Opisthorchis viverrini*-like (Ov-like) infection, 4.8% with *Strongyloides stercoralis*, 2.3% with *Ascaris lumbricoides*, 1.5% with *Trichuris trichiura*, and 3.3% with *Taenia* spp. Ov-like infection was of high prevalence in the southern (28.8%) and central (21.3%) provinces, while hookworm (26.3%), *A. lumbricoides* (7.3%), *T. trichiura* (3.1%), and *Taenia* spp. (4.2%) were prevalent in the northern provinces. Risk analysis showed that men were more likely to be infected with hookworm [adjusted odds ratio (aOR) = 1.2,  $P = 0.019$ ]. The Lao-Tai ethnic group had a 5.2-times ( $P < 0.001$ ) higher chance of having Ov-like infection than the minorities. Possession of toilet facility at home was associated with reduced odds for Ov-like (aOR = 0.4,  $P < 0.001$ ) and hookworm (aOR = 0.6,  $P < 0.001$ ) infections. **Conclusions:** Our study provides a nationwide update of the intestinal helminth prevalence among adults in Lao PDR. To the best of our knowledge, this is the first Lao nationwide survey on intestinal helminth infections and risk factors in adults. It provides crucial information for national control programs for intestinal helminth infections in Lao PDR.

### Dogs as a source for the spreading of enteric parasites including zoonotic ones in Giza Province, Egypt.

Khalifa MM, Fouad EA, Kamel NO, Auda HM, El-Bahy MM, Ramadan RM.

22-06-2023

*Res Vet Sci.*

<https://pubmed.ncbi.nlm.nih.gov/37379694/>

### A Rare Complication of Ascariasis: A Case of Acute Interstitial Nephritis.

Carullo N, Divenuto F, Marascio N, Adams NJ, Giancotti A, Comi N, Faga T, Bolignano D, Coppolino G, Serapide F, Costa C, Torti C, Matera G, Quirino A, Andreucci M.

14-06-2023

*Diagnostics (Basel).*

<https://pubmed.ncbi.nlm.nih.gov/37370949/>

### Epidemiology of soil-transmitted helminths using quantitative PCR and risk factors for hookworm and *Necator americanus* infection in school children in Dak Lak province, Vietnam.

Hughes A, Ng-Nguyen D, Clarke NE, Dyer CEF, Hii SF, Clements ACA, Anderson RM, Gray DJ, Coffeng LE, Kaldor JM, Traub RJ, Vaz Nery S.

27-06-2023

*Parasit Vectors.*

<https://pubmed.ncbi.nlm.nih.gov/37370075/>

**Background:** Soil-transmitted helminth (STH) infection is driven by a complex interaction of demographic, socioeconomic and behavioural factors, including those related to water, sanitation and hygiene (WASH). Epidemiological studies that measure both infection and potential risk factors associated with infection help to understand the drivers of transmission in a population and therefore can provide information to optimise STH control programmes. **Methods:** During October and November 2019, we conducted a cross-sectional survey of the prevalence and intensity of STH infection and associated risk factors among 7710 primary-school-age children from 64 primary schools across 13 districts in Dak Lak province, Vietnam. Quantitative PCR (qPCR) was used to detect and quantify STH infections. **Results:** The predominant STH species was the hookworm *Necator americanus* (overall cluster-adjusted prevalence of 13.7%), and its prevalence was heterogeneously distributed across surveyed schools (0% to 56.3%). All other STH species had a prevalence of less than 1%. Using mixed-effects logistic regression, we found that the adjusted odds ratio (aOR) was significantly higher for both infection and moderate-to-heavy-intensity infection with *N. americanus* among children from multiple ethnic minority groups, compared to children from the majority group (Kinh). Adjusted odds of infection with *N. americanus* were also higher in children who reported practising open defecation at school (aOR 1.42, 95% CI 1.05, 1.93,  $P = 0.02$ ) and in those who had an unimproved household water supply (aOR 1.28, 95% CI 1.04, 1.57,  $P = 0.02$ ). Conversely, children with a flushing household toilet had a reduced risk of infection (aOR 0.58, 95% CI 0.47, 0.70,  $P < 0.01$ ), as did those whose primary female carer attended secondary (aOR 0.65, 95% CI 0.51, 0.84,  $P < 0.01$ ) or tertiary education (aOR 0.39, 95% CI 0.24, 0.63,  $P < 0.01$ ). **Conclusions:** This study is the largest reported prevalence survey of STH infections conducted using qPCR as a diagnostic technique. The findings of higher adjusted odds of infection amongst ethnic minority children highlight that STH control programmes may not be reaching certain population groups and that additional culturally appropriate approaches may be required. Additionally, the associations between specific WASH factors and infection indicate potential programmatic targets to complement preventive chemotherapy programmes.

## Leishmaniose

### Delving in folate metabolism in the parasite *Leishmania major* through a chemogenomic screen and methotrexate selection.

Bigot S, Leprohon P, Ouellette M.

29-06-2023

*PLoS Negl Trop Dis.*



<https://pubmed.ncbi.nlm.nih.gov/37384801/>

Most of our understanding of folate metabolism in the parasite *Leishmania* is derived from studies of resistance to the antifolate methotrexate (MTX). A chemical mutagenesis screen of *L. major* Friedlin and selection for resistance to MTX led to twenty mutants with a 2- to 400-fold decrease in MTX susceptibility in comparison to wild-type cells. The genome sequence of the twenty mutants highlighted recurrent mutations (SNPs, gene deletion) in genes known to be involved in folate metabolism but also in novel genes. The most frequent events occurred at the level of the locus coding for the folate transporter FT1 and included gene deletion and gene conversion events, as well as single nucleotide changes. The role of some of these FT1 point mutations in MTX resistance was validated by gene editing. The gene DHFR-TS coding for the dihydrofolate reductase-thymidylate synthase was the second locus with the most mutations and gene editing confirmed a role in resistance for some of these. The pteridine reductase gene PTR1 was mutated in two mutants. The episomal overexpression of the mutated versions of this gene, but also of DHFR-TS, led to parasites several fold more resistant to MTX than those overexpressing the wild-type versions. Genes with no known link with folate metabolism and coding for a L-galactolactone oxidase or for a methyltransferase were mutated in specific mutants. Overexpression of the wild-type versions of these genes in the appropriate mutants reverted their resistance. Our Mut-seq approach provided a holistic view and a long list of candidate genes potentially involved in folate and antifolate metabolism in *Leishmania*.

### **Rational repurposing, synthesis, in vitro and in silico studies of chromone-peptidyl hybrids as potential agents against *Leishmania donovani*.**

Hassan AHE, Bayoumi WA, El-Sayed SM, Phan TN, Kim YJ, Lee CH, Cho SB, Oh T, Ham G, Mahmoud K, No JH, Lee YS.

Dec-2023

*J Enzyme Inhib Med Chem.*

<https://pubmed.ncbi.nlm.nih.gov/37381756/>

### **Naïve antibody library derived monoclonal antibody against VP35 of Ebola virus.**

Lai JY, Corona A, Ng CL, Tramontano E, Choong YS, Lim TS.

26-06-2023

*Int J Biol Macromol.*

<https://pubmed.ncbi.nlm.nih.gov/37379953/>

Ebola virus is notorious for causing severe and even deadly haemorrhagic fever in infected humans and non-human primates. The high fatality rate of Ebola virus disease (EVD) has highlighted the need for effective diagnosis and treatment. Two monoclonal antibodies (mAbs) have been approved by USFDA for treatment of EVD. Virus surface glycoprotein is the common target for diagnostic and therapy including vaccines. Even so, VP35, a viral RNA polymerase cofactor and interferon inhibitor could be a

potential target to curb EVD. The present work describes the isolation of three mAb clones from a phage-displayed human naïve scFv library against recombinant VP35. The clones showed binding against rVP35 in vitro and inhibition of VP35 in luciferase reporter gene assay. Structural modelling analysis was also carried out to identify the binding interactions involved in the antibody-antigen interaction model. This allows some insight into the "fitness" of the binding pocket between the paratope and target epitope which would be useful for the design of new mAbs through in silico means in the future. In conclusion, the information obtained from the 3 isolated mAbs could be potentially useful in the quest to improve VP35 targeting for therapeutic development in the future.

### **Editorial: New strategies for the treatment of diseases caused by trypanosomatid parasites.**

Cardoso FO, Almeida-Souza F, Maretti-Mira AC, Abreu-Silva AL.

12-06-2023

*Front Cell Infect Microbiol.*

<https://pubmed.ncbi.nlm.nih.gov/37377646/>

### **Cysteinyl-leukotrienes promote cutaneous Leishmaniasis control.**

Noronha LPT, Martins MDA, Castro-Junior AB, Thorstenberg ML, Costa-Soares L, Rangel TP, Carvalho-Gondim F, Rossi-Bergmann B, Savio LEB, Canetti CA, Coutinho-Silva R.

12-06-2023

*Front Cell Infect Microbiol.*

<https://pubmed.ncbi.nlm.nih.gov/37377641/>

### **Antiprotozoal activity of auranofin on *Trypanosoma cruzi*, *Leishmania tropica* and *Toxoplasma gondii*: in vitro and ex vivo study.**

Yıldırım A, Özbilgin A, Yereli K.

28-06-2023

*Trans R Soc Trop Med Hyg.*

<https://pubmed.ncbi.nlm.nih.gov/37377375/>

**Background:** Three obligate intracellular protozoan parasite species, which are responsible for significant morbidity and mortality and settle in macrophage cells, affect more than one-half of the world's population, namely, *Trypanosoma cruzi*, *Leishmania tropica* and *Toxoplasma gondii*, which are causative agents of Chagas disease, leishmaniasis and toxoplasmosis, respectively. In the current study, it was aimed to investigate the in vitro and ex vivo antiprotozoal activity of auranofin on *T. cruzi*, *L. tropica* and *T. gondii*. **Methods:** The in vitro drug efficacy (IC<sub>50</sub>) of auranofin was investigated by haemocytometry and the CellTiter-Glo assay methods and the ex vivo drug efficacy (IC<sub>50</sub>) by light microscopic examination of Giemsa-stained slides. Also, the cytotoxic activity (CC<sub>50</sub>) of auranofin was examined by the CellTiter-Glo assay. The selectivity index (SI) was calculated for auranofin. **Results:** According to IC<sub>50</sub>, CC<sub>50</sub> and SI data, auranofin did not exhibit cytotoxic activity on Vero cells, but exhibited antiprotozoal activity on epimastigotes and intracellular

amastigotes of *T. cruzi*, promastigotes and intracellular amastigotes of *L. tropica* and intracellular tachyzoites of *T. gondii* ( $p < 0.05$ ). **Conclusions:** The detection antiprotozoal activity of auranofin on *T. cruzi*, *L. tropica* and *T. gondii* according to the IC50, CC50 and SI values is considered an important and promising development. This is significant because auranofin may be an effective alternative treatment for Chagas disease, leishmaniasis and toxoplasmosis in the future.

### **Feline leishmaniosis: hematological and biochemical analysis.**

**Silva DTD, Alves ML, Spada JCP, Leonel JAF, Vioti G, Benassi JC, Carregaro VML, Alves-Martin MF, Starke-Buzetti WA, Oliveira TMFS.**

26-06-2023

*Rev Bras Parasitol Vet.*

<https://pubmed.ncbi.nlm.nih.gov/37377321/>

One hundred and sixty-six cats from two animal shelters were subjected to enzyme-linked immunosorbent assay (ELISA), indirect immunofluorescence antibody test (IFAT), conventional polymerase chain reaction (cPCR), quantitative PCR (qPCR) and parasitological tests (PA) for the diagnosis of *Leishmania* spp. Among them, 15% (25/166), 53.6% (89/166), 3.6% (06/166) and 1.8% (03/166) were positive by ELISA, IFAT, both PCRs and PA, respectively. The sequencing of ITS-1 PCR amplicons revealed a 100% match with *Leishmania infantum*. After the *Leishmania* spp. survey, 12 cats were selected and divided into two groups for clinical, hematological, and biochemical analysis: six *L. infantum* positive cats (G1) and six *Leishmania* spp. negative cats (G2). All the cats were negative for feline immunodeficiency virus (FIV) and feline leukemia virus (FeLV). A statistical analysis indicated significantly low platelet counts and significant hyperproteinemia associated with hypoalbuminemia in positive cats ( $p < 0.05$ ). Our results suggest that in endemic areas, cats with clinical signs of feline leishmaniosis (such as skin lesions, weight loss and/or enlarged lymph nodes) and that exhibit hematological and biochemical changes, such as low platelet counts and hyperproteinemia with hypoalbuminemia, should be tested for *Leishmania* spp. infection.

### **Use of liposomal amphotericin B in disseminated cutaneous leishmaniasis caused by *Leishmania braziliensis* in a pediatric patient with Down syndrome.**

**Sandoval-Juárez A, Rojas-Palomino N, Roca LK, Pílares-Barco G, Cuadros-Castro J, Araujo-Castillo R.**

Jan-Mar 2023

*Rev Peru Med Exp Salud Publica.*

<https://pubmed.ncbi.nlm.nih.gov/37377243/>

We present a case of disseminated cutaneous leishmaniasis with extensive manifestation in a pediatric patient with Down syndrome. The case was confirmed by parasitological and immunological tests. The species was identified as *Leishmania* (*Viannia*) *braziliensis* by polymerase chain reaction-restriction fragment length polymorphisms (PCR-RFLP). The immune deficit that occurs as part of Down syndrome may have been the

reason for the aggressive and prolonged clinical manifestations as well as the poor response to stibogluconate and deoxycholate amphotericin. The patient was treated with liposomal amphotericin B and at the end of therapy, showed clinical improvement of the lesions. This report highlights the challenges of the diagnosis and treatment of cutaneous leishmaniasis in immunosuppressed pediatric patients, especially under difficult social, economic and geographic conditions. Leishmaniasis should be considered as a differential diagnosis when treating atypical chronic dermatologic ulcers; the use of liposomal amphotericin in immunocompromised patients should also be considered in these cases.

### **Degron Pathways and Leishmaniasis: Debating Potential Roles of *Leishmania* spp. Proteases Activity on Guiding Hosts Immune Response and Their Relevance to the Development of Vaccines.**

**Oliveira AS, Aredes-Riguetti LM, Pereira BAS, Alves CR, Souza-Silva F.**

23-05-2023

*Vaccines (Basel).*

<https://pubmed.ncbi.nlm.nih.gov/37376405/>

### **Effect of Local Administration of Meglumine Antimoniate and Polyhexamethylene Biguanide Alone or in Combination with a Toll-like Receptor 4 Agonist for the Treatment of Papular Dermatitis due to *Leishmania infantum* in Dogs.**

**Martínez-Flórez I, Guerrero MJ, Dalmau A, Cabré M, Alcover MM, Berenguer D, Good L, Fisa R, Riera C, Ordeix L, Solano-Gallego L.**

10-06-2023

*Pathogens.*

<https://pubmed.ncbi.nlm.nih.gov/37375511/>

### **Genetic Diversity and Population Structure of *Leishmania infantum* in Morocco as Revealed by Multilocus Sequence Typing (MLST) Approach.**

**El Mazini S, Barhoumi M, Mhaidi I, Daoui O, Kbaich MA, El Kacem S, El Idrissi Saik I, Riyad M, Bekhti K, Guizani I, Lemrani M.**

31-05-2023

*Pathogens.*

<https://pubmed.ncbi.nlm.nih.gov/37375475/>

*Leishmania infantum* is endemic in Morocco, and it causes both visceral (VL) and cutaneous leishmaniasis (CL). In this study, the multilocus sequence typing (MLST) approach was used to investigate the phylogeny and population structure of *Leishmania infantum* strains isolated from CL and VL patients and the canine reservoir in different leishmaniasis endemic foci in Morocco. For this purpose, eight loci (pgm, alat, me, fh, g6pd, pgd, gpi and cytb) were amplified in 40 samples, out of which 31 were successfully sequenced. The genetic diversity analysis detected a high

degree of intraspecific genetic variability among the studied strains. The phylogenetic and the haplotype analyses showed that most of the strains from the same geographical areas clustered together. The recombination among *Leishmania infantum* strains was revealed through a splits tree analysis and the number of recombination events. Moreover, the assessment of the gene flow between *Leishmania infantum* and *Leishmania tropica* through phylogenetic analysis and haplotype diversity in two endemic foci where the two species were sympatric showed no genetic exchange between the two species.

### **Leishmania and Leishmaniasis Research: The Past 50 Years and the Future.**

Chang KP.

30-05-2023

*Pathogens.*

<https://pubmed.ncbi.nlm.nih.gov/37375466/>  
**Leishmaniasis in Greece: The Veterinary Perspective.**

Symeonidou I, Sioutas G, Gelasakis AI, Tsokana CN, Papadopoulos E.

26-05-2023

*Pathogens.*

### **Natural-Product-Inspired Microwave-Assisted Synthesis of Novel Spirooxindoles as Antileishmanial Agents: Synthesis, Stereochemical Assignment, Bioevaluation, SAR, and Molecular Docking Studies.**

Sahu NK, Sharma R, Suhas KP, Joshi J, Prakash K, Sharma R, Pratap R, Hu X, Kaur S, Jain M, Coluccini C, Coghi P, Chaudhary S.

16-06-2023

*Molecules.*

<https://pubmed.ncbi.nlm.nih.gov/37375374/>

Leishmaniasis is a neglected tropical disease, and there is an emerging need for the development of effective drugs to treat it. To identify novel compounds with antileishmanial properties, a novel series of functionalized spiro[indoline-3,2'-pyrrolidin]-2-one/spiro[indoline-3,3'-pyrrolizin]-2-one **23a-f**, **24a-f**, and **25a-g** were prepared from natural-product-inspired pharmaceutically privileged bioactive sub-structures, i.e., isatins **20a-h**, various substituted chalcones **21a-f**, and **22a-c** amino acids, via 1,3-dipolar cycloaddition reactions in MeOH at 80 °C using a microwave-assisted approach. Compared to traditional methods, microwave-assisted synthesis produces higher yields and better quality, and it takes less time. We report here the in vitro antileishmanial activity against *Leishmania donovani* and SAR studies. The analogues **24a**, **24e**, **24f**, and **25d** were found to be the most active compounds of the series and showed IC<sub>50</sub> values of 2.43 µM, 0.96 µM, 1.62 µM, and 3.55 µM, respectively, compared to the standard reference drug Amphotericin B (IC<sub>50</sub> = 0.060 µM). All compounds were assessed for *Leishmania* DNA topoisomerase type IB inhibition activity using the standard drug Camptothecin, and **24a**, **24e**, **24f**,

and **25d** showed potential results. In order to further validate the experimental results and gain a deeper understanding of the binding manner of such compounds, molecular docking studies were also performed. The stereochemistry of the novel functionalized spirooxindole derivatives was confirmed by single-crystal X-ray crystallography studies.

### **Two New Cytotoxic Sesquiterpene-Amino Acid Conjugates and a Coumarin-Glucoside from Crossostephium chinense.**

Wang Z, Chitama BA, Suganuma K, Yamano Y, Sugimoto S, Kawakami S, Kaneko O, Otsuka H, Matsunami K.

11-06-2023

*Molecules.*

<https://pubmed.ncbi.nlm.nih.gov/37375252/>

### **Bioactivity Screening and Chemical Characterization of Biocompound from Endophytic Neofusicoccum parvum and Buergeriella spartinae Isolated from Mangrove Ecosystem.**

Cadamuro RD, Bastos IMADS, de Freitas ACO, Rosa MDS, Costa GO, da Silva IT, Robl D, Stoco PH, Sandjo LP, Treichel H, Steindel M, Fongaro G.

16-06-2023

*Microorganisms.*

<https://pubmed.ncbi.nlm.nih.gov/37375101/>

The discovery of biomolecules has been the subject of extensive research for several years due to their potential to combat harmful pathogens that can lead to environmental contamination and infections in both humans and animals. This study aimed to identify the chemical profile of endophytic fungi, namely *Neofusicoccum parvum* and *Buergeriella spartinae*, which were isolated from *Avecinnia schaueriana* and *Laguncularia racemosa*. We identified several HPLC-MS compounds, including Ethylidene-3,39-biplumbagin, Pestauicolactone A, Phenylalanine, 2-Isopropylmalic acid, Fusaproliferin, Suspendole, Ansellone, Calanone derivative, Terpestacin, and others. Solid-state fermentation was conducted for 14-21 days, and methanol and dichloromethane extraction were performed to obtain a crude extract. The results of our cytotoxicity assay revealed a CC<sub>50</sub> value > 500 µg/mL, while the virucide, Trypanosoma, leishmania, and yeast assay demonstrated no inhibition. Nevertheless, the bacteriostatic assay showed a 98% reduction in *Listeria monocytogenes* and *Escherichia coli*. Our findings suggest that these endophytic fungi species with distinct chemical profiles represent a promising niche for further exploring new biomolecules.

### **Regulatory Functions of Hypoxia in Host-Parasite Interactions: A Focus on Enteric, Tissue, and Blood Protozoa.**

DeMichele E, Sosnowski O, Buret AG, Allain T.

16-06-2023

*Microorganisms.*

<https://pubmed.ncbi.nlm.nih.gov/37375100/>

### **Aurachins, Bacterial Antibiotics Interfering with Electron Transport Processes.**

**Kruth S, Nett M.**

17-06-2023

*Antibiotics (Basel).*

<https://pubmed.ncbi.nlm.nih.gov/37370386/>

### **Effect of 3-Carene and the Micellar Formulation on Leishmania (Leishmania) amazonensis.**

**Silva ARST, Costa AMB, Scher R, Andrade-Neto VV, Sarmiento VHV, Santos AJ, Torres-Santos EC, Jain S, Nunes RS, Menna-Barreto RFS, Dolabella SS.**

16-06-2023

*Trop Med Infect Dis.*

<https://pubmed.ncbi.nlm.nih.gov/37368742/>

Leishmaniasis are neglected tropical diseases caused by obligate intracellular *protozoa* of the genus *Leishmania*. The drugs used in treatment have a high financial cost, a long treatment time, high toxicity, and variable efficacy. 3-Carene (3CR) is a hydrocarbon monoterpene that has shown in vitro activity against some *Leishmania* species; however, it has low water solubility and high volatility. This study aimed to develop Poloxamer 407 micelles capable of delivering 3CR (P407-3CR) to improve antileishmanial activity. The micelles formulated presented nanometric size, medium or low polydispersity, and Newtonian fluid rheological behavior. 3CR and P407-3CR inhibited the growth of *L. (L.) amazonensis* promastigote with  $IC_{50}/48h$  of  $488.1 \pm 3.7$  and  $419.9 \pm 1.5$  mM, respectively. Transmission electron microscopy analysis showed that 3CR induces multiple nuclei and kinetoplast phenotypes and the formation of numerous cytosolic invaginations. Additionally, the micelles were not cytotoxic to L929 cells or murine peritoneal macrophages, presenting activity on intracellular amastigotes. P407-3CR micelles ( $IC_{50}/72 h = 0.7 \pm 0.1$  mM) increased the monoterpene activity by at least twice (3CR:  $IC_{50}/72 h > 1.5$  mM). These results showed that P407 micelles are an effective nanosystem for delivering 3CR and potentiating antileishmanial activity. More studies are needed to evaluate this system as a potential therapeutic option for leishmaniasis.

### **Reemergence of Visceral Leishmaniasis in Henan Province, China.**

**Yang C, Li S, Lu D, He Z, Wang D, Qian D, Liu Y, Zhou R, Ji P, Chen JH, Zhang H.**

12-06-2023

*Trop Med Infect Dis.*

<https://pubmed.ncbi.nlm.nih.gov/37368736/>

Visceral leishmaniasis (VL) was widely prevalent in Henan Province in the 1950s. Through active efforts by the government, there were no local cases reported from 1984 to 2015. In 2016, local VL cases reoccurred, and there was an increasing trend of VL cases in Henan Province. To provide a scientific control of VL, an investigation was conducted in Henan Province from 2016 to 2021. The data from VL cases were obtained from the Disease Surveillance Reporting System of the Chinese

Center for Disease Control and Prevention. The rK39 immunochromatographic test (ICT) and PCR assay were performed among high-risk residents and all dogs in the patients' village. ITS1 was amplified, sequenced, and subjected to phylogenetic analyses. A total of 47 VL cases were reported in Henan Province during 2016-2021. Of the cases, 35 were local, and they were distributed in Zhengzhou, Luoyang, and Anyang. The annual average incidence was 0.008/100,000, showing an upward trend year by year ( $\chi^2 = 3.987$ ,  $p = 0.046$ ). Their ages ranged from 7 months to 71 years, with 44.68% (21/47) in the age group of 0-3 years and 46.81% (22/47) in the age group  $\geq 15$  years. The cases occurred throughout the year. The high-risk populations were infants and young children (age  $\leq 3$ ), accounting for 51.06% (24/47), followed by farmers at 36.17% (17/47). The ratio of males to females was 2.13:1. The positive rates of rK39 ICT and PCR were 0.35% (4/1130) and 0.21% (1/468) in the residents. The positive rates of rK39 ICT and PCR were 18.79% (440/2342) and 14.92% (139/929) in the dogs. The ITS1 amplification products in the patients and positive dogs were sequenced. The homology between the target sequence and *Leishmania infantum* was more than 98%. The phylogenetic analysis indicated that the patients and the positive dogs were infected by the same type of *Leishmania*, which was consistent with the strains in the hilly endemic areas in China. This paper showed that patients and domestic dogs were infected by the same type of *L. infantum* and that the positive rate in dogs was relatively high in Henan Province. Because the measures of patient treatment and culling of infected dogs were not effective in reducing VL incidence in Henan Province, it is urgent to develop new approaches for the control of VL, such as wearing insecticide-impregnated collars on dogs, treating the positive dogs, spraying insecticide for sandflies control, and improving residents' self-protection awareness to prevent the further spread of VL in Henan Province.

### **Leishmanicidal and immunomodulatory activities of the formononetin (a natural isoflavone) against Leishmania tropica.**

**Mahmoudvand H, Khalaf AK, Rajabi PZ, Karbasian N, Ghasemian Yadegari J.**

26-06-2023

*BMC Res Notes.*

<https://pubmed.ncbi.nlm.nih.gov/37365655/>

### **Antileishmanial evaluation of triazole-butenolide conjugates: design, synthesis, in vitro screening, SAR and in silico ADME predictions.**

**Pandey AR, Singh SP, Ramalingam K, Yadav K, Bisen AC, Bhatta RS, Srivastava M, Tripathi R, Goyal N, Sashidhara KV.**

06-04-2023

*RSC Med Chem.*

<https://pubmed.ncbi.nlm.nih.gov/37360388/>

### **Flavonoids from Pistacia chinensis subsp. integerrima with leishmanicidal**



### **activity: computational and experimental evidence.**

**Rauf A, Rashid U, Shbeer AM, Al-Ghorbani M, Muhammad N, Khalil AA, Naz H, Sharma R, Ribaud G.**  
26-06-2023

*Nat Prod Res.*

<https://pubmed.ncbi.nlm.nih.gov/37357619/>

### **Effects of Synthetic Ligustrazine-Based Chalcone Derivatives on Trypanosoma brucei brucei and Leishmania spp. Promastigotes.**

**Alkhalidi AAM.**

08-06-2023

*Molecules.*

<https://pubmed.ncbi.nlm.nih.gov/37375205/>

### **Efficacy of an Immunotherapy Combining Immunogenic Chimeric Protein Plus Adjuvant and Amphotericin B against Murine Visceral Leishmaniasis.**

**Vale DL, Freitas CS, Martins VT, Moreira GJL, Machado AS, Ramos FF, Pereira IAG, Bandeira RS, de Jesus MM, Tavares GSV, Ludolf F, Chávez-Fumagalli MA, Galdino AS, Fujiwara RT, Bueno LL, Roatt BM, Christodoulides M, Coelho EAF, Lage DP.**

13-06-2023

*Biology (Basel).*

<https://pubmed.ncbi.nlm.nih.gov/37372136/>

Visceral leishmaniasis (VL) in the Americas is a chronic systemic disease caused by infection with *Leishmania infantum* parasites. The toxicity of antileishmanial drugs, long treatment course and limited efficacy are significant concerns that hamper adequate treatment against the disease. Studies have shown the promise of an immunotherapeutics approach, combining antileishmanial drugs to reduce the parasitism and vaccine immunogens to activate the host immune system. In the current study, we developed an immunotherapy using a recombinant T cell epitope-based chimeric protein, ChimT, previously shown to be protective against *Leishmania infantum*, with the adjuvant monophosphoryl lipid A (MPLA) and amphotericin B (AmpB) as the antileishmanial drug. BALB/c mice were infected with *L. infantum* stationary promastigotes and later they received saline or were treated with AmpB, MPLA, ChimT/Amp, ChimT/MPLA or ChimT/MPLA/AmpB. The combination of ChimT/MPLA/AmpB significantly reduced the parasite load in mouse organs ( $p < 0.05$ ) and induced a Th1-type immune response, which was characterized by higher ratios of anti-ChimT and anti-parasite IgG2a:IgG1 antibodies, increased IFN- $\gamma$  mRNA and IFN- $\gamma$  and IL-12 cytokines and accompanied by lower levels of IL-4 and IL-10 cytokines, when compared to other treatments and controls (all  $p < 0.05$ ). Organ toxicity was also lower with the ChimT/MPLA/AmpB immunotherapy, suggesting that the inclusion of the vaccine and adjuvant ameliorated the toxicity of AmpB to some degree. In addition, the ChimT vaccine alone stimulated in vitro murine macrophages to significantly kill three different internalized species of

*Leishmania* parasites and to produce Th1-type cytokines into the culture supernatants. To conclude, our data suggest that the combination of ChimT/MPLA/AmpB could be considered for further studies as an immunotherapy for *L. infantum* infection.

### **Laurequinone, a Lead Compound against Leishmania.**

**García-Davis S, López-Arencibia A, Bethencourt-Estrella CJ, San Nicolás-Hernández D, Viveros-Valdez E, Díaz-Marrero AR, Fernández JJ, Lorenzo-Morales J, Piñero JE.**  
30-05-2023

*Mar Drugs.*

<https://pubmed.ncbi.nlm.nih.gov/37367658/>

Among neglected tropical diseases, leishmaniasis is one of the leading causes, not only of deaths but also of disability-adjusted life years. This disease, caused by protozoan parasites of the genus *Leishmania*, triggers different clinical manifestations, with cutaneous, mucocutaneous, and visceral forms. As existing treatments for this parasitosis are not sufficiently effective or safe for the patient, in this work, different sesquiterpenes isolated from the red alga *Laurencia johnstonii* have been studied for this purpose. The different compounds were tested in vitro against the promastigote and amastigote forms of *Leishmania amazonensis*. Different assays were also performed, including the measurement of mitochondrial potential, determination of ROS accumulation, and chromatin condensation, among others, focused on the detection of the cell death process known in this type of organism as apoptosis-like. Five compounds were identified that displayed leishmanicidal activity: laurequinone, laurinterol, debromolaurinterol, isolaurinterol, and aplysin, showing IC<sub>50</sub> values against promastigotes of 1.87, 34.45, 12.48, 10.09, and 54.13  $\mu$ M, respectively. Laurequinone was the most potent compound tested and was shown to be more effective than the reference drug miltefosine against promastigotes. Different death mechanism studies carried out showed that laurequinone appears to induce programmed cell death or apoptosis in the parasite studied. The obtained results underline the potential of this sesquiterpene as a novel anti-kinetoplastid therapeutic agent.

### **The Src and Abl family kinases activate the spleen tyrosine kinase to maximize phagocytosis and Leishmania infection.**

**Ullah I, Barrie U, Kernan RM, Mamula ET, Khuong Li FTH, Booshehri LM, Rhodes EL, Bradford JM, Datta A, Wetzel DM.**

26-06-2023

*J Cell Sci.*

<https://pubmed.ncbi.nlm.nih.gov/37357611/>

### **Detection of Leishmania major and Leishmania infantum in cats during an outbreak of cutaneous leishmaniasis in Southern Israel.**



**Kleinerman G, Melloul S, Chaim L, Mergy SE, Kaufman RG, Dagan N, Nachum-Biala Y, Kitaichik S, Gross S, Astman N, Baneth G.**

14-06-2023

*Comp Immunol Microbiol Infect Dis.*

<https://pubmed.ncbi.nlm.nih.gov/37356168/>

Prevalence of *Leishmania* spp. infection was studied in stray cats in two military bases in Southern Israel during a cutaneous leishmaniasis (CL) human outbreak caused by *Leishmania major*. Human CL cases increased from 0/100 in 2008 to 1.28/100 in 2022 in camp #1, and from 0.17/100 in 2008 to 6.4/100 in 2022, in camp #2. Eight out of 29 cats sampled were *Leishmania*-seropositive (28 %) and 7/29 (24 %) were internal transcribed spacer 1 (ITS1) PCR-positive, out of which four (14 %) were positive for *L. major* and three (10 %) for *L. infantum*. Five positive-cats had skin lesions including ulcers, alopecia and scabs, and five had eye lesions. This is the first report of *L. major* infection in cats in Israel and one of the first descriptions in felines worldwide. A larger cohort of cats and vector studies are necessary to determine if felids may act as reservoirs or sentinels of human *L. major* infection.

## 2-Aroyl quinazolinone: Synthesis and in vitro anti-parasitic activity.

**Setshedi KJ, Beteck RM, Jesumoroti OJ, Ilbeigi K, Mabille D, Caljon G, Van der Kooy F, Legoabe LJ.**

23-06-2023

*Chem Biol Drug Des.*

<https://pubmed.ncbi.nlm.nih.gov/37353860/>

Trypanosomes and *Leishmania* are parasitic protozoans that affect millions of people globally. Herein we report the synthesis of 2-aryl quinazolinones and their antiprotozoal efficacy against *Trypanosoma brucei*, *Trypanosoma brucei rhodesiense*, *Trypanosoma cruzi*, and *Leishmania infantum*. These compounds were counter-screened against a human cell line for cytotoxicity. Thirteen of the twenty target compounds in this study inhibited the growth of these parasites, with compounds KJ1, and KJ10 exhibiting IC50 values of 4.7  $\mu$ M (*T. b. brucei*) and 1.1  $\mu$ M (*T. b. rhodesiense*), respectively.

## Visceral Leishmaniasis Caused by *Leishmania Tropic*.

**Özbilgin A, Tunalı V, Çavuş İ, Tetik AV, Dinç M, Yalçın T, Gündüz C, Beyaz M, Köse Ş.**

23-06-2023

*Acta Parasitol.*

<https://pubmed.ncbi.nlm.nih.gov/37351773/>

## Thermoneutrality and severe malaria: investigating the effect of warmer environmental temperatures on the inflammatory response and disease progression.

**Vialard F, Allaëys I, Dong G, Phan MP, Singh U, Hébert MJ, Dieudé M, Langlais D, Boilard E, Labbé DP, Olivier M.**

07-06-2023

*Front Immunol.*

<https://pubmed.ncbi.nlm.nih.gov/37350957/>

**Introduction:** Most studies using murine disease models are conducted at housing temperatures (20 - 22°C) that are sub-optimal (ST) for mice, eliciting changes in metabolism and response to disease. Experiments performed at a thermoneutral temperature (TT; 28 - 31°C) have revealed an altered immune response to pathogens and experimental treatments in murine disease model that have implications for their translation to clinical research. How such conditions affect the inflammatory response to infection with *Plasmodium berghei* ANKA (PbA) and disease progression is unknown. We hypothesized that changes in environmental temperature modulate immune cells and modify host response to malaria disease. To test this hypothesis, we conducted experiments to determine: (1) the inflammatory response to malarial agents injection in a peritonitis model and (2) disease progression in PbA-infected mice at TT compared to ST. **Methods:** In one study, acclimatized mice were injected intraperitoneally with native hemozoin (nHZ) or *Leishmania* at TT (28 - 31°C) or ST, and immune cells, cytokine, and extracellular vesicle (EV) profiles were determined from the peritoneal cavity (PEC) fluid. In another study, PbA-infected mice were monitored until end-point (i.e. experimental malaria score  $\geq 4$ ). **Results:** We found that *Leishmania* injection resulted in decreased cell recruitment and higher phagocytosis of nHZ in mice housed at TT. We found 398 upregulated and 293 downregulated proinflammatory genes in mice injected with nHZ, at both temperatures. We report the presence of host-derived EVs never reported before in a murine parasitic murine model at both temperatures. We observed metabolic changes in mice housed at TT, but these did not result to noticeable changes in disease progression compared to ST. **Discussion:** To our knowledge, these experiments are the first to investigate the effect of thermoneutrality on a malaria murine model. We found important metabolic difference in mice housed at TT. Our results offer insights on how thermoneutrality might impact a severe malaria murine model and directions for more targeted investigations.

## Characterization of thiamine pyrophosphokinase of vitamin B1 biosynthetic pathway as a drug target of *Leishmania donovani*.

**Ranjan Kumar R, Jain R, Akhtar S, Parveen N, Ghosh A, Sharma V, Singh S.**

23-06-2023

*J Biomol Struct Dyn.*

<https://pubmed.ncbi.nlm.nih.gov/37350670/>

## [Visceral Leishmaniasis in an Immunocompetent Patient: A Case Report].

**Rodrigues Monteiro M, Serra JT, Gomes F, Tinoco J.**

23-06-2023

*Acta Med Port.*

<https://pubmed.ncbi.nlm.nih.gov/37350643/>

Leishmaniasis is a parasitic disease transmitted by the bite of female sandflies that occurs in tropical and subtropical

climate regions. Visceral leishmaniasis is the most serious manifestation of the disease, leading to a 95% mortality rate after two years of infection if untreated. Visceral leishmaniasis is frequently associated with immunocompromised states, with the human immunodeficiency virus being the most prevalent. Most cases of visceral leishmaniasis are caused by the species *Leishmania donovani* and *Leishmania infantum*, the latter being the endemic species in the Mediterranean basin. In Portugal, the number of reported cases of visceral leishmaniasis has decreased in the last few years, with 15 cases reported between 2017 and 2021. The authors present a case of visceral leishmaniasis in an immunocompetent patient who manifested the classic pentad: fever, weight loss, hepatosplenomegaly, pancytopenia and hypergammaglobulinemia. The diagnosis was made by the observation of amastigotes of the *Leishmania infantum* species in the bone marrow aspirate examination, and the patient was successfully treated with liposomal amphotericin B.

### Versatile anti-infective properties of pyrido- and dihydropyrido[2,3-d]pyrimidine-based compounds.

Al Nasr IS, Corona A, Koko WS, Khan TA, Ben Said R, Daoud I, Rahali S, Tramontano E, Schobert R, Amdouni N, Biersack B.

15-06-2023

*Bioorg Med Chem.*

<https://pubmed.ncbi.nlm.nih.gov/37336083/>

### Synthesis and biological evaluation of carbohydrate-Coumarin/vanillic acid hybrid as a promising antiparasitic agent.

Sharma A, Saikia P, Saha S, Kumar D, Panchadhayee R.

Aug-2023

*Carbohydr Res.*

<https://pubmed.ncbi.nlm.nih.gov/37327765/>

### Updated estimation of cutaneous leishmaniasis incubation period in French Guiana.

Blaizot R, Fontaine A, Demar M, Delon F, d'Oleón AB, Mayet A, de Laval F, de Santi VP, Briolant S.

14-06-2023

*PLoS Negl Trop Dis.*

<https://pubmed.ncbi.nlm.nih.gov/37315094/>

**Background:** The cutaneous leishmaniasis (CL) incubation period (IP) is defined as the time between parasite inoculation by sandfly bite and the onset of the first CL lesion. IP distribution is difficult to assess for CL because the date of exposure to an infectious bite cannot be accurately determined in endemic areas. IP current estimates for CL range from 14 days to several months with a median around 30-60 days, as established by a few previous studies in both New and Old Worlds. **Methodology:** We estimated CL incubation period distribution using time-to-event models adapted to interval-censored data based on declared date of travels from symptomatic military personnel living in non-

endemic areas that were exposed during their short stays in French Guiana (FG) between January 2001 and December 2021. **Principal findings:** A total of 180 patients were included, of which 176 were men (97.8%), with a median age of 26 years. When recorded, the parasite species was always *Leishmania guyanensis* (31/180, 17.2%). The main periods of CL diagnosis spread from November to January (84/180, 46.7%) and over March-April (54/180, 30.0%). The median IP was estimated at 26.2 days (95% Credible Level, 23.8-28.7 days) using a Bayesian accelerated failure-time regression model. Estimated IP did not exceed 62.1 days (95% CI, 56-69.8 days) in 95% of cases (95th percentile). Age, gender, lesion number, lesion evolution and infection date did not significantly modify the IP. However, disseminated CL was significantly associated with a 2.8-fold shortening of IP. **Conclusions:** This work suggests that the CL IP distribution in French Guiana is shorter and more restricted than anticipated. As the incidence of CL in FG usually peaks in January and March, these findings suggest that patients are contaminated at the start of the rainy season.

### Combined immunohistochemical protocols to differentiate macrophages within the mononuclear-phagocyte system.

Lazzarini G, Abramo F, Albanese F, Pirone A, Miragliotta V.

Aug-2023

*Ann Anat.*

<https://pubmed.ncbi.nlm.nih.gov/37207851/>

**Background:** The "mononuclear phagocyte system" (MPS) refers to dispersed mononuclear monocytes and macrophages and is used to distinguish them from polymorphonuclear cells. The term "histiocyte" indicates large cells with voluminous granulated cytoplasm, sometimes containing engulfed particles, recognized as fully differentiated end cells of the MPS. Dendritic cells (DC) represent another diversified population whose inclusion in the MPS is still debated. The diverse cells of the MPS cannot all be characterized by single antigen markers or unique functions expressed at all stages of cell differentiation or activation. Nevertheless, in a diagnostic setting, their reliable identification plays a major role when a specific therapy must be established. Understanding the heterogeneity among MPS cell populations is indeed relevant to define different therapeutic approaches that can range from the use of antibiotics to immunomodulatory agents. For this reason, we attempted to establish a protocol to reliably identify the proportion of macrophages within the mononuclear phagocyte system in a tissue and/or in a given inflammatory population. **Methods:** the Tafari method was used in different double immunofluorescence protocols using an anti-Iba-1, anti-MAC387, and anti-CD11b-CD68-CD163-CD14-CD16 antibody. **Results and discussion:** in normal canine skin the anti-Iba-1 antibody stained an epidermal cell population (i.e. Langerhans cells) and scattered cells within the dermal compartment. MAC387 was unable to stain cells containing *Leishmania* amastigotes in leishmaniasis-diagnosed samples as the anti-CD11b-CD68-

CD163-CD14-CD16 antibody did. By using a combination of staining protocols to differentiate macrophages within the whole histiocytic infiltrate we validated the use of a cocktail of rabbit monoclonal antibodies raised against CD11b, CD68, CD163, CD14, CD16 to stain skin macrophages.

### Development of a novel immunoFET technology-based POC assay for detection of *Leishmania donovani* and *Leishmania major*.

**Yentur Doni N, Bertani PJ, Volpedo G, Saljoughian N, Varikuti S, Matlashewski G, Lu W, Satoskar AR.**

Jul-2023

*Parasite Immunol.*

<https://pubmed.ncbi.nlm.nih.gov/37183939/>

Leishmaniasis is considered as one of the 20 neglected tropical diseases. Current methods of leishmanial diagnosis depend on conventional laboratory-based techniques, which are time-consuming, costly and require special equipment and trained personnel. In this context, we aimed to provide an immuno field effect transistors (ImmunoFET) biosensor that matches the conventional standards for point-of-care (POC) monitoring and detection of *Leishmania* (L.) *donovani*/*Leishmania major*. Crude antigens prepared by repeated freeze thawing of L. *donovani*/L. *major* stationary phase promastigotes were used for ELISA and ImmunoFETs. *Leishmania*-specific antigens were serially diluted in 1× PBS from a concentration of  $10^6$  - $10^2$  parasites/mL. A specific polyclonal antibody-based sandwich ELISA was established for the detection of *Leishmania* antigens. An immunoFET technology-based POC novel assay was constructed for the detection of *Leishmania* antigens. Interactions between antigen-antibody at the gate surface generate an electrical signal that can be measured by semiconductor field-effect principles. Sensitivity was considered and measured as the change in current divided by the initial current. The final L. *donovani*/L. *major* crude antigen protein concentrations were measured as 1.50 mg/mL. Sandwich ELISA against the *Leishmania* 40S ribosomal protein detected *Leishmania* antigens could detect as few as 100 L. *donovani*/L. *major* parasites. An immunoFET biosensor was constructed based on the optimization of aluminium gallium nitride/gallium nitride (AlGaIn/GaN) surface oxidation methods. The device surface was composed by an AlGaIn/GaN wafer with a 23 nm AlGaIn barrier layer, a 2 µm GaN layer on the silicon carbide (SiC) substrate for *Leishmania* binding, and coated with a specific antibody against the *Leishmania* 40S ribosomal protein, which was successfully detected at concentrations from  $10^6$  to  $10^2$  parasites/mL in 1× PBS. At the concentration of  $10^4$  parasites, the immunoFETs device sensitivities were 13% and 0.052% in the sub-threshold regime and the saturation regime, respectively. *Leishmania* parasites were successfully detected by the ImmunoFET biosensor at a diluted concentration as low as 150 ng/mL. In this study, the developed ImmunoFET biosensor performed well. ImmunoFET biosensors can be used as an alternative diagnostic method to ELISA. Increasing the sensitivity and optimization of immuno-FET

biosensors might allow earlier and faster detection of leishmaniasis.

### Targeting the nucleotide metabolism of *Trypanosoma brucei* and other trypanosomatids.

**Hofer A.**

19-05-2023

*FEMS Microbiol Rev.*

<https://pubmed.ncbi.nlm.nih.gov/37156497/>

### The sphingolipids ceramide and inositol phosphorylceramide protect the *Leishmania major* membrane from sterol-specific toxins.

**Haram CS, Moitra S, Keane R, Kuhlmann FM, Frankfater C, Hsu FF, Beverley SM, Zhang K, Keyel PA.**

Juin-2023

*J Biol Chem.*

<https://pubmed.ncbi.nlm.nih.gov/37094699/>

### Mucosal Leishmaniasis of the lip: Report of an Exuberant case in a Young man.

**de Arruda JAA, Tomo S, Cunha JLS, Guevara JR, Martínez I, Reyes O, Bracho V, Sanchez C, de Andrade BAB, Villarreal-Dorrego M.**

Juin-2023

*Head Neck Pathol.*

<https://pubmed.ncbi.nlm.nih.gov/36346574/>

**Background:** Leishmaniasis is a tropical disease caused by protozoan parasites of the genus *Leishmania*. Mucosal leishmaniasis has been described as secondary to the cutaneous form; however, isolated mucosal involvement can also occur. Specifically, mucosal leishmaniasis of the lip is poorly described and its diagnosis challenges clinicians. **Methods:** We herein report a case of mucosal leishmaniasis affecting the lower lip without cutaneous involvement in a 20-year-old Venezuelan man. The patient had no relevant past medical history. Clinically, a mass-like lesion with ulcerations and crusts was observed. **Results:** Microscopically, the lesion was composed of granulomatous inflammation along with macrophages containing intracytoplasmic inclusions similar to round-shaped *Leishmania*. The species *Leishmania* (*Viannia*) *braziliensis* was confirmed. Treatment with meglumine antimonate was effective. The lesion healed satisfactorily, and no side effects or recurrences were observed. **Conclusion:** Clinicians should be aware of isolated forms of mucosal leishmaniasis of the lip, even in cases where the cutaneous lesion is undetected or clinically manifests as self-limiting. Knowing the endemic areas in the scenario of the dynamics of the ecoepidemiology of leishmaniasis is also essential for surveillance and counselling of the population.

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## Lèpre

### Assessing the cost-effectiveness of integrated case management of Neglected Tropical Diseases in Liberia.

Godwin-Akpan TG, Diaconu K, Edmiston M, Smith JS Jr, Sosu F, Weiland S, Kollie KK.

29-06-2023

*BMC Health Serv Res.*

<https://pubmed.ncbi.nlm.nih.gov/37386431/>

**Background:** In 2017, Liberia became one of the first countries in the African region to develop and implement a national strategy for integrated case management of Neglected Tropical Diseases (CM-NTDs), specifically Buruli ulcer, leprosy, lymphatic filariasis morbidities, and yaws. Implementing this plan moves the NTD program from many countries' fragmented (vertical) disease management. This study explores to what extent an integrated approach offers a cost-effective investment for national health systems. **Methods:** This study is a mixed-method economic evaluation that explores the cost-effectiveness of the integrated CM-NTDs approach compared to the fragmented (vertical) disease management. Primary data were collected from two integrated intervention counties and two non-intervention counties to determine the relative cost-effectiveness of the integrated program model vs. fragmented (vertical) care. Data was sourced from the NTDs program annual budgets and financial reports for integrated CM-NTDs and Mass Drug Administration (MDA) to determine cost drivers and effectiveness. **Results:** The total cost incurred by the integrated CM-NTD approach from 2017 to 2019 was US\$ 789,856.30, with the highest percentage of costs for program staffing and motivation (41.8%), followed by operating costs (24.8%). In the two counties implementing fragmented (vertical) disease management, approximately US\$ 325,000 was spent on the diagnosis of 84 persons and the treatment of twenty-four persons suffering from NTDs. While 2.5 times as much was spent in integrated counties, 9-10 times more patients were diagnosed and treated. **Conclusions:** The cost of a patient being diagnosed under the fragmented (vertical) implementation is five times higher than integrated CM-NTDs, and providing treatment is ten times as costly. Findings indicate that the integrated CM-NTDs strategy has achieved its primary objective of improved access to NTD services. The success of implementing an integrated CM-NTDs approach in Liberia, presented in this paper, demonstrates that NTD integration is a cost-minimizing solution.

### Effectiveness of population-wide screening and mass drug administration for leprosy control in Kiribati: the COMBINE protocol.

Coleman M, Hill J, Timeon E, Rimon E, Bauro T, Ioteba N, Cunanan A, Douglas NM, Islam T, Tomlinson J, Campbell PO, Williman J, Priest P, Marais BJ, Britton WJ, Chambers ST.

29-06-2023

*BMJ Open.*

<https://pubmed.ncbi.nlm.nih.gov/37385746/>

### Platelet-rich Fibrin versus Platelet-rich Plasma: A Study to Assess Efficacy as a Regenerative Medicine Strategy for Chronic Cutaneous Ulcers.

Ratan VR, Inamadar AC.

Jan-Mar 2023

*J Cutan Aesthet Surg.*

<https://pubmed.ncbi.nlm.nih.gov/37383978/>

**Background:** The management of nonhealing ulcers has been a major challenge clinically. Current therapies include debridement, offloading, etc., which show a poor response. Newer modalities include stem cells, platelet-derived growth factors, and fibrin glues, which reduce healing time. Platelets play a major role in wound healing through the secretion of growth factors, chemokines, etc. and have been an area of interest as a modality in regenerative medicine. **Aims and objective:** The aim was to study the comparative efficacy of autologous platelet-rich fibrin (PRF) and platelet-rich plasma (PRP) as a regenerative medicine strategy for chronic cutaneous ulcers. **Materials and methods:** Forty-four ulcers of duration greater than six weeks were enrolled for a comparative study comprising two groups, each divided either into group A receiving PRF dressings or group B receiving PRP dressing for six weeks. The ulcer evaluation was performed at baseline, each weekly dressing, and a two-week follow-up. **Results:** Primary efficacy was assessed by the percentage reduction in the volume of ulcers and re-epithelization at eight weeks. In total, 95.2% of ulcers in group A and 90.4% of ulcers in group B showed complete re-epithelization. One ulcer in group A and two ulcers in group B developed an infection. The recurrence of the ulcer was seen in four ulcers in the PRF group and three ulcers in the PRP group. **Conclusion:** Dressings done with PRF and PRP showed similar efficacy in the percentage reduction in the volume and re-epithelization of chronic cutaneous ulcers. Both dressings were associated with similar complications. PRF and PRP dressings provide a safe, efficacious, and inexpensive regenerative medicine strategy in the healing of chronic cutaneous ulcers.

### Increasing the Safety Profile of Follicular Unit Extraction by Eliminating the Use of Bupivacaine and Nerve Block: Experience from a Tertiary Care Center of North India.

Shah FY, Shah AA, Tasaduq I, Bhat MA, Rather AY, Dar UK, Shah SA, Hassan I.

Jan-Mar 2023

*J Cutan Aesthet Surg.*

<https://pubmed.ncbi.nlm.nih.gov/37383976/>

**Introduction:** Follicular unit extraction (FUE) is a safe and effective procedure in the hands of an expert. Side effects, particularly those which can lead to significant morbidity or mortality, are unacceptable as the procedure is done purely for cosmetic reasons. Any modification that decreases the risk associated with the procedure should be promoted. **Aim and objective:** The study was conducted



to determine whether FUE can be carried out effectively with the elimination of nerve blocks and bupivacaine from the procedure. **Materials and methods:** The study was conducted in 30 patients suffering from androgenetic alopecia. The donor areas were anesthetized using lignocaine with adrenaline just below the area to be harvested. The anesthetic was injected intradermally resulting in the development of wheals in continuity, forming a linear line. From our previous experience, we found intradermal administration of lignocaine to give better anesthetic effect as compared to subcutaneous administration, although the former is more painful. This was followed by injection of tumescent into the donor area and donor harvesting, which lasted for a couple of hours. The recipient area was anesthetized using a similar technique of linear injection of anesthetic just ahead of the proposed hair line. **Results:** The total amount of lignocaine with adrenaline consumed during the surgery ranged from a minimum of 6.1 ml to 8.5 ml, with an average of 7.6 ml. The average duration of the entire surgery was 6.5 h, ranging from 4.5 to 8.5 h. None of the patients experienced any pain during the entire surgery, and there were no significant side effects related to anesthetic administration in any patient. **Discussion:** We found lignocaine with adrenaline to be a very safe and effective anesthetic agent for field block anesthesia in FUE. The exclusion of bupivacaine and nerve blocks from the procedure of FUE can further increase the safety of the procedure, particularly for beginners and in cases where the area to be covered is not extensive (Norwood-Hamilton grades 3, 4, and 5).

### Silicone in Dermatology: An Update.

Bains P, Kaur S.

Jan-Mar 2023

*J Cutan Aesthet Surg.*

<https://pubmed.ncbi.nlm.nih.gov/37383974/>

### Atypical Hansen's Disease Mimicking Xanthogranuloma: Role of Cytology.

Vijayvergiya G, Panwar H, Santosh T, Patra S, Joshi D, Asati DP, Kapoor N.

Jan-Mar 2023

*J Cutan Aesthet Surg.*

<https://pubmed.ncbi.nlm.nih.gov/37383972/>

### Fractional Laser Resurfacing for Acne Scars: Our Experience at Tertiary Care Hospital of North India.

Bhat YJ, Rehman F, Hassan I, Krishan K, Daing A, Yaseen A, Jeelani S, Akhtar S, Bashir S, Zareek S, Devi R, Nabi N.

Jan-Mar 2023

*J Cutan Aesthet Surg.*

<https://pubmed.ncbi.nlm.nih.gov/37383970/>

**Background:** Acne is very common among adolescents, which may sometimes persist into adulthood, and acne scars continue to have a profoundly negative impact on quality of life. Of all the various modalities available, fractional lasers have shown effective results. **Aims and objectives:** The aim of this study was to assess the efficacy and safety of fractional carbon dioxide (CO<sub>2</sub>) laser

resurfacing in atrophic facial acne scars. **Materials and methods:** The study included 104 subjects aged ≥18 years with atrophic acne scars on face of more than 6 months of duration recruited over a period of 1 year. All the patients were treated with fractional CO<sub>2</sub> laser (600 W power and wavelength 10,600 nm). Four sessions of fractional CO<sub>2</sub> laser resurfacing were done at 6-week intervals in each patient. We compared the improvement rate of scars after every session at 6-week interval, 2 weeks after the last session, and finally 6 months after the last laser session. **Results:** The difference between the mean baseline score (3.43) and mean final score (1.83) using Goodman and Baron's qualitative scar scale was found to be statistically significant ( $P = 0.001$ ). Mean improvement increased from first treatment session to the end of the treatment course from 0.56 to 1.62 indicating the role of the number of sessions in the overall improvement of acne scars. With regard to overall satisfaction, maximum number of patients were either very satisfied (55.8%) or satisfied (25%) as compared to those who were only slightly satisfied (11.5%) or completely unsatisfied (7.7%). **Conclusion:** Fractional ablative laser gives excellent results in the management of acne scars and has emerged as an appealing non-invasive option for this indication. Being a safe and effective option for atrophic acne scar treatment, it can be recommended wherever available.

### Effectiveness of Secretome from Human Umbilical Cord Mesenchymal Stem Cells in Gel (10% SM-hUCMSC Gel) for Chronic Wounds (Diabetic and Trophic Ulcer) - Phase 2 Clinical Trial.

Tan ST, Aisyah PB, Firmansyah Y, Nathasia N, Budi E, Hendrawan S.

23-06-2023

*J Cutan Aesthet Surg.*

<https://pubmed.ncbi.nlm.nih.gov/37383529/>

### Kikuchi-Fujimoto disease: A comprehensive review.

Mahajan VK, Sharma V, Sharma N, Rani R.

06-06-2023

*World J Clin Cases.*

<https://pubmed.ncbi.nlm.nih.gov/37383134/>

Kikuchi-Fujimoto disease, a rare form of necrotizing lymphadenitis, is an uncommon, benign, self-limiting disorder of obscure etiology. It affects mostly young adults of both genders. Clinically, it presents with fever and lymphadenopathy of a firm to rubbery consistency frequently involving cervical lymph nodes while weight loss, splenomegaly, leucopenia, and elevated erythrocyte sedimentation rate feature in severely affected patients. Cutaneous involvement occurs in about 30%-40% of cases as facial erythema and nonspecific erythematous papules, plaques, acneiform or morbilliform lesions of great histologic heterogeneity. Both Kikuchi-Fujimoto disease and systemic lupus erythematosus share an obscure and complex relationship as systemic lupus erythematosus may occasionally precede, develop subsequently, or sometimes be associated concurrently with Kikuchi-Fujimoto disease. It is often mistaken for non-Hodgkin

lymphoma while lupus lymphadenitis, cat-scratch disease, Sweet's syndrome, Still's disease, drug eruptions, infectious mononucleosis, and viral or tubercular lymphadenitis are other common differentials. Fine needle aspiration cytology mostly has features of nonspecific reactive lymphadenitis and immunohistochemistry studies usually show variable features of uncertain diagnostic value. Since its diagnosis is exclusively from histopathology, it needs to be evaluated more carefully; an early lymph node biopsy will obviate the need for unnecessary investigations and therapeutic trials. Its treatment with systemic corticosteroids, hydroxychloroquine, or antimicrobial agents mostly remains empirical. The article reviews clinicoepidemiological, diagnostic, and management aspects of KFD from the perspective of practicing clinicians.

### **Autochthonous Leprosy in the United States.**

**Belzer A, Ochoa MT, Adler BL.**

29-06-2023

*N Engl J Med.*

<https://pubmed.ncbi.nlm.nih.gov/37379141/>

### **Leprosy, the Great Imitator of Rheumatic Diseases: A Case Study.**

**Youssef H, Mahani T, Hoojati M.**

26-05-2023

*Cureus.*

<https://pubmed.ncbi.nlm.nih.gov/37378226/>

A 68-year-old Hispanic man was referred to our center for cutaneous vasculitis of the lower extremities, diagnosed via skin biopsy. He had a 10-year history of erythematous plaques complicated by persistent, non-healing ulcers previously treated with prednisone and hydroxychloroquine. Laboratory testing was significant for positive U1-ribonucleoprotein antibody, antinuclear antibody human epithelial-2, and an elevated erythrocyte sedimentation rate. A repeat skin biopsy revealed nonspecific ulcerations. The patient was diagnosed with a mixed connective tissue disease with features of scleroderma. Mycophenolate was initiated, and prednisone was tapered. After two years of relapsing ulcerations on his lower extremities, a third skin punch biopsy showed dermal granulomas with numerous acid-fast organisms, and a polymerase chain reaction identified *Mycobacterium lepromatosis*, indicating polar lepromatous leprosy with an erythema nodosum leprosum reaction. After three months of minocycline and rifampin therapy, his lower extremity ulcerations and erythema resolved. Our case highlights the variable and elusive nature of this disease, which can mimic many systemic rheumatologic conditions.

### **Study on Autoimmune Thyroid Disorders in Chronic Spontaneous Urticaria at a Tertiary Care Central Rural Hospital in India.**

**Pendam M, Madke B, Singh A, Jawade S.**

23-05-2023

*Cureus.*

<https://pubmed.ncbi.nlm.nih.gov/37378208/>

### **Prevalence and Predictors of COVID-19 Long-Term Symptoms: A Cohort Study from the Amazon Basin.**

**Silva KM, Freitas DCA, Medeiros SS, Miranda LVA, Carmo JBM, Silva RG, Becker LL, Abreu ES, Buranello L, Souza MSM, Nadruz W, Fernandes-Silva MM, Maguire JH, Toledo-Cornell C, Silvestre OM.**

26-06-2023

*Am J Trop Med Hyg.*

<https://pubmed.ncbi.nlm.nih.gov/37364863/>

### **Explore the reasons for SARS-CoV-2 vaccine hesitancy among healthcare workers: a cross-sectional study.**

**Bereda G.**

14-04-2023

*Ann Med Surg (Lond).*

<https://pubmed.ncbi.nlm.nih.gov/37363532/>

Vaccine hesitancy is described by the WHO as "a delay in acceptance or refusal of safe immunizations notwithstanding the availability of vaccine services." In Ethiopia, the cumulative acceptance rate of the COVID-19 vaccination was 57.8%. Ethiopia had a lower rate of COVID-19 vaccination acceptance than was required to create herd immunity. This study was carried out to determine the prevalence of COVID-19 vaccine reluctance and its contributing factors. Based on the findings of the study, recommendations were made to the relevant bodies in order to reduce vaccine hesitancy and increase vaccination acceptability. **Objectives:** A cross-sectional online-based study was conducted to better understand the reasons for SARS-CoV-2 vaccine hesitancy among healthcare workers (HCWs) in Oromia regional state, Ethiopia. **Materials and methods:** A cross-sectional survey using an internet platform was conducted from 18 June 2021, to 29 June 2022. A multistage cluster sampling strategy was used to find participants, with each cluster representing a sampling unit made up of a set of population elements. Participants are then randomly chosen from those clusters. The data were entered in Epi Info 7.2.0.1, then exported to Microsoft Excel and imported into statistical programs for social sciences (26.0 version) for statistical analysis. Statistical significance was considered to be a *P* value of less than 0.05. **Results:** Four hundred twenty-two HCWs completed the online survey. The majority of the HCWs were male (*n*=234, 55.5%), urban residents (*n*=396, 93.8%), protestants (*n*=168, 39.8%), and married people (*n*=232, 55.0%). The prevalence of HCWs reluctant to receive the SARS-CoV-2 vaccination was 69.7% (*n*=294). Age from 19 to 34 [adjusted odds ratio (AOR) =1.48, 95% CI: 1.69-7.42, *P*=<0.001], female sex (AOR =3.68, 95% CI =1.370-6.413, *P*=0.002), income between 3501 and 8500 ETB (AOR =1.67, 95% CI =1.380-5.697, *P*=0.048), information from websites (AOR =1.79, 95% CI =1.720-31.179, *P*=0.013), vaccine skepticism (AOR =4.75, 95% CI =3.210-8.152, *P*=0.009), and potential adverse effects of a SARS-CoV-2 vaccine (AOR =2.18, 95% CI =1.732-5.248, *P*=0.043) were

independent predictors of SARS-CoV-2 vaccine hesitancy among HCWs. **Conclusion and recommendations:** HCWs were reluctant to get the SARS-CoV-2 immunization at a high percentage overall. To reduce hesitancy to receive the SARS-CoV-2 vaccination among HCWs, the Oromia regional state health bureau should be required to increase HCWs' knowledge of the COVID-19 vaccine by providing proper training for all HCWs.

### How is ischemic stroke linked to a COVID-19-infected patient different from other cardiovascular risk factors? a case report.

Bereda G.

19-04-2023

*Ann Med Surg (Lond).*

<https://pubmed.ncbi.nlm.nih.gov/37363457/>

### Unique genomic sequences in a novel *Mycobacterium avium* subsp. *hominissuis* lineage enable fine scale transmission route tracing during pig movement.

Komatsu T, Ohya K, Ota A, Nishiuchi Y, Yano H, Matsuo K, Odoi JO, Suganuma S, Sawai K, Hasebe A, Asai T, Yanai T, Fukushi H, Wada T, Yoshida S, Ito T, Arikawa K, Kawai M, Ato M, Baughn AD, Iwamoto T, Maruyama F.

10-05-2023

*One Health.*

<https://pubmed.ncbi.nlm.nih.gov/37363238/>

*Mycobacterium avium* subsp. *hominissuis* (MAH) is one of the most prevalent mycobacteria causing non-tuberculous mycobacterial disease in humans and animals. Of note, MAH is a major cause of mycobacterial granulomatous mesenteric lymphadenitis outbreaks in pig populations. To determine the precise source of infection of MAH in a pig farm and to clarify the epidemiological relationship among pig, human and environmental MAH lineages, we collected 50 MAH isolates from pigs reared in Japan and determined draft genome sequences of 30 isolates. A variable number of tandem repeat analysis revealed that most pig MAH isolates in Japan were closely related to North American, European and Russian human isolates but not to those from East Asian human and their residential environments. Historical recombination analysis revealed that most pig isolates could be classified into SC2/4 and SC3, which contain MAH isolated from pig, European human and environmental isolates. Half of the isolates in SC2/4 had many recombination events with MAH lineages isolated from humans in East Asia. To our surprise, four isolates belonged to a new lineage (SC5) in the global MAH population. Members of SC5 had few footprints of inter-lineage recombination in the genome, and carried 80 unique genes, most of which were located on lineage specific-genomic islands. Using unique genetic features, we were able to trace the putative transmission route via their host pigs. Together, we clarify the possibility of species-specificity of MAH in addition to local adaptation. Our results highlight two transmission routes of MAH, one exposure on pig farms from the environment

and the other via pig movement. Moreover, our study also warns that the evolution of MAH in pigs is influenced by MAH from patients and their residential environments, even if the MAH are genetically distinct.

### Nasopharyngeal *Mycobacterium abscessus* Infection: A Case Report and Literature Review.

Kaji M, Namkoong H, Nagao G, Azekawa S, Nakagawara K, Tanaka H, Morita A, Asakura T, Kamata H, Uwamino Y, Yoshida M, Fukunaga K, Hasegawa N.

20-06-2023

*Infect Drug Resist.*

<https://pubmed.ncbi.nlm.nih.gov/37361939/>

**Background:** *Mycobacterium abscessus* (*M. abscessus*) is a rapidly growing bacterium (RGM) that causes refractory pulmonary and extrapulmonary infections. However, studies investigating pharyngeal and laryngeal *M. abscessus* infections are limited. **Case presentation:** A 41-year-old immunocompetent woman complaining of bloody sputum was referred to our hospital. Although her sputum culture tested positive for *M. abscessus* subsp. *abscessus*, radiological findings were not indicative of pulmonary infection or sinusitis. Further diagnostic workup, including laryngeal endoscopy and positron emission tomography/computed tomography (PET/CT), confirmed the presence of nasopharyngeal *M. abscessus* infection. The patient was initially treated with intravenous amikacin, imipenem/cilastatin, azithromycin, and clofazimine for 28 days, after which the patient was provided with amikacin, azithromycin, clofazimine, and sitafloxacin for four months. After the completion of antibiotic therapy, the patient showed negative results on sputum smear and culture and normal findings on PET/CT and laryngeal endoscopy. Whole-genome sequencing of this strain revealed that it belonged to the ABS-GL4 cluster, which has a functional erythromycin ribosomal methylase gene, although it is not a major lineage in non-cystic fibrosis (CF) patients in Japan and Taiwan and in CF patients in European countries. We conducted a literature review and identified seven patients who developed pharyngeal/laryngeal non-tuberculous mycobacterium (NTM) infection. Four of the eight patients had a history of immunosuppressant use, including steroids. Seven of the eight patients responded well to their treatment regimens. **Conclusion:** Patients whose sputum culture tests are positive for NTM and who meet the diagnostic criteria for NTM infection but do not have intrapulmonary lesions should be evaluated for otorhinolaryngological infections. Our case series revealed that immunosuppressant use is a risk factor for pharyngeal/laryngeal NTM infection and that patients with pharyngeal/laryngeal NTM infections respond relatively well to antibiotic therapy.

### Erratum for Andrade et al., "Antimicrobial Resistance among Leprosy Patients in Brazil: Real-World Data Based on the National Surveillance Plan".

**Andrade ESN, Brandão JG, Silva JSD, Coriolano CRF, Rosa PS, Moraes MO, Ferreira CO, Gomes CM, Araújo WN.**  
26-06-2023  
*Antimicrob Agents Chemother.*  
<https://pubmed.ncbi.nlm.nih.gov/37358442/>

### **Clinicopathological Study of Chronic Kidney Disease of Unknown Etiology in Odisha.**

**Parida S, Das S, Kar A, Routray RK.**  
Oct-2022  
*J Assoc Physicians India.*  
<https://pubmed.ncbi.nlm.nih.gov/37355866/>

### **Naftifine: A Topical Allylamine for Superficial Dermatophytosis.**

**Trailokya AA, Shirsat AB, Madhu R, Shah B.**  
Mai-2023  
*J Assoc Physicians India.*  
<https://pubmed.ncbi.nlm.nih.gov/37355825/>

Dermatophytosis is a very common public health problem with high prevalence. Dermatophytes are a highly specialized set of filamentous fungi, which are adapted to keratinized tissues of humans and animals. Dermatophytosis is the most common fungal infection worldwide, affecting approximately 20-25% of the world's population. The etiological agents of dermatophytosis, called dermatophytes, change with geography and socioeconomic status. *Trichophyton rubrum* (T. rubrum) is the prime species for skin and nail infections followed by *T. mentagrophytes*/ *T. interdigital* complex. There is a shift from *T. rubrum* to *T. mentagrophytes* in India for superficial fungal infections. In order to deal with fungal infections, treatment strategies involve the use of systemic antifungals and/or topical antifungal agents. Naftifine is a synthetic allylamine antifungal first reported in 1974 and in 1985 became the first commercially available allylamine. The highly lipophilic nature of allylamine allows efficient penetration and reasonably high concentrations in the stratum corneum (SC) and hair follicles. Naftifine is fungicidal as well as fungistatic. The higher efficacy rates of allylamines over imidazoles for the treatment of fungal infections, even for months after cessation of treatment, is thought to be due to their fungicidal effect, as well as to potentially greater keratin binding and slower release from the SC. The effectiveness of naftifine is also demonstrated against various bacteria belonging to both gram-negative and gram-positive classes. The antiinflammatory property of naftifine has been reported in various preclinical studies where it has been shown to target the prostaglandin pathway. Naftifine 1 and 2% gel and cream is approved by The United States Food and Drug Administration (USFDA), recently naftifine has been approved in India by the Indian regulatory authority Drug Controller General of India (DCGI) for the treatment of dermatophytosis. Naftifine 2% also appears to be a promising treatment, requiring fewer applications than the 1% formulation. Naftifine appears to be effective in a single dose and has a shorter treatment duration than azoles. Naftifine demonstrated its efficacy and safety in various clinical studies of tinea infections. Naftifine offers

a very useful and promising option for treating dermatophytosis.

### **Why TB programmes should assess for comorbidities, determinants and disability at the start and end of TB treatment.**

**Harries AD, Lin Y, Thekkur P, Nair D, Chakaya J, Dongo JP, Luzze H, Chimzizi R, Mubanga A, Timire C, Kavenga F, Satyanarayana S, Kumar AMV, Khogali M, Zachariah R.**  
01-07-2023  
*Int J Tuberc Lung Dis.*  
<https://pubmed.ncbi.nlm.nih.gov/37353872/>

### **Systematic Review of Hansen Disease Attributed to Mycobacterium lepromatosis.**

**Collin SM, Lima A, Heringer S, Sanders V, Pessotti HA, Deps P.**  
Juil-2023  
*Emerg Infect Dis.*  
<https://pubmed.ncbi.nlm.nih.gov/37347507/>

### **Evaluating the availability and quality of services for lymphatic filariasis morbidity in Ghana.**

**Edmiston M, Atinbire S, Mensah EO, Mensah E, Alomatu B, Asemanyi Mensah K, Palmer S.**  
12-06-2023  
*PLoS Negl Trop Dis.*  
<https://pubmed.ncbi.nlm.nih.gov/37307289/>

### **Spatial analysis of the epidemiological risk of leprosy in the municipalities of Minas Gerais.**

**Bueno IC, Lages DDS, Lana FCF.**  
05-06-2023  
*PLoS Negl Trop Dis.*  
<https://pubmed.ncbi.nlm.nih.gov/37276221/>

**Background:** Leprosy remains a significant public health problem of high importance. This investigation aims to analyze the spatial distribution of the leprosy epidemiological risk in the municipalities of Minas Gerais. **Methods:** This ecological study was conducted with new leprosy cases diagnosed from 2004 to 2019 in the municipalities of the state of Minas Gerais. Based on the epidemiological indicators, a composite indicator called the leprosy epidemiological risk index was estimated, classifying municipalities as high, medium, low and very low risk. For the spatial analysis, the global and local spatial autocorrelation statistics were used to identify the spatial distribution of the leprosy epidemiological risk in the periods 2004-2011 and 2012-2019 and classified as High/High, Low/Low, High/Low and Low /High. **Results:** Although leprosy is declining in the state of Minas Gerais, the Global Moran Index confirmed the spatial dependence between municipalities for the two analyzed periods, characterizing the formation of clusters. When performing the local spatial autocorrelation, it was found that the macroregions with the highest number of municipalities



with high indices, surrounded by other municipalities with high indices (high-high), were Northwest, East, South East, North, and Northeast. The low risk macroregions were Southeast, Center, South-Center and South. **Conclusion:** Leprosy has a heterogeneous spatial pattern and remains concentrated in historically endemic areas of the state. It underscores the importance of intensifying actions to combat leprosy in these municipalities and macroregions. Promote improved access to health services and combat stigma and prejudice to eliminate leprosy as a public health problem.

### Cutaneous paecilomyces infection in an immunocompetent patient.

**Dsouza PA, Monteiro RC, Martis J, Fernandes S.**

Août-2023

*Int J Dermatol.*

<https://pubmed.ncbi.nlm.nih.gov/37140100/>

## Morsures de serpent

### Ethnomedicinal uses, phytochemistry, and pharmacological relevance of *Justicia procumbens* (Oriental Water Willow) - A promising traditional plant.

**Ibrahim SRM, Mohamed SGA, Abdallah HM, Mohamed GA.**

27-06-2023

*Ethnopharmacol.*

<https://pubmed.ncbi.nlm.nih.gov/37385576/>

### Posterior Reversible Leucoencephalopathy Syndrome: Case Series, Comments, and Diagnostic Dilemma.

**Chaudhuri J, Basu S, Roy MK, Chakravarty A.**

28-06-2023

*Curr Neurol Neurosci Rep.*

<https://pubmed.ncbi.nlm.nih.gov/37378723/>

**Purpose of review:** To report a series of patients with clinical and radiological features suggestive of posterior reversible encephalopathy syndrome (PRES) related to diverse etiologies emphasizing its pathophysiological basis. **Recent findings:** Posterior reversible encephalopathy syndrome (PRES) may present with a broad range of clinical symptoms from headache and visual disturbances to seizure and altered mentation. Typical imaging findings include posterior-circulation predominant vasogenic edema. Although there are many well-documented diseases associated with PRES, the exact pathophysiologic mechanism has yet to be fully elucidated. Generally accepted theories revolve around disruption of the blood-brain barrier secondary to elevated intracranial pressures or endothelial injury induced by ischemia from a vasoconstrictive response to rising blood pressure or toxins/cytokines. While clinical and radiographic reversibility is common, long-standing morbidity and mortality can occur in severe forms. In patients with malignant forms of PRES, aggressive care has

markedly reduced mortality and improved functional outcomes. Various factors that have been associated with poor outcome include altered sensorium, hypertensive etiology, hyperglycemia, longer time to control the causative factor, elevated C reactive protein, coagulopathy, extensive cerebral edema, and hemorrhage on imaging. Reversible cerebral vasoconstriction syndromes (RCVS) and primary angiitis of the central nervous system (PACNS) are invariably considered in the differential diagnosis of new cerebral arteriopathies. Recurrent thunderclap headache (TCH), and single TCH combined with either normal neuroimaging, border zone infarcts, or vasogenic edema, have 100% positive predictive value for diagnosing RCVS or RCVS-spectrum disorders. Diagnosis of PRES in some circumstances can be challenging and structural imaging may not be sufficient to distinguish it from other differential diagnostic considerations like ADEM. Advanced imaging techniques, such as MR spectroscopy or positron emission tomography (PET) can provide additional information to determine the diagnosis. Such techniques are more useful to understand the underlying vasculopathic changes in PRES and may answer some of the unresolved controversies in pathophysiology of this complex disease. Eight patients with PRES resulting from different etiologies varying from pre-eclampsia/eclampsia, post-partum headache with seizures, neuropsychiatric systemic lupus erythematosus, snake bite, Dengue fever with encephalopathy, alcoholic liver cirrhosis with hepatic encephalopathy, and lastly reversible cerebral vasoconstriction syndrome (RCVS). Additionally, a diagnostic dilemma between PRES and acute disseminated encephalomyelitis (ADEM) was notable in one patient. Some of these patients did not have or only very transiently had arterial hypertension. PRES may underlie the clinical conundrum of headache, confusion, altered sensorium, seizures, and visual impairment. PRES need not necessarily be always associated with high blood pressure. Imaging findings may also be variable. Both clinicians and radiologists need to familiarize themselves with such variabilities.

### Venomous Bites, Stings and Poisoning by European Vertebrates as an Overlooked and Emerging Medical Problem: Recognition, Clinical Aspects and Therapeutic Management.

**Paolino G, Di Nicola MR, Avella I, Mercuri SR.**

23-05-2023

*Life (Basel).*

<https://pubmed.ncbi.nlm.nih.gov/37374011/>

### Clinical Characteristics and Management of Snake Bite Injuries in the Jerusalem Area.

**Gross I, Maree A, Rekhtman D, Mujahed W, Hashavya S, Assaf J.**

19-06-2023

*J Clin Med.*

<https://pubmed.ncbi.nlm.nih.gov/37373825/>

## New Insights into Immunopathology Associated to Bothrops lanceolatus Snake Envenomation: Focus on PLA<sub>2</sub> Toxin.

Gabrili JJM, Pidde G, Magnoli FC, Marques-Porto R, Villas-Boas IM, Squaiella-Baptistão CC, Silva-de-França F, Burgher F, Blomet J, Tambourgi DV.

09-06-2023

*Int J Mol Sci.*

<https://pubmed.ncbi.nlm.nih.gov/37373079/>

The systemic increase in inflammatory mediator levels can induce diverse pathological disorders, including potentially thrombus formation, which may be lethal. Among the clinical conditions in which the formation of thrombi dictates the patient's prognosis, envenomation by *Bothrops lanceolatus* should be emphasized, as it can evolve to stroke, myocardial infarction and pulmonary embolism. Despite their life-threatening potential, the immunopathological events and toxins involved in these reactions remain poorly explored. Therefore, in the present study, we examined the immunopathological events triggered by a PLA<sub>2</sub> purified from *B. lanceolatus* venom, using an ex vivo human blood model of inflammation. Our results showed that the purified PLA<sub>2</sub> from the venom of *B. lanceolatus* damages human erythrocytes in a dose dependent way. The cell injury was associated with a decrease in the levels of CD55 and CD59 complement regulators on the cell surface. Moreover, the generation of anaphylatoxins (C3a and C5a) and the soluble terminal complement complex (sTCC) indicates that human blood exposure to the toxin activates the complement system. Increased production of TNF- $\alpha$ , CXCL8, CCL2 and CCL5 followed complement activation. The venom PLA<sub>2</sub> also triggered the generation of lipid mediators, as evidenced by the detected high levels of LTB<sub>4</sub>, PGE<sub>2</sub> and TXB<sub>2</sub>. The scenario here observed of red blood cell damage, dysfunctions of the complement regulatory proteins, accompanied by an inflammatory mediator storm, suggests that *B. lanceolatus* venom PLA<sub>2</sub> contributes to the thrombotic disorders present in the envenomed individuals.

## Snake Antivenoms-Toward Better Understanding of the Administration Route.

Gamulin E, Mateljak Lukačević S, Halassy B, Kurtović T.

15-06-2023

*Toxins (Basel).*

<https://pubmed.ncbi.nlm.nih.gov/37368699/>

Envenomations induced by animal bites and stings constitute a significant public health burden. Even though a standardized protocol does not exist, parenterally administered polyclonal antivenoms remain the mainstay in snakebite therapy. There is a prevailing opinion that their application by the *i.m.* route has poor efficacy and that *i.v.* administration should preferentially be chosen in order to achieve better accomplishment of the antivenom therapeutic activity. Recently, it has been demonstrated that neutralization not only in the systemic circulation but also in the lymphatic system might be of great importance for the clinical outcome since it represents another

relevant body compartment through which the absorption of the venom components occurs. In this review, the present-day and summarized knowledge of the laboratory and clinical findings on the *i.v.* and *i.m.* routes of antivenom administration is provided, with a special emphasis on the contribution of the lymphatic system to the process of venom elimination. Until now, antivenom-mediated neutralization has not yet been discussed in the context of the synergistic action of both blood and lymph. A current viewpoint might help to improve the comprehension of the venom/antivenom pharmacokinetics and the optimal approach for drug application. There is a great need for additional dependable, practical, well-designed studies, as well as more practice-related experience reports. As a result, opportunities for resolving long-standing disputes over choosing one therapeutic principle over another might be created, improving the safety and effectiveness of snakebite management.

## Children Growing Up with Severe Disabilities as a Result of Snakebite Envenomations in Indigenous Villages of the Brazilian Amazon: Three Cases and Narratives.

de Farias AS, Cristino JS, da Costa Arévalo M, Carneiro Junior A, Gomes

Filho MR, Ambrosio SA, Nickenig Vissoci J, Wen FH, Azevedo Machado V, Sachett J, Monteiro W.

23-05-2023

*Toxins (Basel).*

<https://pubmed.ncbi.nlm.nih.gov/37368653/>

## Clinical Profile and Outcome of Snake Bite Patients from Tertiary Healthcare Center: In Sub-Himalayan Region: A Medical College-based Study.

Negi RC, Machhan P, Raj M, Barwal VK, Chander S, Thakur S, Mokta J.

Mai-2023

*J Assoc Physicians India.*

<https://pubmed.ncbi.nlm.nih.gov/37355819/>

## Prototyping of a lateral flow assay based on monoclonal antibodies for detection of Bothrops venoms.

Knudsen C, Jürgensen JA, D Knudsen P, Oganessian I, Harrison JA, Dam SH, Haack AM, Friis RUW, Vitved L, Belfakir SB, Ross GMS, Zenobi R, H Laustsen A.

01-09-2023

*Anal Chim Acta.*

<https://pubmed.ncbi.nlm.nih.gov/37355315/>

**Background:** Brazil is home to a multitude of venomous snakes; perhaps the most medically relevant of which belong to the *Bothrops* genus. *Bothrops* spp. are responsible for roughly 70% of all snakebites in Brazil, and envenomings caused by their bites can be treated with three types of antivenom: bothropic antivenom, bothrolachetic antivenom, and bothro-crotalic antivenom. The choice to administer antivenom depends on the severity

of the envenoming, while the choice of antivenom depends on availability and on how certain the treating physician is that the patient was bitten by a bothropic snake. The diagnosis of a bothropic envenoming can be made based on expert identification of the dead snake or a photo thereof or based on a syndromic approach wherein the clinician examines the patient for characteristic manifestations of envenoming. This approach can be very effective but requires staff that has been trained in clinical snakebite management, which, unfortunately, far from all relevant staff has. **Results:** In this article, we describe a prototype of the first lateral flow assay (LFA) capable of detecting venoms from Brazilian Bothrops spp. The monoclonal antibodies for the assay were generated using hybridoma technology and screened in sandwich enzyme-linked immunosorbent assays (ELISAs) to identify Bothrops spp.-specific antibody sandwich pairs. The prototype LFA is able to detect venom from several Bothrops spp. The LFA has a limit of detection (LoD) of 9.5 ng/mL in urine, when read with a commercial reader, and a visual LoD of approximately 25 ng/mL. **Significance:** The work presented here serves as a proof of concept for a genus-specific venom detection kit that could support physicians in diagnosing Bothrops envenomings. Although further optimisation and testing is needed before the LFA can find clinical use, such a device could aid in decentralising antivenoms in the Brazilian Amazon and help ensure optimal snakebite management for even more victims of this highly neglected disease.

### A Case of Contact Dermatitis to Venomous Snake.

B SN, Jyothi CS, Biradar S.

Fév-2023

*J Assoc Physicians India.*

<https://pubmed.ncbi.nlm.nih.gov/37354480/>

### Total CroFab and Anavip Antivenom Vial Administration in US Rattlesnake Envenomations: 2019-2021.

Brandeheoff N, Dalton A, Daugherty C, Dart RC, Monte AA; ToxIC Snakebite Study Group.

Juil-2023

*J Med Toxicol.*

<https://pubmed.ncbi.nlm.nih.gov/37115482/>

## Mycétome

### MALDI-TOF MS identification of Exophiala species isolated in Japan: Library enrichment and faster sample preparation.

Futatsuya T, Mura T, Anzawa K, Mochizuki T, Shimizu A, Iinuma Y.

29-06-2023

*J Dermatol.*

<https://pubmed.ncbi.nlm.nih.gov/37381719/>

Exophiala species cause chromoblastomycosis, mycetoma, and phaeohyphomycosis, which are

occasionally fatally in immunocompromised patients. Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) provides rapid and accurate examination of isolated bacteria and some fungal isolates, but the preparation method for filamentous fungi is complicated. In this study, 31 clinical isolates of Exophiala spp. in Japan were identified by MALDI-TOF MS with a library enriched by adding data. To simplify the sample preparation method, two modified methods were compared with the standard method for filamentous fungi. The agar cultivation sample preparation method reduced the time required for liquid culture and was considered suitable for clinical use. In 30 of 31 clinical isolates of Exophiala spp., the species identified by MALDI-TOF MS with the highest score matched the species identified by sequencing the internal transcribed spacer region. Exophiala dermatitidis, E. lecanii-corni, and E. oligosperma were identified above the genus level, while E. jeanselmei and E. xenobiotica were often not identified at the species level. The identification scores tended to be lower for less-registered strains in the in-house library. It is suggested that library enrichment and the modified preparation method may facilitate early diagnosis of rare fungal infections by Exophiala spp. in clinical laboratories using MALDI-TOF MS.

### Unveiling a common neglected tropical disease- Actinomycotic Mycetoma.

C GD, K M, N AK, P T S.

24-06-2023

*QJM.*

<https://pubmed.ncbi.nlm.nih.gov/37354532/>

## Onchocercose

### The Development of Cutaneous Lesions in Tropically Adapted Beef Cattle Is Associated with Hypersensitive Immune Response to Buffalo Fly Antigens.

Naseem MN, Raza A, Kamran M, Allavena R, Constantinoiu C, McGowan M, Turni C, Tabor AE, James P.

16-06-2023

*Animals (Basel).*

<https://pubmed.ncbi.nlm.nih.gov/37370520/>

This study investigated the role of cattle immune responses in the pathogenesis of buffalo fly (*Haematobia irritans exigua*) (BF) lesions. Brangus steers phenotyped for lesion development were divided into three groups: high lesion susceptibility (HL), low lesion susceptibility (LL) and no lesions (NL), based on lesion severity scores. Each steer was injected intradermally with different concentrations of BF, *Onchocerca gibsoni* (Og), and *Musca domestica* (Md) antigens. At 1 h post-injection, wheal areas at BF injection sites were found to be significantly larger in HL than NL cattle, but there were no significant differences ( $p < 0.05$ ) found between either the HL or NL cattle and LL cattle. At 24, 48, and 72 h post-injection, the skinfold thickness response to both BF and Md antigens was significantly greater in the HL group than the NL group. However, skin thickness was significantly greater

for the BF antigens than the Md antigens ( $p < 0.05$ ). There were no significant differences found between the LL and NL animals in response to the BF antigens at any time, and no significant differences were determined between any of the lesion groups in response to the Og antigens. Histological examination of skin sections taken from the BF antigen injection sites in HL cattle at 72 h post-injection revealed necrosis of the epidermis and superficial dermis, along with severe eosinophilic inflammation. This study suggests that differences in the hypersensitivity to BF antigens underlie differences amongst the cattle in their susceptibility to the development of BF lesions, and breeding for immune-related biomarkers may assist in selecting more BF lesion-resistant cattle.

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## Pian

### Assessing the cost-effectiveness of integrated case management of Neglected Tropical Diseases in Liberia.

**Godwin-Akpan TG, Diaconu K, Edmiston M, Smith JS Jr, Sosu F, Weiland S, Kollie KK.**

29-09-2023

*BMC Health Serv Res.*

<https://pubmed.ncbi.nlm.nih.gov/37386431/>

**Background:** In 2017, Liberia became one of the first countries in the African region to develop and implement a national strategy for integrated case management of Neglected Tropical Diseases (CM-NTDs), specifically Buruli ulcer, leprosy, lymphatic filariasis morbidities, and yaws. Implementing this plan moves the NTD program from many countries' fragmented (vertical) disease management. This study explores to what extent an integrated approach offers a cost-effective investment for national health systems. **Methods:** This study is a mixed-method economic evaluation that explores the cost-effectiveness of the integrated CM-NTDs approach compared to the fragmented (vertical) disease management. Primary data were collected from two integrated intervention counties and two non-intervention counties to determine the relative cost-effectiveness of the integrated program model vs. fragmented (vertical) care. Data was sourced from the NTDs program annual budgets and financial reports for integrated CM-NTDs and Mass Drug Administration (MDA) to determine cost drivers and effectiveness. **Results:** The total cost incurred by the integrated CM-NTD approach from 2017 to 2019 was US\$ 789,856.30, with the highest percentage of costs for program staffing and motivation (41.8%), followed by operating costs (24.8%). In the two counties implementing fragmented (vertical) disease management, approximately US\$ 325,000 was spent on the diagnosis of 84 persons and the treatment of twenty-four persons suffering from NTDs. While 2.5 times as much was spent in integrated counties, 9–10 times more patients were diagnosed and treated. **Conclusions:** The cost of a patient being diagnosed under the fragmented (vertical) implementation is five times higher than integrated CM-NTDs, and providing treatment is ten times as costly. Findings indicate that the integrated CM-NTDs strategy has achieved its primary objective of improved access to

NTD services. The success of implementing an integrated CM-NTDs approach in Liberia, presented in this paper, demonstrates that NTD integration is a cost-minimizing solution.

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## Rage

### Discovery of a novel bat lyssavirus in a Long-fingered bat (*Myotis capaccinii*) from Slovenia.

**Černe D, Hostnik P, Toplak I, Presetnik P, Maurer-Wernig J, Kuhar U.**

29-06-2023

*PLoS Negl Trop Dis.*

<https://pubmed.ncbi.nlm.nih.gov/37384601/>

Lyssaviruses are the causative agents of rabies, a zoonotic, fatal disease that is thought to be ancestral to bats. In the last decade, the detection of bat associated lyssaviruses is increasing also in Europe. Within a retrospective bat associated lyssavirus surveillance study a total of 225 dead bats of 21 bat species were collected in Slovenia between 2012 and 2019 and tested by specific real-time RT-PCR method. The first lyssavirus positive sample in bats in Slovenia was detected using the real-time RT-PCR, the fluorescent antibody test, and next generation sequencing, while the rabies tissue culture inoculation test was unsuccessful due to sample degradation and storage conditions. The nearly complete genome of Divača bat lyssavirus from Slovenia consists of 11,871 nucleotides and reflects the characteristic gene organization known for lyssaviruses, encoding the five viral proteins. Phylogenetic analysis of Divača bat lyssavirus revealed that it belongs to phylogroup I lyssaviruses and is most closely related to Kotalahti bat lyssavirus (KBLV) with 87.20% nucleotide and 99.22% amino acid identity. Together with KBLV, Khujand virus, European bat lyssavirus 2, Bakeloh bat lyssavirus, and Aravan virus, Divača bat lyssavirus was detected in the genus *Myotis* suggesting its key role in the transmission and maintenance of certain lyssaviruses.

### Emergence of rabies among vaccinated humans in India: a public health concern.

**Goel K, Sen A, Satapathy P, Kumar P, Aggarwal AK, Sah R, Padhi BK.**

22-11-2022

*Lancet Reg Health Southeast Asia.*

<https://pubmed.ncbi.nlm.nih.gov/37383039/>

### Whole-Brain Inputs to Major Descending Pathways of the Anterior Lateral Motor Cortex.

**Xu T, Jin Z, Yang M, Chen Z, Xiong H.**

28-06-2023

*J Neurophysiol.*

<https://pubmed.ncbi.nlm.nih.gov/37377198/>

The anterior lateral motor cortex (ALM) is critical to subsequent correct movements and plays a vital role in predicting specific future movements. Different



descending pathways of the ALM are preferentially involved in different roles in movements. However, the circuit function mechanisms of these different pathways may be concealed in the anatomy circuit. Clarifying the anatomy inputs of these pathways should provide some helpful information for elucidating these function mechanisms. Here, we used a retrograde trans-synaptic rabies virus to systematically generate, analyze and compare whole-brain maps of inputs to the thalamus (TH)-, medulla oblongata (Med)-, superior colliculus (SC)-, and pontine nucleus (Pons)-projecting ALM neurons in C57BL/6J mice. Fifty-nine separate regions from nine major brain areas projecting to the descending pathways of the ALM were identified. Brain-wide quantitative analyses revealed identical whole-brain input patterns between these descending pathways. Most inputs to the pathways originated from the ipsilateral side of the brain, with most innervations provided by the cortex and TH. The contralateral side of the brain also sent sparse projections, but these were rare, emanating only from the cortex and cerebellum. Nevertheless, the inputs received by TH-, Med-, SC- and Pons-projecting ALM neurons had different weights, potentially laying an anatomical foundation for understanding the diverse functions of well-defined descending pathways of the ALM. Our findings provide anatomical information to help elucidate the precise connections and diverse functions of the ALM.

### **Immunogenicity of Oral Rabies Vaccine Strain SPBN GASGAS in Local Dogs in Bali, Indonesia.**

Megawati Saputra IL, Suwarno S, Husein WF, Suseno PP, Prayoga IMA, Vos A, Arthawan IM, Schoonman L, Weaver J, Zainuddin N.

20-06-2022

*Viruses.*

<https://pubmed.ncbi.nlm.nih.gov/37376704/>

### **Transcriptomic Analysis of mRNA Expression Profiles in the Microglia of Mouse Brains Infected with Rabies Viruses of Varying Virulence.**

Liu J, Li W, Yu D, Jin R, Hou H, Ling X, Kiflu AB, Wei X, Yang X, Li X, He Y, Luo TR.

23-05-2023

*Viruses.*

<https://pubmed.ncbi.nlm.nih.gov/37376523/>

### **Effect of Phone Text Message Reminders on Compliance with Rabies Post-Exposure Prophylaxis following Dog Bites in Rural Kenya.**

Chuchu VM, Mutono N, Bichanga P, Kitala PM, Ksee D, Muturi M, Mwatondo A, Nasimiyu C, Akunga L, Amiche A, Hampson K, Thumbi SM.

18-06-2023

*Vaccines (Basel).*

<https://pubmed.ncbi.nlm.nih.gov/37376501/>

The prompt administration of post-exposure prophylaxis (PEP) is one of the key strategies for ending human deaths from rabies. A delay in seeking the first dose of rabies PEP,

or failure to complete the recommended dosage, may result in clinical rabies and death. We assessed the efficacy of short message system (SMS) phone texts in improving the adherence to scheduled PEP doses among bite patients in rural eastern Kenya. We conducted a single-arm, before-after field trial that compared adherence among bite patients presenting at Makueni Referral Hospital between October and December 2018 (control) and between January and March 2019 (intervention). Data on their demographics, socio-economic status, circumstances surrounding the bite, and expenditures related to the bite were collected. A total of 186 bite patients were enrolled, with 82 (44%) in the intervention group, and 104 (56%) in the control group. The odds of PEP completion were three times (OR 3.37, 95% CI 1.28, 10.20) more likely among patients who received the SMS reminder, compared to the control. The intervention group had better compliance on the scheduled doses 2 to 5, with a mean deviation of 0.18 days compared to 0.79 days for the control group ( $p = 0.004$ ). The main reasons for non-compliance included lack of funds (30%), and forgetfulness (23%) on days for follow-up treatment, among others. Nearly all (96%,  $n = 179$ ) the bite patients incurred indirect transport costs, at an average of USD 4 (USD 0-45) per visit. This study suggests that the integration of SMS reminders into healthcare service delivery increases compliance with PEP, and may strengthen rabies control and elimination strategies.

### **Canine Distemper Virus Infection in the Free-Living Wild Canines, the Red Fox (*Vulpes vulpes*) and Jackal (*Canis aureus moreoticus*), in Croatia.**

Prpić J, Lojkić I, Keros T, Krešić N, Jemeršić L.

15-06-2023

*Pathogens.*

<https://pubmed.ncbi.nlm.nih.gov/37375523/>

The canine distemper virus (CDV), a paramyxovirus that is closely related to the human measles virus and rinderpest virus of cattle, is a highly contagious viral disease in dogs and wild carnivores worldwide. CDV represents a serious threat to domestic and wild animals, especially to the conservation of endangered wild carnivores. Our study aims to investigate the occurrence of CDV in free-living wild canines in Croatia. For this purpose, 176 red foxes and 24 jackal brain samples collected in the frame of the active surveillance of rabies during winter 2021/2022 were tested. This study provided the first comprehensive overview of the prevalence and spatial distribution of CDV in the wildlife of Croatia, including the molecular phylogenetic analysis of the H gene sequence of field CDV strains circulating in red fox and jackal populations of Croatia. The molecular characterization of hemagglutinin gene genomic regions confirmed the phylogenetic clustering of obtained sequences into the Europa 1 genotype. The obtained CDV red fox sequences were mutually very similar (97.60%). This study indicates the high genetic similarity of Croatian CDV red fox sequences and CDV red fox sequences from Italy and Germany, badger sequences from Germany, polecat sequences from Hungary, and dog sequences from Hungary and Germany.

## **In Silico Identification and In Vitro Validation of Repurposed Compounds Targeting the RSV Polymerase.**

**Xu E, Park S, Calderon J, Cao D, Liang B.**

18-06-2023

*Microorganisms.*

<https://pubmed.ncbi.nlm.nih.gov/37375110/>

## **Emerging Rhabdoviruses and Human Infection.**

**Shepherd JG, Davis C, Streicker DG, Thomson EC.**

17-06-2023

*Biology (Basel).*

<https://pubmed.ncbi.nlm.nih.gov/37372162/>

*Rhabdoviridae* is a large viral family, with members infecting a diverse range of hosts including, vertebrate species, arthropods, and plants. The predominant human pathogen within the family is *Rabies lyssavirus*, the main cause of human rabies. While rabies is itself a neglected disease, there are other, less well studied, rhabdoviruses known to cause human infection. The increasing application of next-generation sequencing technology to clinical samples has led to the detection of several novel or rarely detected rhabdoviruses associated with febrile illness. Many of these viruses have been detected in low- and middle-income countries where the extent of human infection and the burden of disease remain largely unquantified. This review describes the rhabdoviruses other than *Rabies lyssavirus* that have been associated with human infection. The discovery of the Bas Congo virus and Ekpoma virus is discussed, as is the re-emergence of species such as Le Dantec virus, which has recently been detected in Africa 40 years after its initial isolation. Chandipura virus and the lyssaviruses that are known to cause human rabies are also described. Given their association with human disease, the viruses described in this review should be prioritised for further study.

## **Spatial ecology of translocated raccoons.**

**Hill JE, Helton JL, Chipman RB, Gilbert AT, Beasley JC, Dharmarajan G, Rhodes OE.**

27-06-2023

*Sci Rep.*

<https://pubmed.ncbi.nlm.nih.gov/37369730/>

Raccoons (*Procyon lotor*) are routinely translocated both legally and illegally to mitigate conflicts with humans, which has contributed to the spread of rabies virus across eastern North America. The movement behavior of translocated raccoons has important ramifications for disease transmission yet remains understudied and poorly quantified. To examine the spatial ecology of raccoons following experimental translocation, we performed reciprocal 16 km-distance translocations of 30 raccoons between habitats of high and low raccoon density (bottomland hardwood and upland pine, respectively) across the Savannah River Site (SRS) in Aiken, South Carolina, USA (2018-2019). Translocation influenced patterns of raccoon space use, with translocated animals exhibiting a 13-fold increase in 95% utilization distributions (UDs) post- compared to pre-translocation

(mean 95% UD  $35.8 \pm 36.1 \text{ km}^2$  vs  $1.96 \pm 1.17 \text{ km}^2$ ). Raccoons originating from upland pine habitats consistently had greater space use and larger nightly movement distances post-translocation compared to raccoons moved from bottomland hardwood habitats, whereas these differences were generally not observed prior to translocation. Estimated home ranges of male raccoons were twice the area as estimated for female raccoons, on average, and this pattern was not affected by translocation. After a transient period lasting on average 36.5 days (SD = 30.0, range = 3.25-92.8), raccoons often resumed pre-experiment movement behavior, with 95% UD sizes not different from those prior to translocation (mean =  $2.27 \pm 1.63 \text{ km}^2$ ). Most animals established new home ranges after translocation, whereas three raccoons moved > 16 km from their release point back to the original capture location. Four animals crossed a 100-m wide river within the SRS post-translocation, but this behavior was not documented among collared raccoons prior to translocation. Large increases in space use combined with the crossing of geographic barriers such as rivers may lead to elevated contact rates with conspecifics, which can heighten disease transmission risks following translocation. These results provide additional insights regarding the potential impacts of raccoon translocation towards population level risks of rabies outbreaks and underscore the need to discourage mesocarnivore translocations to prevent further spread of wildlife rabies.

## **Dog bites as a zoonotic risk in Ecuador: Need for the implementation of a One Health approach.**

**Joselyn Calderón G, Poveda S, Sosa AL, Mora N, López Bejar M, Orlando SA, Garcia-Bereguain MA.**

19-04-2023

*One Health.*

<https://pubmed.ncbi.nlm.nih.gov/37363229/>

## **Emergency response using oral rabies vaccination of dogs -field data from Namibia demonstrate high efficiency.**

**Freuling CM, Busch F, Shikongo MB, Silume N, van der Westhuizen J, Khaiseb S, Shilongo A, Müller T.**

11-05-2023

*One Health.*

<https://pubmed.ncbi.nlm.nih.gov/37363208/>

Dog-mediated rabies is responsible for tens of thousands of human deaths annually, and in resource-constrained settings, vaccinating dogs to control the disease at source remains challenging for various reasons. Currently, rabies elimination efforts rely on mass dog vaccination by the parenteral route. While oral rabies vaccination (ORV) of dogs is primarily considered a tool to increase herd immunity, particularly by targeting free-roaming and stray dogs, here, we are showcasing an ORV-only approach as an emergency response model. Using a third-generation vaccine and a standardized egg-flavored bait, we assessed the effectiveness and vaccination under field conditions in the Zambezi region of Namibia. During this trial, with four teams and within four working days, 3097 dogs were offered a bait, of which 88,0% were considered

vaccinated. Teams managed to vaccinate, on average, over 20 dogs/h, despite using a door-to-door vaccination approach. The favorable results both in terms of bait acceptance and successful vaccination as well as field applicability and effectiveness further support the great potential of ORV in dog rabies control programmes.

### Children's Internet use and physical and psychosocial development.

Novaković S, Milenković S, Srećković M, Backović D, Ignjatović V, Capo N, Stojanović T, Vukomanović V, Sekulić M, Gavrilović J, Vuleta K, Ignjatović V.

08-06-2023

*Front Public Health.*

<https://pubmed.ncbi.nlm.nih.gov/37361154/>

**Introduction:** Internet use (IU) commonly refers to sedentary lifestyle and may be addictive, especially among children. The aim of this study was to investigate the relationship between IU and some aspects of child physical and psychosocial development. **Methodology:** We conducted a cross-sectional survey by using a screen-time based sedentary behavior questionnaire and Strengths and Difficulties Questionnaire (SDQ)-among 836 primary school children in the Braničevo District. The children's medical records were analysed for vision problems and spinal deformities. Their body weight (BW) and height (BH) were measured and body mass index (BMI) was calculated as BW in kilograms divided by BH in meters squared ( $\text{kg/m}^2$ ). **Results:** The average age of respondents was 13.4 (SD 1.2) years. The mean duration of daily Internet use and sedentary behavior was 236 (SD 156) and 422 (SD 184) minutes, respectively. There was no significant correlation between daily IU and vision problems (near sightedness, farsightedness, astigmatism, strabismus), and spinal deformities. However, daily Internet use is significantly associated with obesity ( $p < 0.001$ ) and sedentary behavior ( $p = 0.01$ ). There was significant correlation between emotional symptoms with total Internet usage time, and total sedentary score ( $p < 0.001$  for both,  $r = 0.141$  and  $r = 0.132$ , respectively). There was a positive correlation between the total sedentary score of children and hyperactivity/inattention ( $r = 0.167$ ,  $p < 0.001$ ), emotional symptoms ( $r = 0.132$ ,  $p < 0.001$ ), and conduct problems ( $r = 0.084$ ,  $p < 0.01$ ). **Conclusion:** In our study, children's Internet use was associated with obesity, psychological disturbances and social maladjustment.

### Factors associated with heartworm preventative use in the golden retriever lifetime study.

Wisniewski L, Faulkner V, Faulkner C.

09-06-2023

*Front Vet Sci.*

<https://pubmed.ncbi.nlm.nih.gov/37360405/>

### Large-scale phylogenetic analysis reveals genetic diversity and geographic distribution of rabies virus in South-East and South Asia.

Zhang L, Sun S, Gong W, Thompson L, Cruz J, Dukpa K, Gonzales RM, Tu Z, He B, Liu Y, Tu C, Feng Y.

22-06-2023

*Infect Genet Evol.*

<https://pubmed.ncbi.nlm.nih.gov/37353186/>

South-East Asia (SEA) and South Asia (SA) are two important geographic regions with the most severe enzootic rabies in the world. In these regions, phylogenetic analysis of rabies virus (RABV) has been conducted only at a country level; the results obtained from different countries are scattered and unequal, with a non-uniform system to name RABV genotypes. Therefore, it is difficult to undertake origin-tracking and compare inter-country RABV evolution and transmission. To avoid the confusion in understanding and to generate a panoramic picture of RABV genetic diversity, distribution, and transmission in SEA and SA, the present study conducted a systematic phylogenetic analysis by combining all sequences representing 2368 RABV strains submitted to GenBank by 14 rabies endemic SEA and SA countries. The results showed that RABVs circulating in two regions were classified into four major clades and many subclades: the Asia clade is circulating only in SEA, the Indian subcontinent, and Arctic-like clades only in SA, while the Cosmopolitan clade has been detected in both regions. The results also showed a wide range of hosts were infected by divergent RABV subclades, with dogs being the major transmission source. However, wildlife rabies was also found to be an important issue with 6 wild carnivore species identified as potential sources of spillover risk for sylvatic rabies to humans, domestic animals, and other wild animals. Current findings indicate that the two regions have separate virus clades circulating thus indicating the absence of cross-transmission between the regions. The study emphasizes the importance of phylogenetic analysis in the regions using uniform genotyping and naming systems for rabies surveillance, to coordinate actions of member countries to eliminate dog-mediated human rabies by 2030.

### A review of the diet of the common vampire bat (*Desmodus rotundus*) in the context of anthropogenic change.

Brown N, Escobar LE.

12-06-2023

*Mamm Biol.*

<https://pubmed.ncbi.nlm.nih.gov/37363038/>

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## Schistosomiasis

### Experimental infection with *Schistosoma mansoni* from Belém, Pará, Brazil: Strains newly isolated vs. laboratory maintained.

Dias IHL, Fonseca ALS, Sousa SRM, Goveia CO, Fernandez MA, Enk MJ.

26-06-2023

*Exp Parasitol.*

<https://pubmed.ncbi.nlm.nih.gov/37380123/>

**Background:** Schistosomiasis is a neglected tropical disease that occurs in locations with inadequate sanitation conditions. The geographic distribution of *Schistosoma*

mansoni trematode depends directly on the presence of its intermediate host, Biomphalaria mollusks. Studies involving recently isolated and laboratory strains are not common due to the difficulty in cycle maintenance. This study evaluated the susceptibility and infectivity responses in intermediate and definitive hosts with strains of *S. mansoni*, one isolated and kept in laboratory environment for 34 years (BE) and the other recently collected (BE-I) METHODS: For experimental infection, a total of 400 *B. glabrata* mollusks were divided in four infection groups. Thirty mice were divided in two groups for infection with the two strains. **Results:** It was possible to notice differences about *S. mansoni* infection in both strains. The laboratory strain was more harmful to freshly collected mollusks. Differences in the patterns of infection in mice could be observed. **Conclusion:** Particularities occurred in each group of infection by *S. mansoni* strains, despite having the same geographic origin. Effects from the parasite-host interaction are visible in terms of infection in definitive and intermediate hosts.

### **The Association Between Female Genital Schistosomiasis and Other Infections of the Lower Genital Tract in Adolescent Girls and Young Women: A Cross-Sectional Study in South Africa.**

**Shukla JD, Kleppa E, Holmen S, Ndhlovu PD, Mtshali A, Sebitloane M, Vennervald BJ, Gundersen SG, Taylor M, Kjetland EF.**

01-07-2023

*J Low Genit Tract Dis.*

<https://pubmed.ncbi.nlm.nih.gov/37379442/>

**Objectives/purposes of the study:** This study aimed to explore the relationship between female genital schistosomiasis (FGS), sexually transmitted infections, bacterial vaginosis, and yeast among young women living in *Schistosoma haematobium*-endemic areas. **Methods:** In a cross-sectional study of young women, sexually active, aged 16 to 22 years in rural KwaZulu-Natal, South Africa, in 32 randomly selected rural schools in schistosomiasis-endemic areas, the authors performed gynecological and laboratory investigations, diagnosed FGS and other infections, and did face-to-face interviews. **Results:** Female genital schistosomiasis was the second most prevalent current genital infection (23%), significantly more common in those who had urinary schistosomiasis (35%), compared with those without (19%,  $p < .001$ ). In the FGS-positive group, 35% had human papillomavirus compared with 24% in the FGS-negative group ( $p = .010$ ). In the FGS-positive group, 37% were seropositive for herpes simplex virus infection, compared with 30% in the FGS-negative group ( $p = .079$ ). There were significantly fewer chlamydia infections among women with FGS (20%,  $p = .018$ ) compared with those who did not have FGS (28%). **Conclusions:** Female genital schistosomiasis was the second most common genital infection after herpes simplex virus. Human papillomavirus infection was significantly associated with FGS, but Chlamydia was negatively associated with FGS. Women with FGS may have had more frequent contact with the health system for genital discharge. The results show the importance of the inclusion of FGS in the national management protocols

for genital infections in areas endemic for *S. haematobium* and highlight a more comprehensive approach to diagnosis and genital disease management.

### **Spatio-temporal GAMLSS modeling of the incidence of schistosomiasis in the central region of the State of Minas Gerais, Brazil.**

**Nogueira DA, Sáfadi T, Lima RR, Mata ASD, Graciano MMC, Barçante JMP, Barçante TA, Dourado SMP.**

26-06-2023

*Cad Saude Publica.*

<https://pubmed.ncbi.nlm.nih.gov/37377298/>

In Brazil, millions of people live in areas with risk of schistosomiasis, a neglected chronic disease with high morbidity. The *Schistosoma mansoni* helminth is present in all macroregions of Brazil, including the State of Minas Gerais, one of the most endemic states. For this reason, the identification of potential foci is essential to support educational and prophylactic public policies to control this disease. This study aims to model schistosomiasis data based on spatial and temporal aspects and assess the importance of some exogenous socioeconomic variables and the presence of the main *Biomphalaria* species. Considering that, when working with incident cases, a discrete count variable requires an appropriate modeling, the GAMLSS modeling was chosen since it jointly considers a more appropriate distribution for the response variable due to zero inflation and spatial heteroscedasticity. Several municipalities presented high incidence values from 2010 to 2012, and a downward trend was observed until 2020. We also noticed that the distribution of incidence behaves differently in space and time. Municipalities with dams presented risk 2.25 times higher than municipalities without dams. The presence of *B. glabrata* was associated with the risk of schistosomiasis. On the other hand, the presence of *B. straminea* represented a lower risk of the disease. Thus, the control and monitoring of *B. glabrata* snails is essential to control and eliminate schistosomiasis; and the GAMLSS model was effective in the treatment and modeling of spatio-temporal data.

### **Blocking BAFF Alleviates Hepatic Fibrosis in Schistosoma japonicum-Infected Mice.**

**Dong P, Mei C, Yang Y, Zhou Y, Xu Y, Song L, Yu C.**

01-06-2023

*Pathogens.*

<https://pubmed.ncbi.nlm.nih.gov/37375483/>

### **Role of the IL-33/ST2 Activation Pathway in the Development of the Hepatic Fibrosis Induced by Schistosoma mansoni Granulomas in Mice.**

**Maggi L, Camelo GMA, Rocha IC, Pereira Alves W, Moreira JMP, Almeida Pereira T, Tafuri WL, Rabelo ÉML, Correa A Jr, Ecco R, Negrão-Corrêa DA.**

16-06-2023

*Int J Mol Sci.*

<https://pubmed.ncbi.nlm.nih.gov/37373379/>



## Malacological Survey and Spatial Distribution of Intermediate Host Snails in Schistosomiasis Endemic Districts of Rwanda.

Kagabo J, Kalinda C, Nshimiyimana P, Mbonigaba JB, Ruberanziza E, Nyandwi E, Rujeni N.

28-05-2023

*Trop Med Infect Dis.*

<https://pubmed.ncbi.nlm.nih.gov/37368713/>

**Background:** Schistosomiasis, due to *S. mansoni*, is prevalent in Rwanda. However, there is a paucity of information related to the abundance, species, distribution, and infectivity of *Schistosoma* intermediate host snails. **Methods:** Snails were collected from 71 sites, including lakeshores and wetlands. Snails obtained were morphologically identified, and cercariae were shed using standard procedures. Cercariae were molecularly characterized using PCR. GPS coordinates were used to generate geospatial maps of snail distribution that were overlaid with geospatial distribution of schistosomiasis among pre-school children in the same areas. **Results:** Overall, 3653 snails were morphologically classified as *Bulinus* spp. and 1449 as *Biomphalaria* spp. A total of 306 snails shed cercariae, 130 of which were confirmed as *S. mansoni* cercaria by PCR. There was no significant difference in the proportion of *S. mansoni* cercariae in wetlands compared to lakeshores. **Conclusion:** Rwandan water bodies harbor an important number of snails that shed *S. mansoni* cercariae. Furthermore, a strong spatial correlation was observed between the distribution of schistosomiasis in children and the spatial distribution of snail infectivity with *S. mansoni*. The presence of *Bulinus* spp. suggests a potential risk of *S. haematobium*, although molecular analysis did not show any current transmission of this parasite.

## Molecular detection of Fasciola, Schistosoma and Paramphistomum species from freshwater snails occurring in Gauteng and Free State provinces, South Africa.

Molaba GG, Molefe-Nyembe NI, Taioe OM, Mofokeng LS, Thekiso OMM, Mtshali K.

22-06-2023

*Vet Parasitol.*

<https://pubmed.ncbi.nlm.nih.gov/37364501/>

## Schistosoma mansoni egg-derived thioredoxin and Sm14 drive the development of IL-10 producing regulatory B cells.

Chayé MAM, Gasan TA, Ozir-Fazalikhani A, Scheenstra MR, Zawistowska-Deniziak A, van Hengel ORJ, Gentenaar M, Manurung MD, Harvey MR, Codée JDC, Chiodo F, Heijke AM, Kalinowska A, van Diepen A, Hensbergen PJ, Yazdanbakhsh M, Guigas B, Hokke CH, Smits HH.

26-06-2023

*PLoS Negl Trop Dis.*

<https://pubmed.ncbi.nlm.nih.gov/37363916/>

During chronic schistosome infections, a complex regulatory network is induced to regulate the host immune system, in which IL-10-producing regulatory B (Breg) cells play a significant role. *Schistosoma mansoni* soluble egg antigens (SEA) are bound and internalized by B cells and induce both human and mouse IL-10 producing Breg cells. To identify Breg-inducing proteins in SEA, we fractionated SEA by size exclusion chromatography and found 6 fractions able to induce IL-10 production by B cells (out of 18) in the high, medium and low molecular weight (MW) range. The high MW fractions were rich in heavily glycosylated molecules, including multi-fucosylated proteins. Using SEA glycoproteins purified by affinity chromatography and synthetic glycans coupled to gold nanoparticles, we investigated the role of these glycan structures in inducing IL-10 production by B cells. Then, we performed proteomics analysis on active low MW fractions and identified a number of proteins with putative immunomodulatory properties, notably thioredoxin (SmTrx1) and the fatty acid binding protein Sm14. Subsequent splenic murine B cell stimulations and hock immunizations with recombinant SmTrx1 and Sm14 showed their ability to dose-dependently induce IL-10 production by B cells both in vitro and in vivo. Identification of unique Breg cells-inducing molecules may pave the way to innovative therapeutic strategies for inflammatory and auto-immune diseases.

## Impact of precipitation on the prevalence of schistosomiasis mekongi in Lao PDR: Structural equation modelling using Earth observation satellite data.

Matsumoto-Takahashi ELA, Kumagai T, Oyoshi K, Sasaki Y, Mizukami Y, Hongvanthong B, Brey PT, Kano S, Iwagami M.

11-05-2023

*One Health.*

<https://pubmed.ncbi.nlm.nih.gov/37363222/>

## MicroRNA-1 targets ribosomal protein genes to regulate the growth, development and reproduction of Schistosoma japonicum.

Sun C, Luo F, You Y, Gu M, Yang W, Yi C, Zhang W, Feng Z, Wang J, Hu W.

22-06-2023

*Int J Parasitol.*

<https://pubmed.ncbi.nlm.nih.gov/37355197/>

Eggs laid by mature female schistosomes are primarily responsible for the pathogenesis of schistosomiasis and critical for transmission. Consequently, elucidating the mechanism of sexual maturation as well as egg production may lead to new strategies for the control of schistosomiasis. MicroRNAs (miRNAs) are involved in multiple biological processes including reproduction in many organisms, yet their roles have not been well characterized in schistosomes. Here, we investigated microRNA-1 (miR-1), which was downregulated gradually in both male and female *Schistosoma japonicum* after they reached sexual maturity. The expression of miR-1, as

shown with quantitative reverse transcription PCR (qRT-PCR), was lower in the reproductive organs of adult females compared with the somatic tissues. Overexpression of miR-1 in adult worms destroyed the morphological architecture of reproductive organs and reduced the subsequent oviposition, which may be due to the activation of apoptosis pathways. Through in silico analysis, 34 potential target genes of miR-1 were identified, including five ribosomal protein genes, called rp-s13, rp-l7ae, rp-l14, rp-l11 and rp-s24e. In vitro dual-luciferase reporter gene assays and miRNA overexpression experiments further validated that these ribosomal protein genes were directly regulated by miR-1. In contrast to the gene expression of miR-1, qRT-PCR and in situ hybridization experiments demonstrated these ribosomal protein genes were enriched in the sexual organs of adult females. Using RNA interference to silence the ribosomal protein genes in different developmental stages in a mouse model system, we demonstrated that these miR-1 target genes not only participated in the reproductive development of *S. japonicum*, but also were required for the growth and survival of the parasite in the early developmental stages. Taken together, our data suggested that miR-1 may affect the growth, reproduction and oviposition of *S. japonicum* by targeting the ribosomal protein genes, which provides insights for exploration of new anti-schistosome strategies.

### **The FMRF-NH<sub>2</sub> gated sodium channel of *Biomphalaria glabrata*: Localization and expression following infection by *Schistosoma mansoni*.**

**Vicente-Rodríguez LC, Torres-Arroyo AC, Hernández-Vázquez A, Rosa-Casillas M, Bracho-Rincón DP, de Jesús PM, Behra ML, Habib MR, Zhou XN, Rosenthal JJC, Miller MW.**

23-06-2023

*PLoS Negl Trop Dis.*

<https://pubmed.ncbi.nlm.nih.gov/37352363/>

The neglected tropical disease schistosomiasis impacts over 700 million people globally. *Schistosoma mansoni*, the trematode parasite that causes the most common type of schistosomiasis, requires planorbid pond snails of the genus *Biomphalaria* to support its larval development and transformation to the cercarial form that can infect humans. A greater understanding of neural signaling systems that are specific to the *Biomphalaria* intermediate host could lead to novel strategies for parasite or snail control. This study examined a *Biomphalaria glabrata* neural channel that is gated by the neuropeptide FMRF-NH<sub>2</sub>. The *Biomphalaria glabrata* FMRF-NH<sub>2</sub> gated sodium channel (Bgl-FaNaC) amino acid sequence was highly conserved with FaNaCs found in related gastropods, especially the planorbid *Planorbella trivolvis* (91% sequence identity). In common with the *P. trivolvis* FaNaC, the *B. glabrata* channel exhibited a low affinity (EC<sub>50</sub>: 3 x 10<sup>-4</sup> M) and high specificity for the FMRF-NH<sub>2</sub> agonist. Its expression in the central nervous system, detected with immunohistochemistry and in situ hybridization, was widespread, with the protein localized mainly to neuronal fibers and the mRNA confined to cell bodies. Colocalization of the Bgl-FaNaC message with its FMRF-NH<sub>2</sub> agonist

precursor occurred in some neurons associated with male mating behavior. At the mRNA level, Bgl-FaNaC expression was decreased at 20 and 35 days post infection (dpi) by *S. mansoni*. Increased expression of the transcript encoding the FMRF-NH<sub>2</sub> agonist at 35 dpi was proposed to reflect a compensatory response to decreased receptor levels. Altered FMRF-NH<sub>2</sub> signaling could be vital for parasite proliferation in its intermediate host and may therefore present innovative opportunities for snail control.

### **Non-covalent inhibitors of thioredoxin glutathione reductase with schistosomicidal activity in vivo.**

**Petukhova VZ, Aboagye SY, Ardini M, Lullo RP, Fata F, Byrne ME, Gabriele F, Martin LM, Harding LNM, Gone V, Dangi B, Lantvit DD, Nikolic D, Ippoliti R, Effantin G, Ling WL, Johnson JJ, Thatcher GRJ, Angelucci F, Williams DL, Petukhov PA.**

22-06-2023

*Nat Commun.*

<https://pubmed.ncbi.nlm.nih.gov/37349300/>

Only praziquantel is available for treating schistosomiasis, a disease affecting more than 200 million people. Praziquantel-resistant worms have been selected for in the lab and low cure rates from mass drug administration programs suggest that resistance is evolving in the field. Thioredoxin glutathione reductase (TGR) is essential for schistosome survival and a validated drug target. TGR inhibitors identified to date are irreversible and/or covalent inhibitors with unacceptable off-target effects. In this work, we identify noncovalent TGR inhibitors with efficacy against schistosome infections in mice, meeting the criteria for lead progression indicated by WHO. Comparisons with previous in vivo studies with praziquantel suggests that these inhibitors outperform the drug of choice for schistosomiasis against juvenile worms.

### ***Schistosoma japonicum*-derived peptide SJMHE1 ameliorates allergic symptoms and responses in mice with allergic rhinitis.**

**Gao X, Mao C, Zheng T, Xu X, Luo X, Zhang S, Liu J, Wang X, Chen X, Dong L.**

06-06-2023

*Front Cell Infect Microbiol.*

<https://pubmed.ncbi.nlm.nih.gov/37346033/>

## **Trachome**

### **The Prevalence of Trachomatous Trichiasis in People Aged 15 Years and Over in Six Evaluation Units of Gaoual, Labé, Dalaba and Beyla Districts, Guinea.**

**Bah MM, Sakho F, Goepogui A, Nieba LC, Cisse A, Courtright P, Harte AJ, Burgert-Brucker C, Jimenez C, Lama PL, Sagnon M, Bakhtiari A, Boyd S, Solomon AW, Kelly M, James F, Tenkiano MSD, Harding-Esch EM, Dicko BM.**

28-06-2023

**Purpose:** Trachoma is a public health problem in 42 countries. Inflammation associated with repeated ocular infection with *Chlamydia trachomatis* can cause the eyelid to scar and turn inwards, resulting in the eyelashes rubbing against the eyeball, known as trichomatous trichiasis (TT). In Guinea, baseline surveys conducted in 2013 reported inflammatory trachoma prevalences below the World Health Organization (WHO) threshold for elimination, but TT prevalences above threshold. Given this epidemiological context and time since baseline survey, TT-only surveys were conducted in selected districts to determine current TT prevalence. The results of this study provide critical data for assessing Guinea's achievement of trachoma elimination targets. **Methods:** Four health districts, consisting of six evaluation units (EU), were surveyed. In each EU, field teams visited 29 clusters with a minimum 30 households included in each. Participants aged ≥15 years were examined by certified graders trained to identify TT and determine whether management had been offered. **Results:** A total of 22,476 people were examined, with 48 TT cases across the six EUs identified. Five of six EUs had an age-and-gender adjusted TT-prevalence unknown to the health system less than 0.2%, whereas one EU, Beyla 2, had an adjusted TT prevalence of 0.24%. **Conclusion:** These TT-only surveys, along with findings from other trachoma interventions, suggest that Guinea is close to achieving elimination of trachoma as a public health problem. This study demonstrates the value of undertaking TT-only surveys in settings where baseline surveys indicated active trachoma prevalences below WHO elimination threshold, but TT prevalences above it.

### Modeling the "F" in "SAFE": The dynamic game of facial cleanliness in trachoma prevention.

Barazanji M, Ngo JD, Powe JA, Schneider KP, Rychtář J, Taylor D.

23-06-2023

*PLoS One.*

<https://pubmed.ncbi.nlm.nih.gov/37352249/>

### Pharmacokinetics, feasibility and safety of co-administering azithromycin, albendazole, and ivermectin during mass drug administration: A review.

McPherson S, Solomon AW, Seife F, Solomon H, Gebre T, Mabey DCW, Marks M.

14-06-2023

*PLoS Negl Trop Dis.*

<https://pubmed.ncbi.nlm.nih.gov/37315102/>

**Introduction:** Traditionally, health ministries implement mass drug administration programmes for each neglected tropical disease (NTD) as separate and distinct campaigns. Many NTDs have overlapping endemicity suggesting co-administration might improve programme reach and efficiency, helping accelerate progress towards 2030 targets. Safety data are required to support a recommendation to undertake co-administration.

**Methodology:** We aimed to compile and summarize existing data on co-administration of ivermectin, albendazole and azithromycin, including both data on pharmacokinetic interactions and data from previous experimental and observational studies conducted in NTD-endemic populations. We searched PubMed, Google Scholar, research and conference abstracts, gray literature, and national policy documents. We limited the publication language to English and used a search period from January 1st, 1995 through October 1st, 2022. Search terms were: azithromycin and ivermectin and albendazole, mass drug administration co-administration trials, integrated mass drug administration, mass drug administration safety, pharmacokinetic dynamics, and azithromycin and ivermectin and albendazole. We excluded papers if they did not include data on co-administration of azithromycin and both albendazole and ivermectin, or azithromycin with either albendazole or ivermectin alone. **Results:** We identified a total of 58 potentially relevant studies. Of these we identified 7 studies relevant to the research question and which met our inclusion criteria. Three papers analyzed pharmacokinetic and pharmacodynamic interactions. No study found evidence of clinically significant drug-drug interactions likely to impact safety or efficacy. Two papers and a conference presentation reported data on the safety of combinations of at least two of the drugs. A field study in Mali suggested the rates of adverse events were similar with combined or separate administration, but was underpowered. A further field study in Papua New Guinea used all three drugs as part of a four-drug regimen also including diethylcarbamazine; in this setting, co-administration appeared safe but there were issues with the consistency in how adverse events were recorded. **Conclusion:** There are relatively limited data on the safety profile of co-administering ivermectin, albendazole and azithromycin as an integrated regimen for NTDs. Despite the limited amount of data, available evidence suggests that such a strategy is safe with an absence of clinically important drug-drug interactions, no serious adverse events reported and little evidence for an increase in mild adverse events. Integrated MDA may be a viable strategy for national NTD programmes.

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

### Intestinal helminth infections and associated risk factors among adults in the Lao People's Democratic Republic.

Phonekeo S, Kounnavong S, Vonglokhram M, Siengsounthone L, Homsana A, Gummin S, Vounatsu P,

**Nittiyanant P, Worawichawong S, Aekplakorn W, Odermatt P, Sayasone S.**

30-06-2023

*Infect Dis Poverty.*

<https://pubmed.ncbi.nlm.nih.gov/37386528/>

### **One Health for fascioliasis control in human endemic areas.**

**Mas-Coma S, Valero MA, Bargues MD.**

27-06-2023

*Trends Parasitol.*

<https://pubmed.ncbi.nlm.nih.gov/37385922/>

*Fasciola hepatica* and *F. gigantica* are liver flukes causing fascioliasis, a worldwide zoonotic, complex disease. Human infection/reinfection occurs in endemic areas where preventive chemotherapy is applied, because of fasciolid transmission ensured by livestock and lymnaeid snail vectors. A One Health control action is the best complement to decrease infection risk. The multidisciplinary framework needs to focus on freshwater transmission foci and their environment, lymnaeids, mammal reservoirs, and inhabitant infection, ethnography and housing. Local epidemiological and transmission knowledge furnished by previous field and experimental research offers the baseline for control design. A One Health intervention should be adapted to the endemic area characteristics. Long-term control sustainability may be achieved by prioritizing measures according to impact depending on available funds.

### **Curcumin and Its Supramolecular Complex with Disodium Glycyrrhizinate as Potential Drugs for the Liver Fluke Infection Caused by *Opisthorchis felineus*.**

**Lvova MN, Ponomarev DV, Tarasenko AA, Kovner AV, Minkova GA, Tsyganov MA, Li M, Lou Y, Evseenko VI, Dushkin AV, Sorokina IV, Tolstikova TG, Mordvinov VA, Avgustinovich DF.**

09-06-2023

*Pathogens.*

<https://pubmed.ncbi.nlm.nih.gov/37375509/>

Opisthorchiosis is a parasitic liver disease found in mammals that is widespread throughout the world and causes systemic inflammation. Praziquantel remains the drug of choice for the treatment of opisthorchiosis, despite its many adverse effects. An anthelmintic effect is attributed to the main curcuminoid of *Curcuma longa* L. roots-curcumin (Cur)-along with many other therapeutic properties. To overcome the poor solubility of curcumin in water, a micellar complex of curcumin with the disodium salt of glycyrrhizic acid (Cur:Na<sub>2</sub>GA, molar ratio 1:1) was prepared via solid-phase mechanical processing. In vitro experiments revealed a noticeable immobilizing effect of curcumin and of Cur:Na<sub>2</sub>GA on mature and juvenile *Opisthorchis felineus* individuals. In vivo experiments showed that curcumin (50 mg/kg) had an anthelmintic effect after 30 days of administration to *O. felineus*-infected hamsters, but the effect was weaker than that of a single administration of praziquantel (400 mg/kg). Cur:Na<sub>2</sub>GA (50 mg/kg, 30 days), which contains less free

curcumin, did not exert this action. The complex, just as free curcumin or better, activated the expression of bile acid synthesis genes (*Cyp7A1*, *Fxr*, and *Rxra*), which was suppressed by *O. felineus* infection and by praziquantel. Curcumin reduced the rate of inflammatory infiltration, whereas Cur:Na<sub>2</sub>GA reduced periductal fibrosis. Immunohistochemically, a decrease in liver inflammation markers was found, which is determined by calculating the numbers of tumor-necrosis-factor-positive cells during the curcumin treatment and of kynurenine-3-monooxygenase-positive cells during the Cur:Na<sub>2</sub>GA treatment. A biochemical blood test revealed a normalizing effect of Cur:Na<sub>2</sub>GA (comparable to that of curcumin) on lipid metabolism. We believe that the further development and investigation of therapeutics based on curcuminoids in relation *Opisthorchis felineus* and other trematode infections will be useful for clinical practice and veterinary medicine.

### ***Opisthorchis viverrini*-Current Understanding of the Neglected Hepatobiliary Parasite.**

**Liau MYQ, Toh EQ, Shelat VG.**

02-06-2023

*Pathogens.*

<https://pubmed.ncbi.nlm.nih.gov/37375485/>

### ***Fasciola hepatica*: An unusual cause of biliary obstruction.**

**Okasha HH, Delsa H, Gobran BA, Nakhla R.**

24-06-2023

*Gastrointest Endosc.*

<https://pubmed.ncbi.nlm.nih.gov/37364704/>

### **Molecular detection of *Fasciola*, *Schistosoma* and *Paramphistomum* species from freshwater snails occurring in Gauteng and Free State provinces, South Africa.**

**Molaba GG, Molefe-Nyembe NI, Taioe OM, Mofokeng LS, Thekiso OMM, Mtshali K.**

22-06-2023

*Vet Parasitol.*

<https://pubmed.ncbi.nlm.nih.gov/37364501/>

Trematodiasis are diseases caused by snail-borne trematode parasites that infect both animals and humans. Fascioliasis, schistosomiasis and paramphistomosis are some of these diseases and they affect millions of livestock, leading to significant economic losses. The aim of the study was to document freshwater snails occurring in selected study sites in the Free State and Gauteng provinces as well as identify and detect larval trematodes that they harbour. Samples were collected from a total of five study sites within two provinces of South Africa. Morphological features were used to identify snail species and were further confirmed genetically by polymerase chain reaction (PCR), sequencing and phylogenetic analysis. The larval trematodes were also detected by PCR, PCR-Restriction Length Fragment Polymorphism (PCR-RLFP), sequencing and phylogenetic analysis. A total of 887 freshwater snails were collected from Free State (n = 343)



and Gauteng (n = 544). Five different genera of snails as well as species in the Succineidae family were documented. The snails in descending order of abundance were identified as: Physa (P.) spp. (51%), Succineidae spp. (20%), Galba (G.) truncatula (12%), Pseudosuccinea (Ps.) columella (10%), Planorbella (Pl.) duryi (6%) and Bulinus (B.) truncatus (1%). Approximately 272 DNA pools were created for genetic identification of snails and detection of trematode parasites. Schistosoma species were not detected from any of the snail species. A total prevalence of 46% was obtained for Fasciola hepatica in the identified snail species across all study sites. Overall, the highest prevalence of F. hepatica was obtained in Physa species (24%), whilst the lowest was observed in B. truncatus snails (1%). Forty three percent (43%) of the snail samples were PCR positive for Paramphistomum DNA. This is the first report of P. mexicana in South Africa. Fasciola hepatica was confirmed from all obtained snail species per study site. This is the first reported detection of F. hepatica in Pl. duryi and P. mexicana snails as well as the first confirmation of natural infection from P. acuta in South Africa.

### **Molecular characterization of Fasciola hepatica in endemic regions of Colombia.**

García-Corredor D, Alvarado M, Pulido-Medellín M, Muñoz M, Cruz-Saavedra L, Hernández C, Giraldo JC, Vásquez-

Arteaga LR, Morillo Coronado AC, Ramírez JD.  
09-06-2023  
*Front Vet Sci.*  
<https://pubmed.ncbi.nlm.nih.gov/37360412/>

### **Multinomial logistic regression based on neural networks reveals inherent differences among dairy farms depending on the differential exposure to Fasciola hepatica and Ostertagia ostertagi.**

Oehm AW, Leinmueller M, Zablotzki Y, Campe A, Hoedemaker M, Springer A, Jordan D, Strube C, Knubben-Schweizer G.  
22-06-2023  
*Int J Parasitol.*  
<https://pubmed.ncbi.nlm.nih.gov/37355196/>

### **A survey for antibodies against Fasciola hepatica in cattle and sheep in Finland indicates a low level of exposure.**

Gröning H, Oksanen A, Skrzypczak T, Autio T.  
22-06-2023  
*Acta Vet Scand.*  
<https://pubmed.ncbi.nlm.nih.gov/37349804/>

**Background:** Fasciolosis is a parasitic infection caused by the liver fluke Fasciola hepatica that can have a major economic impact on livestock industry. The prevalence of the disease has recently been increasing in many North European countries. The objective of this study was to determine the prevalence of antibody against F. hepatica

in Finnish cattle herds and sheep flocks during 2019 by using a commercial enzyme-linked immunosorbent assay (ELISA). Randomly selected bulk tank milk samples were obtained from 660 dairy herds. Blood samples were collected at slaughterhouses from 1944 suckler cows from 309 herds and from 1120 sheep from 95 flocks. **Results:** Antibodies against F. hepatica were found in 0.45% (95% confidence interval (CI): 0.15-1.33) of the dairy herds and 0.97% (95% CI: 0.33-2.82) of the suckler cow herds. The seropositive herds were located in eastern and central Finland. None of the sampled sheep flocks tested had antibodies against F. hepatica (95% CI: 0-3.89). The results of the assays were compared with meat inspection data received from the slaughterhouses. All positive herds also had liver condemnations due to F. hepatica based on the meat inspection reports. **Conclusions:** Compared to other North European countries, the prevalence of fasciolosis in Finland can be considered low, and according to meat inspection reports, there are no indications of the prevalence increasing in Finland.

### **"Open a Can of Worms": Eosinophilic Liver Infiltration Due to Clonorchis sinensis Infection.**

Lan T, Tai Y, Tang C.  
01-07-2023  
*Am J Gastroenterol.*  
<https://pubmed.ncbi.nlm.nih.gov/36746416/>

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## **Trypanosomes (trypanosomiasis et maladie de Chagas)**

### **Platinum and Palladium Compounds: Disrupting the Ergosterol Pathway in Trypanosoma cruzi.**

Mosquillo F, Scalese G, Moreira R, Denis PA, Machado I, Paulino M, Gambino D, Perez Diaz L.  
29-06-2023  
*Chembiochem.*  
<https://pubmed.ncbi.nlm.nih.gov/37382991/>

### **Trypanosoma lewisi in blood of Rattus rattus complex residing in human settlements, Nakhon Si Thammarat, Thailand: Microscopic and molecular investigations.**

Tanthanathipchai N, Mitsuwan W, Chaisiri K, Thaikod S, de Lourdes Pereira M, Paul AK, Saengsawang P.  
22-06-2023  
*Comp Immunol Microbiol Infect Dis.*  
<https://pubmed.ncbi.nlm.nih.gov/37379668/>

Trypanosomes are blood parasites infected in various mammals, including rats. The presence of rats in human settlements can increase the chance of Trypanosoma transmission to humans. The molecular study of multispacer in Trypanosoma spp. in naturally infected

rodents in Thailand is scanty. The objective of this study was to detect *Trypanosoma* in the blood of the captured rats in Nakhon Si Thammarat, Thailand, using microscopic and molecular techniques. This was a cross-sectional study conducted in human settlement areas. Ninety-nine blood samples were collected using cardiac puncture. A blood sample was smeared on a glass slide and examined using a compound light microscope and a scanning electron microscope. Moreover, polymerase chain reaction was applied to detect *Trypanosoma evansi* and *T. lewisi* in the blood. An additional primer set was used to confirm the species of the detected trypanosome. Approximately 18% of the rats had positive *Trypanosoma* infections. All *Trypanosoma*-positive blood samples were matched with sequences of *T. lewisi*. The stumpy form of trypanosome had higher nucleus related parameters than the slender form. Interestingly, the partial sequences of the alpha-tubulin gene of *T. lewisi* were first reported in the naturally infected RrC in this study. Based on the results obtained, *T. lewisi* biology, particularly the virulent components and route of transmission, pathogenesis, and in vitro experiments, are strongly recommended for further study.

### Editorial: New strategies for the treatment of diseases caused by trypanosomatid parasites.

Cardoso FO, Almeida-Souza F, Maretti-Mira AC, Abreu-Silva AL.

12-06-2023

*Front Cell Infect Microbiol.*

<https://pubmed.ncbi.nlm.nih.gov/37377646/>

### Targeting Metalloenzymes: The "Achilles' Heel" of Viruses and Parasites.

Moianos D, Prifti GM, Makri M, Zoidis G.

19-06-2023

*Pharmaceuticals (Basel).*

<https://pubmed.ncbi.nlm.nih.gov/37375848/>

Metalloenzymes are central to the regulation of a wide range of essential viral and parasitic functions, including protein degradation, nucleic acid modification, and many others. Given the impact of infectious diseases on human health, inhibiting metalloenzymes offers an attractive approach to disease therapy. Metal-chelating agents have been expansively studied as antivirals and antiparasitics, resulting in important classes of metal-dependent enzyme inhibitors. This review provides the recent advances in targeting the metalloenzymes of viruses and parasites that impose a significant burden on global public health, including influenza A and B, hepatitis B and C, and human immunodeficiency viruses as well as *Trypanosoma brucei* and *Trypanosoma cruzi*.

### Nitazoxanide: A Drug Repositioning Compound with Potential Use in Chagas Disease in a Murine Model.

Arce-Fonseca M, Gutiérrez-Ocejo RA, Rosales-Encina JL, Aranda-Fraustro A, Cabrera-Mata JJ, Rodríguez-Morales O.

01-06-2023

*Pharmaceuticals (Basel).*

<https://pubmed.ncbi.nlm.nih.gov/37375773/>

### Antiplasmodial, Trypanocidal, and Genotoxicity In Vitro Assessment of New Hybrid $\alpha,\alpha$ -Difluorophenylacetamide-statin Derivatives.

Araujo-Lima CF, de Cassia Castro Carvalho R, Rosario SL, Leite DI, Aguiar ACC, de Souza Santos LV, de Araujo JS, Salomão K, Kaiser CR, Krettli AU, Bastos MM, Aiub CAF, de Nazaré Correia Soeiro M, Boechat N, Felzenszwalb I.

24-05-2023

*Pharmaceuticals (Basel).*

<https://pubmed.ncbi.nlm.nih.gov/37375730/>

**Background:** Statins present a plethora of pleiotropic effects including anti-inflammatory and antimicrobial responses.  $\alpha,\alpha$ -difluorophenylacetamides, analogs of diclofenac, are potent pre-clinical anti-inflammatory non-steroidal drugs. Molecular hybridization based on the combination of pharmacophoric moieties has emerged as a strategy for the development of new candidates aiming to obtain multitarget ligands. **Methods:** Considering the anti-inflammatory activity of phenylacetamides and the potential microbicidal action of statins against obligate intracellular parasites, the objective of this work was to synthesize eight new hybrid compounds of  $\alpha,\alpha$ -difluorophenylacetamides with the moiety of statins and assess their phenotypic activity against *in vitro* models of *Plasmodium falciparum* and *Trypanosoma cruzi* infection besides exploring their genotoxicity safety profile.

**Results:** None of the sodium salt compounds presented antiparasitic activity and two acetated compounds displayed mild anti-*P. falciparum* effect. Against *T. cruzi*, the acetate halogenated hybrids showed moderate effect against both parasite forms relevant for human infection. Despite the considerable trypanosomicidal activity, the brominated compound revealed a genotoxic profile impairing future *in vivo* testing. **Conclusions:** However, the chlorinated derivative was the most promising compound with chemical and biological profitable characteristics, without presenting genotoxicity *in vitro*, being eligible for further *in vivo* experiments.

### Antiprotozoal activity of auranofin on *Trypanosoma cruzi*, *Leishmania tropica* and *Toxoplasma gondii*: in vitro and ex vivo study.

Yıldırım A, Özbilgin A, Yereli K.

28-06-2023

*Trans R Soc Trop Med Hyg.*

<https://pubmed.ncbi.nlm.nih.gov/37377375/>

**Background:** Three obligate intracellular protozoan parasite species, which are responsible for significant morbidity and mortality and settle in macrophage cells, affect more than one-half of the world's population, namely, *Trypanosoma cruzi*, *Leishmania tropica* and *Toxoplasma gondii*, which are causative agents of Chagas disease, leishmaniasis and toxoplasmosis, respectively. In the current study, it was aimed to investigate the in vitro and ex vivo antiprotozoal activity of auranofin on *T. cruzi*, *L. tropica* and *T. gondii*. **Methods:** The in vitro drug efficacy (IC50) of auranofin was investigated by haemocytometry

and the CellTiter-Glo assay methods and the ex vivo drug efficacy (IC<sub>50</sub>) by light microscopic examination of Giemsa-stained slides. Also, the cytotoxic activity (CC<sub>50</sub>) of auranofin was examined by the CellTiter-Glo assay. The selectivity index (SI) was calculated for auranofin. **Results:** According to IC<sub>50</sub>, CC<sub>50</sub> and SI data, auranofin did not exhibit cytotoxic activity on Vero cells, but exhibited antiprotozoal activity on epimastigotes and intracellular amastigotes of *T. cruzi*, promastigotes and intracellular amastigotes of *L. tropica* and intracellular tachyzoites of *T. gondii* ( $p < 0.05$ ).

**Conclusions:** The detection antiprotozoal activity of auranofin on *T. cruzi*, *L. tropica* and *T. gondii* according to the IC<sub>50</sub>, CC<sub>50</sub> and SI values is considered an important and promising development. This is significant because auranofin may be an effective alternative treatment for Chagas disease, leishmaniasis and toxoplasmosis in the future.

### Effects of Synthetic Ligustrazine-Based Chalcone Derivatives on *Trypanosoma brucei brucei* and *Leishmania* spp. Promastigotes.

**Alkhaldi AAM.**

08-06-2023

*Molecules.*

<https://pubmed.ncbi.nlm.nih.gov/37375205/>

Current medication therapy for leishmaniasis and trypanosomiasis remains a major challenge due to its limited efficacy, significant adverse effects, and inaccessibility. Consequently, locating affordable and effective medications is a pressing concern. Because of their easy-to-understand structure and high functionalization potential, chalcones are promising candidates for use as bioactive agents. Thirteen synthetic ligustrazine-containing chalcones were evaluated for their ability to inhibit the growth of leishmaniasis and trypanosomiasis in etiologic agents. The tetramethylpyrazine (TMP) analogue ligustrazine was chosen as the central moiety for the synthesis of these chalcone compounds. The most effective compound (EC<sub>50</sub> = 2.59  $\mu$ M) was the chalcone derivative **2c**, which featured a pyrazin-2-yl amino on the ketone ring and a methyl substitution. Multiple actions were observed for certain derivatives, including **1c**, **2a-c**, **4b**, and **5b**, against all strains tested. Eflornithine served as a positive control, and three ligustrazine-based chalcone derivatives, including **1c**, **2c**, and **4b**, had a higher relative potency. Compounds **1c** and **2c** are particularly efficacious; even more potent than the positive control, they are therefore promising candidates for the treatment of trypanosomiasis and leishmaniasis.

### Experimental *Trypanosoma cruzi* Infection and Chagas Disease-A Word of Caution.

**Talvani A, Teixeira MM.**

19-05-2023

*Microorganisms*

<https://pubmed.ncbi.nlm.nih.gov/37375115/>

### Bioactivity Screening and Chemical Characterization of Biocompound from Endophytic *Neofusicoccum parvum* and *Buergenerula spartinae* Isolated from Mangrove Ecosystem.

**Cadamuro RD, Bastos IMADS, de Freitas ACO, Rosa MDS, Costa GO, da Silva IT, Robl D, Stoco PH, Sandjo LP, Treichel H, Steindel M, Fongaro G.**

16-05-2023

*Microorganisms.*

<https://pubmed.ncbi.nlm.nih.gov/37375101/>

The discovery of biomolecules has been the subject of extensive research for several years due to their potential to combat harmful pathogens that can lead to environmental contamination and infections in both humans and animals. This study aimed to identify the chemical profile of endophytic fungi, namely *Neofusicoccum parvum* and *Buergenerula spartinae*, which were isolated from *Avecinnia schaueriana* and *Laguncularia racemosa*. We identified several HPLC-MS compounds, including Ethylidene-3,39-biplumbagin, Pestauvicolactone A, Phenylalanine, 2-Isopropylmalic acid, Fusaproliferin, Suspendole, Ansellone, Calanone derivative, Terpestacin, and others. Solid-state fermentation was conducted for 14-21 days, and methanol and dichloromethane extraction were performed to obtain a crude extract. The results of our cytotoxicity assay revealed a CC<sub>50</sub> value > 500  $\mu$ g/mL, while the virucide, *Trypanosoma*, leishmania, and yeast assay demonstrated no inhibition. Nevertheless, the bacteriostatic assay showed a 98% reduction in *Listeria monocytogenes* and *Escherichia coli*. Our findings suggest that these endophytic fungi species with distinct chemical profiles represent a promising niche for further exploring new biomolecules.

### Validation of the NAT Chagas IVD Kit for the Detection and Quantification of *Trypanosoma cruzi* in Blood Samples of Patients with Chagas Disease.

**Moreira OC, Fernandes AG, Gomes NLDS, Dos Santos CM, Jacomasso T, Costa ADT, Nascimento LOR, Hasslocher-Moreno AM, do Brasil PEAA, Morello LG, Marchini FK, Krieger MA, Britto C.**

24-05-2023

*Life (Basel).*

<https://pubmed.ncbi.nlm.nih.gov/37374019/>

### Targeting RNA Structure to Inhibit Editing in Trypanosomes.

**Acquah FA, Mooers BHM.**

14-06-2023

*Int J Mol Sci.*

<https://pubmed.ncbi.nlm.nih.gov/37373258/>

Mitochondrial RNA editing in trypanosomes represents an attractive target for developing safer and more efficient drugs for treating infections with trypanosomes because this RNA editing pathway is not found in humans. Other workers have targeted several enzymes in this editing system, but not the RNA. Here, we target a universal

domain of the RNA editing substrate, which is the U-helix formed between the oligo-U tail of the guide RNA and the target mRNA. We selected a part of the U-helix that is rich in G-U wobble base pairs as the target site for the virtual screening of 262,000 compounds. After chemoinformatic filtering of the top 5000 leads, we subjected 50 representative complexes to 50 nanoseconds of molecular dynamics simulations. We identified 15 compounds that retained stable interactions in the deep groove of the U-helix. The microscale thermophoresis binding experiments on these five compounds show low-micromolar to nanomolar binding affinities. The UV melting studies show an increase in the melting temperatures of the U-helix upon binding by each compound. These five compounds can serve as leads for drug development and as research tools to probe the role of the RNA structure in trypanosomal RNA editing.

### Acute Phase Proteins in Dogs with Natural Infection by *Trypanosoma cruzi*.

Rivadeneira-Barreiro P, Montes-de-Oca-Jiménez R, Zambrano-Rodríguez P, Vázquez-Chagoyán JC, Gutiérrez-Castillo ADC, Pardo-Marin L, Franco-Martínez L, Cerón JJ, Martínez-Subiela S.

31-05-2023

*Trop Med Infect Dis.*

<https://pubmed.ncbi.nlm.nih.gov/37368717/>

Acute phase proteins have been used as tools for the diagnosis, monitoring, and prognosis of several diseases in domestic animals. However, the dynamics of these proteins in infection by *Trypanosoma cruzi*, the causative agent of Chagas disease in dogs, is still unknown. The aim of this study was to determine concentrations of acute phase proteins (C-reactive protein, haptoglobin, ferritin and paraoxonase-1) in dogs in a coastal town of Ecuador, with natural *Trypanosoma cruzi* infection with or without seroreactivity of *Ehrlichia canis*, *Ehrlichia ewingii*, *Anaplasma phagocytophilum*, *Anaplasma platys*, *Borrelia burgdorferi* and *Dirofilaria immitis*. For the detection of *Trypanosoma cruzi* serum antibodies, two different antigen-based enzyme-linked immunosorbent assay tests were implemented. For the detection of seroreactivity of *Ehrlichia canis*, *Ehrlichia ewingii*, *Anaplasma phagocytophilum*, *Anaplasma platys*, *Borrelia burgdorferi* and *Dirofilaria immitis*, an IDEXX SNAP® 4Dx® test was used. To determine the concentration of C-reactive protein and ferritin, an immunoturbidimetric assay was used; haptoglobin concentration was measured using a commercial colorimetric method validated in dogs; a spectrophotometric method was used to determine the serum concentration of paraoxonase-1. Results showed a reduction in the serum levels of paraoxonase-1 in *Trypanosoma cruzi*-seroreactive dogs, either with or without seroreactivity to other vector-borne diseases. A serum ferritin increment was observed in *Trypanosoma cruzi*-seroreactive dogs with seroreactivity to any other vector-borne diseases. Our findings suggest that paraoxonase-1 levels are reduced in *Trypanosoma cruzi*-seroreactive dogs without evident clinical signs of Chagas disease, despite their seroreactivity to the other vector-borne diseases studied. These findings could indicate an

oxidative stress response in *Trypanosoma cruzi*-seroreactive dogs with no evident signs of inflammation.

### Molecular Detection of Animal Trypanosomes in Different Animal Species in the Visayas Region of the Philippines.

Elata A, Galon EM, Moumouni PFA, Ybanez RHD, Mossaad E, Salces CB, Bajenting GP, Ybanez AP, Xuan X, Inoue N, Suganuma K.

27-06-2023

*Acta Parasitol.*

<https://pubmed.ncbi.nlm.nih.gov/37368129>

### Trypanosomes infection, endosymbionts, and host preferences in tsetse flies (*Glossina spp.*) collected from Akagera park region, Rwanda: A correlational xenomonitoring study.

Gashururu RS, Maingi N, Githigia SM, Getange DO, Ntivuguruzwa JB, Habimana R, Cecchi G, Gashumba J, Bargul JL, Masiga DK.

28-04-2023

*One Health.*

### Protein abundance in the midgut of wild tsetse flies (*Glossina palpalis palpalis*) naturally infected by *Trypanosoma congolense* s.l.

Tsagmo JM, Njiokou F, Dziedzich A, Rofidal V, Hem S, Geiger A.

26-06-2023

*Med Vet Entomol.*

<https://pubmed.ncbi.nlm.nih.gov/37357577/>

Tsetse flies (*Glossina spp.*) are major vectors of African trypanosomes, causing either Human or Animal African Trypanosomiasis (HAT or AAT). Several approaches have been developed to control the disease, among which is the anti-vector Sterile Insect Technique. Another approach to anti-vector strategies could consist of controlling the fly's vector competence through hitherto unidentified regulatory factors (genes, proteins, biological pathways, etc.). The present work aims to evaluate the protein abundance in the midgut of wild tsetse flies (*Glossina palpalis palpalis*) naturally infected by *Trypanosoma congolense* s.l. Infected and non-infected flies were sampled in two HAT/AAT foci in Southern Cameroon. After dissection, the proteomes from the guts of parasite-infected flies were compared to that of uninfected flies to identify quantitative and/or qualitative changes associated with infection. Among the proteins with increased abundance were fructose-1,6-biphosphatase, membrane trafficking proteins, death proteins (or apoptosis proteins) and SERPINS (inhibitor of serine proteases, enzymes considered as trypanosome virulence factors) that displayed the highest increased abundance. The present study, together with previous proteomic and transcriptomic studies on the secretome of trypanosomes from tsetse fly gut extracts, provides data to be explored in further investigations on, for example, mammal host



immunisation or on fly vector competence modification via para-transgenic approaches.

### Seroprevalence of *Trypanosoma cruzi* infection among blood donors in the state of Pará, Brazil.

Valente JD, Silva NDS, Vasconcelos de Sousa S, Amaral CEM, Pinto LC.

22-06-2023

*Transfus Apher Sci.*

<https://pubmed.ncbi.nlm.nih.gov/37357058/>

**Introduction:** Chagas disease (CD) is a neglected pathology worldwide, considered a public health problem due to the high morbidity and mortality rate and its social impact. Thus, the objective was to estimate the prevalence of reactive serology for *T. cruzi* in blood donors in the units of the public blood network in the state of Pará (Brazil), as well as to describe the epidemiological profile of these donors. **Methods:** This is a retrospective and descriptive study carried out at the Pará State Center for Hematology and Hemotherapy (HEMOPA) between 2016 and 2021, with analysis of secondary data (epidemiological and serological) of inapt blood donors for CD. **Results:** Among the 533,674 screened samples, the reactivity for anti-*T. cruzi* was detected in 0.1% (548), of which 0.03% (166) were inconclusive and 0.07% (382) were positive. The hemonucleus of the city of Abaetetuba had the highest seroprevalence (0.6%). Regarding epidemiological characteristics, most blood donors were men (63.7%), aged between 31 and 45 (44.7%), racially mixed (79.2%), high school graduate (45.8%), single/widowed/divorced (62%), first-time donors (69%), spontaneous donations (58%) and from the state's countryside (69.9%). **Conclusion:** Over the years analyzed, we observed an increase in seroprevalence for *T. cruzi* emphasizing the need to maintain epidemiological control in the region and the application of more accurate serological tests in the screening of donor blood bags.

### Two New Cytotoxic Sesquiterpene-Amino Acid Conjugates and a Coumarin-Glucoside from *Crossostephium chinense*.

Wang Z, Chitama BA, Suganuma K, Yamano Y, Sugimoto S, Kawakami S, Kaneko O, Otsuka H, Matsunami K.

1106-2023

*Molecules.*

<https://pubmed.ncbi.nlm.nih.gov/37375252/>

### Enyne acetogenins from *Porcelia macrocarpa* displayed anti-*Trypanosoma cruzi* activity and cause a reduction in the intracellular calcium level.

Thevenard F, Brito IA, Costa-Silva TA, Tempone AG, Lago JHG.

24-06-2023

*Sci Rep.*

<https://pubmed.ncbi.nlm.nih.gov/37355735/>

Natural products are a promising source of new compounds with a wide spectrum of pharmacological properties, including antiprotozoal activities. Chagas disease, caused by the protozoan parasite *Trypanosoma cruzi*, is one of several neglected tropical diseases with reduced options for treatment, which presents limitations such as toxicity and ineffectiveness in the chronic stage of the disease. Aiming to investigate the Brazilian flora for the discovery of new anti-*T. cruzi* compounds, the MeOH extract from *Porcelia macrocarpa* R.E. Fries (Annonaceae) fruit peels displayed potent activity against trypomastigotes and intracellular amastigotes and was subjected to bioactivity-guided fractionation. Using different chromatographic steps, a fraction composed of a mixture of four new chemically related acetogenins was obtained. The compounds were characterized as (2S\*,3R\*,4R\*)-3-hydroxy-4-methyl-2-(n-octadeca-13',17'-dien-11'-inil)butanolide (1), (2S\*,3R\*,4R\*)-3-hydroxy-4-methyl-2-(n-eicosa-13',19'-dien-11'-inil)butanolide (2), (2S\*,3R\*,4R\*)-3-hydroxy-4-methyl-2-(n-octadec-13'-en-11'-inil)butanolide (3), and (2S\*,3R\*,4R\*)-3-hydroxy-4-methyl-2-(n-eicosa-13'-en-11'-inil)butanolide (4) by NMR analysis and UHPLC/ESI-HRMS data. The mixture of compounds 1-4, displayed an EC<sub>50</sub> of 4.9 and 2.5 µg/mL against trypomastigote and amastigote forms of *T. cruzi*, respectively, similar to the standard drug benznidazole (EC<sub>50</sub> of 4.8 and 1.4 µg/mL). Additionally, the mixture of compounds 1-4 displayed no mammalian toxicity for murine fibroblasts (CC<sub>50</sub> > 200 µg/mL), resulting in a SI > 40.8 and > 83.3 against trypomastigotes and amastigotes, respectively. Based on these results, the mechanism of action of this bioactive fraction was investigated. After a short-time incubation with the trypomastigotes, no alterations in the cell membrane permeability were observed. However, it was verified a decrease in the intracellular calcium of the parasites, without significant pH variations of the acidocalcisomes. The intracellular damages were followed by an upregulation of the reactive oxygen species and ATP, but no depolarization effects were observed in the mitochondrial membrane potential. These data suggest that the mixture of compounds 1-4 caused an irreversible oxidative stress in the parasites, leading to death. If adequately studied, these acetogenins can open new insights for the discovery of new routes of death in *T. cruzi*.

### 2-Aroyl quinazolinone: Synthesis and in vitro anti-parasitic activity.

Setshedi KJ, Beteck RM, Jesumoroti OJ, Ilbeigi K, Mabille D, Caljon G, Van der Kooy F, Legoabe LJ.

23-06-2023

*Chem Biol Drug Des.*

<https://pubmed.ncbi.nlm.nih.gov/37353860/>

Trypanosomes and Leishmania are parasitic protozoans that affect millions of people globally. Herein we report the synthesis of 2-aroyl quinazolinones and their antiprotozoal efficacy against *Trypanosoma brucei*, *Trypanosoma brucei rhodesiense*, *Trypanosoma cruzi*, and *Leishmania infantum*. These compounds were counter-screened against a human cell line for cytotoxicity. Thirteen of the twenty target compounds in this study inhibited the growth of these parasites, with compounds

KJ1, and KJ10 exhibiting IC<sub>50</sub> values of 4.7 μM (T. b. brucei) and 1.1 μM (T. b. rhodesiense), respectively.

### **A Trypanosoma cruzi phosphoglycerate kinase isoform with a Per-Arnt-Sim domain acts as a possible sensor for intracellular conditions.**

Rojas-Pirela M, Delgado A, Rondón-Guerrero YDC, Cáceres AJ, Michels PAM, Concepción JL, Quiñones W.  
21-06-2023

*Exp Parasitol.*

<https://pubmed.ncbi.nlm.nih.gov/37353138/>

### **Resistance to deltamethrin in Triatoma infestans (Hemiptera: Reduviidae): does it influence the phenotype of antennae, wings, and heads?**

Hernández ML, Dujardin JP, Villacís AG, Yumiseva CA, Remón C, Mougabure-Cueto G.  
21-06-2023

*Acta Trop.*

<https://pubmed.ncbi.nlm.nih.gov/37352997/>

### **ELISA F29 -A therapeutic efficacy biomarker in Chagas disease: Evaluation in pediatric patients treated with nifurtimox and followed for 4 years post-treatment.**

Rivero R, Esteva MI, Huang E, Colmegna L, Altcheh J, Grossmann U, Ruiz AM; CHICO and CHICO SECURE Study Groups.  
23-06-2023

*PLoS Negl Trop Dis.*

<https://pubmed.ncbi.nlm.nih.gov/37352322/>

### **KREH1 RNA helicase activity promotes utilization of initiator gRNAs across multiple mRNAs in trypanosome RNA editing.**

Dubey AP, Tylec BL, Mishra A, Sortino K, Chen R, Sun Y, Read LK.  
23-06-2023

*Nucleic Acids Res.*

<https://pubmed.ncbi.nlm.nih.gov/37140035/>

Mitochondrial U-indel RNA editing in kinetoplastid protozoa is directed by trans-acting gRNAs and mediated by a holoenzyme with associated factors. Here, we examine the function of the holoenzyme-associated KREH1 RNA helicase in U-indel editing. We show that KREH1 knockout (KO) impairs editing of a small subset of mRNAs. Overexpression of helicase-dead mutants results in expanded impairment of editing across multiple transcripts, suggesting the existence of enzymes that can compensate for KREH1 in KO cells. In depth analysis of editing defects using quantitative RT-PCR and high-throughput sequencing reveals compromised editing initiation and progression in both KREH1-KO and mutant-expressing cells. In addition, these cells exhibit a distinct defect in the earliest stages of editing in which the initiator gRNA is bypassed, and a small number of editing events

takes place just outside this region. Wild type KREH1 and a helicase-dead KREH1 mutant interact similarly with RNA and holoenzyme, and overexpression of both similarly disorders holoenzyme homeostasis. Thus, our data support a model in which KREH1 RNA helicase activity facilitates remodeling of initiator gRNA-mRNA duplexes to permit accurate utilization of initiating gRNAs on multiple transcripts.

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## **Ulcère de Buruli**

### **Assessing the cost-effectiveness of integrated case management of Neglected Tropical Diseases in Liberia.**

Godwin-Akpan TG, Diaconu K, Edmiston M, Smith JS Jr, Sosu F, Weiland S, Kollie KK.  
29-06-2023

*BMC Health Serv Res.*

<https://pubmed.ncbi.nlm.nih.gov/37386431/>

**Background:** In 2017, Liberia became one of the first countries in the African region to develop and implement a national strategy for integrated case management of Neglected Tropical Diseases (CM-NTDs), specifically Buruli ulcer, leprosy, lymphatic filariasis morbidities, and yaws. Implementing this plan moves the NTD program from many countries' fragmented (vertical) disease management. This study explores to what extent an integrated approach offers a cost-effective investment for national health systems. **Methods:** This study is a mixed-method economic evaluation that explores the cost-effectiveness of the integrated CM-NTDs approach compared to the fragmented (vertical) disease management. Primary data were collected from two integrated intervention counties and two non-intervention counties to determine the relative cost-effectiveness of the integrated program model vs. fragmented (vertical) care. Data was sourced from the NTDs program annual budgets and financial reports for integrated CM-NTDs and Mass Drug Administration (MDA) to determine cost drivers and effectiveness.

**Results:** The total cost incurred by the integrated CM-NTD approach from 2017 to 2019 was US\$ 789,856.30, with the highest percentage of costs for program staffing and motivation (41.8%), followed by operating costs (24.8%). In the two counties implementing fragmented (vertical) disease management, approximately US\$ 325,000 was spent on the diagnosis of 84 persons and the treatment of twenty-four persons suffering from NTDs. While 2.5 times as much was spent in integrated counties, 9-10 times more patients were diagnosed and treated. **Conclusions:** The cost of a patient being diagnosed under the fragmented (vertical) implementation is five times higher than integrated CM-NTDs, and providing treatment is ten times as costly. Findings indicate that the integrated CM-NTDs strategy has achieved its primary objective of improved access to NTD services. The success of implementing an integrated CM-NTDs approach in Liberia, presented in this paper, demonstrates that NTD integration is a cost-minimizing solution.

**A human model of Buruli ulcer: The case for controlled human infection and considerations for selecting a *Mycobacterium ulcerans* challenge strain.**

Muhi S, Osowicki J, O'Brien D, Johnson PDR, Pidot S, Doerflinger M, Marshall JL, Pellegrini M, McCarthy J, Stinear TP.

29-06-2023

*PLoS Negl Trop Dis.*

<https://pubmed.ncbi.nlm.nih.gov/37384606/>

**From Bacterial Toxin to Therapeutic Agent: The Unexpected Fate of Mycolactone.**

Ricci D, Demangel C.

30-05-2023

*Toxins (Basel).*

<https://pubmed.ncbi.nlm.nih.gov/37368670/>

"Recognizing a surprising fact is the first step towards discovery." This famous quote from Louis Pasteur is particularly appropriate to describe what led us to study mycolactone, a lipid toxin produced by the human pathogen *Mycobacterium ulcerans*. *M. ulcerans* is the causative agent of Buruli ulcer, a neglected tropical disease manifesting as chronic, necrotic skin lesions with a "surprising" lack of inflammation and pain. Decades after its first description, mycolactone has become much more than a mycobacterial toxin. This uniquely potent inhibitor of the mammalian translocon (Sec61) helped reveal the central importance of Sec61 activity for immune cell functions, the spread of viral particles and, unexpectedly, the viability of certain cancer cells. We report in this review the main discoveries that marked our research into mycolactone, and the medical perspectives they opened up. The story of mycolactone is not over and the applications of Sec61 inhibition may go well beyond immunomodulation, viral infections, and oncology.