



## **Veille scientifique**

# **Maladies tropicales négligées**

**Semaine 12**  
*20 au 26 mars 2023*

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# Dengue, chikungunya et maladie à virus Zika

## Recent advances in the development of methyltransferase (MTase) inhibitors against (re)emerging arboviruses diseases dengue and Zika.

Delgado-Maldonado T, Moreno-Herrera A, Pujadas G, Vázquez-Jiménez LK, González-González A, Rivera G.  
20-03-2023

*Eur J Med Chem.*

<https://pubmed.ncbi.nlm.nih.gov/36958266/>

## Secondary metabolites as potential drug candidates against Zika virus, an emerging looming human threat: Current landscape, molecular mechanism and challenges ahead.

Sadeer NB, El Kalamouni C, Khalid A, Abdalla AN, Zengin G, Khoa Bao LV, Mahomoodally MF.

15-03-2023

*J Infect Public Health.*

<https://pubmed.ncbi.nlm.nih.gov/36958171/>

Nature has given us yet another wild card in the form of Zika virus (ZIKV). It was found in 1947, but has only recently become an important public health risk, predominantly to pregnant women and their unborn offspring. Currently, no specific therapeutic agent exists for ZIKV and treatment is mainly supportive. Natural products (NPs) can serve as a major source of potent antiviral drugs. To create this review, a comprehensive search was conducted from different databases (PubMed, ScienceDirect, Google scholar). A statistical analysis on the number of publications related to NPs and ZIKV was conducted to analyse the trend in research covering the period 1980-2020. From the data collated in this review, a number of NPs have been found to be inhibitive towards different stages of the ZIKV lifecycle in vitro studies. For instance, baicalin, (-)-epigallocatechin gallate, curcumin, nanchangmycin, gossypol, cephaeline, emetine, resveratrol, berberine, amongst others, can prevent viral entry by attacking ZIKV E protein. Compounds luteolin, myricetin, astragalin, rutin, (-)-epigallocatechin gallate, carnosine, pedalitin, amongst others, inhibited NS2B-NS3 protease activity which consequently hamper replication. Interestingly, a few NPs had the ability to arrest both viral entry and replication, namely baicalin, (-)-epigallocatechin gallate, curcumin, cephaeline, emetine, and resveratrol. To the best of our knowledge, we obtained only one in vivo study conducted on emetine and results showed that it decreased the levels of circulating ZIKV by approximately 10-fold. Our understanding on NPs exhibiting anti-ZIKV effects in in vivo testing as well as clinical trials is limited. Our trend analysis showed that interest in searching for a cure or prevention against Zika in NPs is negligible and there are no publications yet covering the clinical evaluation. NPs with anti-ZIKV property can a winning strategy in controlling the bio-burden of an epidemic or pandemic. We therefore opine that in the future, more research should be devoted to ZIKV. This review attempts

to provide baseline data and roadmap to pursue detailed investigations for developing potent and novel therapeutic agents to prevent and cure ZIKV infection.

## Chikungunya Outbreak in Country with Multiple Vectorborne Diseases, Djibouti, 2019-2020.

Javelle E, de Laval F, Durand GA, Dia A, Ficko C, Bousquet A, Delaune D, Briolant S, Mérens A, Brossier C, Pommier H, Gala F, Courtiol A, Savreux Q, Sicard S, Sanchez JP, Robin F, Simon F, de Lamballerie X, Grard G, Leparco-Goffart I, de Santi VP.

Apr-2023

*Emerg Infect Dis.*

<https://pubmed.ncbi.nlm.nih.gov/36958020/>

## Transmission of Zika virus by dendritic cell subsets in skin and vaginal mucosa.

Eder J, Zijlstra-Willems E, Koen G, Kootstra NA, Wolthers KC, Geijtenbeek TB.

06-03-2023

*Front Immunol.*

<https://pubmed.ncbi.nlm.nih.gov/36949942/>

## Editorial: Biological drivers of vector-pathogen interactions - vol II.

Rego ROM, Lopez JE, Cabelas-Cruz A.

06-03-2023

*Front Cell Infect Microbiol.*

<https://pubmed.ncbi.nlm.nih.gov/36949813/>

## Epidemiological profile of arboviruses in two different scenarios: dengue circulation vs. dengue, chikungunya and Zika co-circulation.

Farias PCS, Pastor AF, Gonçalves JP, do Nascimento IDS, de Souza Ferraz ES, Lopes TRR, do Carmo RF, Côelho MRCD, Silva Júnior JVI.

22-03-2023

*BMC Infect Dis.*

<https://pubmed.ncbi.nlm.nih.gov/36949383/>

**Background:** The severity and distribution of dengue virus (DENV) infections have been attributed to a complex interaction among viral, host and environmental factors. Herein, we investigated the influence of chikungunya (CHIKV) and Zika (ZIKV) viruses on the epidemiological profile of dengue cases, using Recife, Pernambuco state, Brazil, as a study model. In addition, we described and compared the epidemiological profile related to each arbovirus (DENV vs. CHIKV vs. ZIKV). **Methods:** All cases of dengue, chikungunya and Zika reported to the Pernambuco Health Department in 2011-2013 (DENV circulation) and 2016-2018 (DENV, CHIKV and ZIKV co-circulation) were included in our study. The cases were classified by sex, age and race/color and their distribution was analyzed by the  $\chi^2$  test. Furthermore, the data were also analyzed for co-infections. Temperature, humidity and rainfall data were analyzed using one-way ANOVA and paired t-test. **Results:** During 2011-2013, 15,315 dengue cases were diagnosed, most of them female, brown and

20-29 age group. Between 2016 and 2018, 15,870 dengue cases were described, which presented the same profile described above. In the two triennia, the female/male dengue ratio fluctuated significantly, ranging from 1.07 to 1.52. Regarding chikungunya, 7076 cases were reported, most of them female and brown. The female/male ratio also fluctuated significantly, ranging from 1.62 to 2.1. Two main age groups were observed in chikungunya:  $\leq 19$  years (minority of diagnoses) and  $\geq 20$  years (majority of diagnoses). In the same triennium, 266 Zika cases were reported to the Pernambuco Health Department, mainly in females and in the 0-9 and 20-39 age groups. In general, 119 co-infections were identified: 117 DENV-CHIKV, 1 CHIKV-ZIKV and 1 DENV-CHIKV-ZIKV. Concerning climate data, only the humidity in 2011 was significantly different from the other years. **Conclusion:** The epidemiological profile of dengue cases did not change after the introduction of CHIKV and ZIKV. Females were the most diagnosed with dengue, chikungunya or Zika, however we found important differences in the age profile of these arboviruses, which should be considered by public health policies, as well as investigated in future studies of virus-host interaction.

### Chimeric protection to dengue.

**Taglialegna A.**

22-03-2023

*Nat Rev Microbiol.*

<https://pubmed.ncbi.nlm.nih.gov/36949283/>

### Zika virus NS1 suppresses VE-cadherin via hsa-miR-29b-3p/DNMT3b/MMP-9 pathway in human brain microvascular endothelial cells.

**Bhardwaj U, Singh SK.**

20-03-2023

*Cell Signal.*

<https://pubmed.ncbi.nlm.nih.gov/36948479/>

Zika virus infection has been reported to cause microcephaly in newborns. ZIKV exploits various strategies to cross the blood-brain barrier. ZIKV NS1 may compromise the barrier integrity of endothelial cells by regulating expression of junctional proteins. MicroRNAs play an important role in post-transcriptional gene regulations. We demonstrated that ZIKV-NS1 affected the adherence junction protein in human brain microvascular endothelial cells via hsa-miR-29b-3p/DNMT3b/MMP-9 pathway. The hCMEC/D3 cells were exposed to ZIKV-NS1 with different doses (500 ng/mL and 1000 ng/mL) for 24 h. The expression pattern of DNMT3b, MMP-9, and VE-cadherin were studied using immunoblotting and the distribution of DNMT3b and MMP-9 were studied using immunofluorescence. The quantification of hsa-miR-29b-3p was done through qRT-PCR. Direct regulation of DNMT3b by hsa-miR-29b-3p was demonstrated by overexpression of hsa-miR-29b-3p using hsa-miR-29b-3p mimic, and knockdown of hsa-miR-29b-3p by using hsa-miR-29b-3p inhibitors. The ZIKV-NS1 affected the barrier function of endothelial cells through the increased expression of hsa-miR29b-3p, which suppressed the

DNMT3b, thus enhanced expression of MMP-9, which finally suppressed the expression of VE-cadherin. These findings suggested that ZIKV-NS1 alters the expression of Adherens Junction protein in human brain microvascular endothelial cells through hsa-miR-29b-3p/DNMT3b/MMP-9 pathway, which compromised the barrier function of human brain microvascular endothelial cells.

### ASFV transcription reporter screening system identifies aylanthone as a broad antiviral compound.

**Zhang Y, Zhang Z, Zhang F, Zhang J, Jiao J, Hou M, Qian N, Zhao D, Zheng X, Tan X.**

20-03-2023

*Virology.* 2023 Mar 20

<https://pubmed.ncbi.nlm.nih.gov/36948461/>

### A sero-epidemiological investigation of West Nile virus among patients without any records of their symptoms from three different hospitals from Tunisia.

**Nasraoui N, Moussa MLB, Ayedi Y, Mastouri M, Trabelsi A, Raies A, Wölfel R, Moussa MB.**

20-03-2023

*Acta Trop.*

<https://pubmed.ncbi.nlm.nih.gov/36948235/>

West Nile virus is one of the most known arboviruses around the world, along with Dengue virus, Toscana virus, Chikungunya (CHIK). In Tunisia, many epidemics of WNV had occurred in the past. The last one dated from 2018. The aim of our work was to perform a sero-epidemiological investigation on WNV without any records of their symptoms from three different hospitals from Tunisia. Patients without any records of their symptoms of the infection of West Nile Virus (WNV) infection were included in the period from October 2017 to January 2020 from three different Virology departments in the country (the Military Hospital in Tunis, Fattouma Bourguiba Hospital in Monastir and Sahloul Hospital in Sousse). A venous blood sample was taken from all patients at the bend of the elbow using a sterile syringe under aseptic conditions. Serological investigation for WNV was conducted through ELISA and IFI assays. RT-PCR was used to confirm the infection. The study included 353 patients. Twenty-eighty percent (28.8%) of the population were tested positive for IgM antibodies, males were having less positive antibodies than women (24.6% vs. 36.3%,  $p < 0.05$ ). In the city of Sousse, positive IgM were found more than in the other cities. As for IgG, 19.2% of the patients were having positive antibodies. No significant association was found between genders ( $p > 0.05$ ). One quarter of the IgM antibodies were tested positive using IFI technique, with no difference between genders ( $p > 0.05$ ). Only 9.2% of the samples were positive by PCR. Our results highlight the importance of establishing sustainable entomological systems and effective clinical ones and of promoting appropriate biological control strategies to optimize the limitation of the circulation of

WNV as well as other arboviruses to inhibit their harmful effects on health.

### **Precursor to Dengue: Projecting Effects of Climate Change on Mosquito Density in Southeast Asia.**

**Osuolale O.**

Mar-2023

*Environ Health Perspect.*

<https://pubmed.ncbi.nlm.nih.gov/36947409/>

### **First official record of *Aedes (Stegomyia) albopictus* (Diptera: Culicidae) in the Acre State, Northern Brazil.**

**Rocha RDC, Cardoso ADS, Souza JL, Pereira EDS, Amorim MF, Souza MSM, Medeiros CL, Monteiro MFM, Meneguetti DUO, Paula MB, Brilhante AF, Lima-Camara TN.**

20-03-2023

*Rev Inst Med Trop Sao Paulo.*

<https://pubmed.ncbi.nlm.nih.gov/36946816/>

*Aedes (Stegomyia) albopictus* (Skuse, 1854) was reported in Brazil for the first time in 1986 and has shown marked expansion throughout the Brazilian territory. During a routine activity to control dengue fever conducted by the Division of Entomology of the Municipal Health Department in Rio Branco city, adults and immatures of Culicidae were collected in a peri-urban area. The identified Culicidae forms indicated that they belonged to the species *Ae. albopictus*. This is the first official record of the presence of *Ae. albopictus* in the Acre State, confirming its current presence in all Brazilian states.

### **Many-core algorithms for high-dimensional gradients on phylogenetic trees.**

**Gangavarapu K, Ji X, Baele G, Fourment M, Lemey P, Iv FAM, Suchard MA.**

08-03-2023

*ArXiv.*

<https://pubmed.ncbi.nlm.nih.gov/36945693/>

The rapid growth in genomic pathogen data spurs the need for efficient inference techniques, such as Hamiltonian Monte Carlo (HMC) in a Bayesian framework, to estimate parameters of these phylogenetic models where the dimensions of the parameters increase with the number of sequences  $N$ . HMC requires repeated calculation of the gradient of the data log-likelihood with respect to (wrt) all branch-length-specific (BLS) parameters that traditionally takes  $\mathcal{O}(N^2)$  operations using the standard pruning algorithm. A recent study proposes an approach to calculate this gradient in  $\mathcal{O}(N)$ , enabling researchers to take advantage of gradient-based samplers such as HMC. The CPU implementation of this approach makes the calculation of the gradient computationally tractable for nucleotide-based models but falls short in performance for larger state-space size models, such as codon models. Here, we describe novel massively parallel algorithms to calculate the gradient of the log-likelihood wrt all BLS parameters

that take advantage of graphics processing units (GPUs) and result in many fold higher speedups over previous CPU implementations. We benchmark these GPU algorithms on three computing systems using three evolutionary inference examples: carnivores, dengue and yeast, and observe a greater than 128-fold speedup over the CPU implementation for codon-based models and greater than 8-fold speedup for nucleotide-based models. As a practical demonstration, we also estimate the timing of the first introduction of West Nile virus into the continental United States under a codon model with a relaxed molecular clock from 104 full viral genomes, an inference task previously intractable. We provide an implementation of our GPU algorithms in BEAGLE v4.0.0, an open source library for statistical phylogenetics that enables parallel calculations on multi-core CPUs and GPUs.

### **Sociodemographic factors associated to knowledge and attitudes towards dengue prevention among the Peruvian population: findings from a national survey.**

**Fernandez-Guzman D, Caira-Chuquineyra B, Calderon-Ramirez PM, Cisneros-Alca S, Benito-Vargas RM.**

21-03-2023

*BMJ Open.*

<https://pubmed.ncbi.nlm.nih.gov/36944464/>

### **Prevalence and Risk Factors of Acute Kidney Injury in Hospitalized Children with Dengue Infection Using Kidney Disease Improving Global Outcomes Criteria.**

**Mekangkul E, Siripen N, Rianthavorn P.**

21-03-2023

*Indian J Pediatr.*

<https://pubmed.ncbi.nlm.nih.gov/36943633/>

### **Unravelling the epidemiological diversity of Zika virus by analyzing key protein variations.**

**Leiva S, Bugnon Valdano M, Gardiol D.**

21-03-2023

*Arch Virol.*

<https://pubmed.ncbi.nlm.nih.gov/36943525/>

The consequences of Zika virus (ZIKV) infections were limited to sporadic mild diseases until almost a decade ago, when epidemic outbreaks took place, with quick spread into the Americas. Simultaneously, novel severe neurological manifestations of ZIKV infections were identified, including congenital microcephaly. However, why the epidemic strains behave differently is not yet completely understood, and many questions remain about the actual significance of genetic variations in the epidemiology and biology of ZIKV. In this study, we analysed a large number of viral sequences to identify genes with different levels of variability and patterns of genomic variations that could be associated with ZIKV diversity. We compared numerous epidemic strains with pre-epidemic strains, using the BWA-mem algorithm, and we also examined specific variations among the epidemic

ZIKV strains derived from microcephaly cases. We identified several viral genes with dissimilar mutation rates among the ZIKV strain groups and novel protein variation profiles that might be associated with epidemiological particularities. Finally, we assessed the impact of the detected changes on the structure and stability of the NS1, NS5, and E proteins using the I-TASSER, trRosetta, and RaptorX modelling algorithms, and we found some interesting variations that might help to explain the heterogeneous features of the diverse ZIKA strains. This work contributes to the identification of genetic differences in the ZIKV genome that might have a phenotypic impact, providing a basis for future experimental analysis to elucidate the genetic causes of the recent ZIKV emergency.

### Loop Dynamics and Conformational Flexibility in Dengue Serine Protease Activity: Noninvasive Perturbation by Solvent Exchange.

Misra R, Maity A, Kundu S, Bhunia M, Nanda B, Maiti NC, Pal U.

21-03-2023

*J Chem Inf Model.*

<https://pubmed.ncbi.nlm.nih.gov/36943246/>

### Broad Host Tropism of Flaviviruses during the Entry Stage.

Zhang Y, Yan Y, Li S, Yuan F, Wen D, Jia N, Xiong T, Zhang X, Zheng A.

21-03-2023

*Microbiol Spectr.*

<https://pubmed.ncbi.nlm.nih.gov/36943072/>

### Insecticide resistance compromises the control of *Aedes aegypti* in Bangladesh.

Al-Amin HM, Gyawali N, Graham M, Alam MS, Lenhart A, Hugo LE, Rašić G, Beebe NW, Devine GJ.

21-03-2023

*Pest Manag Sci.*

<https://pubmed.ncbi.nlm.nih.gov/36942761/>

**Background:** With no effective drugs or widely available vaccines, dengue control in Bangladesh is dependent on targeting the primary vector *Aedes aegypti* with insecticides and larval source management. Despite these interventions, the dengue burden is increasing in Bangladesh, and the country experienced its worst outbreak in 2019 with 101,354 hospitalized cases. This may be partially facilitated by the presence of intense insecticide resistance in vector populations. Here, we describe the intensity and mechanisms of resistance to insecticides commonly deployed against *Ae. aegypti* in Dhaka, Bangladesh. **Results:** Dhaka *Ae. aegypti* colonies exhibited high-intensity resistance to pyrethroids. Using CDC bottle assays, we recorded 2 - 24% mortality (recorded at 24 hours) to permethrin and 48 - 94% mortality to deltamethrin, at 10x the diagnostic dose. Bioassays conducted using insecticide-synergist combinations suggested that metabolic mechanisms were contributing to pyrethroid resistance, specifically multi-function oxidases, esterases, and glutathione S-

transferases. In addition, *kdr* alleles were detected, with a high frequency (78-98%) of homozygotes for the V1016G mutation. A large proportion ( $\leq 74\%$ ) of free-flying and resting mosquitoes from Dhaka colonies survived exposure to standard applications of pyrethroid aerosols in an experimental free-flight room. Although that exposure affected *Ae. aegypti*'s immediate host-seeking behavior, the effect was transient in surviving mosquitoes.

**Conclusion:** The intense resistance characterized in this study is likely compromising the operational effectiveness of pyrethroids against *Ae. aegypti* in Dhaka. Switching to alternative chemical classes may offer a medium-term solution, but ultimately a more sustainable and effective approach to controlling dengue vectors is required. This article is protected by copyright.

### Correction: Anti-viral activity of culinary and medicinal mushroom extracts against dengue virus serotype 2: an in-vitro study.

Ellan K, Thayan R, Raman J, Hidari KIPJ, Ismail N, Sabaratnam V.

20-03-2023

*BMC Complement Med Ther.*

<https://pubmed.ncbi.nlm.nih.gov/36941686/>

### The Development and Evaluation of a Combined Infection-Rheumatology Assessment Service in Response to the Chikungunya Fever Epidemic.

Krutikov M, Donovan J, Lambourne J, Ciurtin C, Brown M, Bailey R, Manson JJ.

20-03-2023

*Am J Trop Med Hyg.*

<https://pubmed.ncbi.nlm.nih.gov/36940667/>

The chikungunya virus is an arthritogenic alphavirus. Acute infection may be followed by persistent arthralgia, often causing significant functional impairment. The 2014-2015 chikungunya fever (CHIKF) epidemic resulted in a marked increase in cases presenting to rheumatology and tropical diseases services. A combined multidisciplinary rheumatology-tropical diseases service for assessment, management, and follow-up of patients with proven CHIKF and persistent ( $\geq 4$  weeks) arthralgia was proposed and rapidly developed at The Hospital for Tropical Diseases in London. Rapid set up of a multidisciplinary clinic in response to the epidemic was achieved. Of a total of 54 patients, 21 (38.9%) patients with CHIKF developed persistent arthralgia and were reviewed by the multidisciplinary service. A combined assessment approach enabled comprehensive multidisciplinary assessment of CHIKF, assessment of joint pathology through ultrasound, and appropriate follow-up. A combined rheumatology-tropical diseases service was successfully used to identify and assess CHIKF-associated morbidity. Future outbreaks may be approached by establishing tailored multidisciplinary clinics.

### The protein disulfide isomerase inhibitor 3-methyltoxoflavin inhibits Chikungunya virus.



**Puhl AC, Fernandes RS, Godoy AS, Gil LHV, Oliva G, Ekins S.**

15-03-2023

*Bioorg Med Chem.*

<https://pubmed.ncbi.nlm.nih.gov/36940609/>

Chikungunya virus (CHIKV) is the etiological agent of chikungunya fever, a (re)emerging arbovirus infection, that causes severe and often persistent arthritis, as well as representing a serious health concern worldwide for which no antivirals are currently available. Despite efforts over the last decade to identify and optimize new inhibitors or to reposition existing drugs, no compound has progressed to clinical trials for CHIKV and current prophylaxis is based on vector control, which has shown limited success in containing the virus. Our efforts to rectify this situation were initiated by screening 36 compounds using a replicon system and ultimately identified the natural product derivative 3-methyltoxoflavin with activity against CHIKV using a cell-based assay ( $EC_{50}$  200 nM, SI = 17 in Huh-7 cells). We have additionally screened 3-methyltoxoflavin against a panel of 17 viruses and showed that it only additionally demonstrated inhibition of the yellow fever virus ( $EC_{50}$  370 nM, SI = 3.2 in Huh-7 cells). We have also showed that 3-methyltoxoflavin has excellent in vitro human and mouse microsomal metabolic stability, good solubility and high Caco-2 permeability and it is not likely to be a P-glycoprotein substrate. In summary, we demonstrate that 3-methyltoxoflavin has activity against CHIKV, good in vitro absorption, distribution, metabolism and excretion (ADME) properties as well as good calculated physicochemical properties and may represent a valuable starting point for future optimization to develop inhibitors for this and other related viruses.

### **Acute telogen effluvium due to Dengue fever mimicking androgenetic alopecia.**

**Starace M, Piraccini BM, Evangelista V, Bruni F, Alessandrini A.**

Feb-2023

*Ital J Dermatol Venerol.*

<https://pubmed.ncbi.nlm.nih.gov/36939507/>

### **Co-infection of dengue, scrub typhus, and typhoid during dengue outbreak in Nepal, 2022: A case report.**

**Bhattarai BR, Bhujel R, Pokhrel S, Mishra A, Priyadarshinee A.**

14-03-2023

*Clin Case Rep.*

<https://pubmed.ncbi.nlm.nih.gov/36937629/>

In midst of the recent dengue outbreak in Nepal, in 2022, the risk of co-infection increases and may lead to fatal outcomes if the diagnosis of multiple infections is delayed. Thus, all available diagnostic approaches must be taken to decrease the burden of illness and lessen mortality.

### **Synthesis and virucide activity on zika virus of 1,2,3-triazole-containing vanillin derivatives.**

**da Silva Rodrigues JV, Rodrigues Gazolla PA, da Cruz Pereira I, Dias RS, Poly da Silva IE, Oliveira Prates JW, de Souza Gomes I, de Azevedo Silveira S, Costa AV, de Oliveira FM, de Aguiar AR, Canedo da Silva C, Teixeira RR, de Paula SO.**

17-03-2023

*Antiviral Res.*

<https://pubmed.ncbi.nlm.nih.gov/36934985/>

### **Bio-efficacy of insecticidal molecule emodin against dengue, filariasis, and malaria vectors.**

**Chinnasamy R, Govindasamy B, Venkatesh M, Magudeeswaran S, Dhanarajan A, Devarajan N, Willie P, Perumal V, Mekchay S, Krutmuang P.**

18-03-2023

*Environ Sci Pollut Res Int.*

<https://pubmed.ncbi.nlm.nih.gov/36934179/>

Emodin, a compound isolated from *Aspergillus terreus*, was studied using chromatographic and spectroscopic methods and compound purity (96%) was assessed by TLC. Furthermore, high larvicidal activity against *Aedes aegypti*-AeA ( $LC_{50}$  6.156 and  $LC_{90}$  12.450 mg/L), *Culex quinquefasciatus*-CuQ (8.216 and 14.816 mg/L), and *Anopheles stephensi*-AnS larvae (6.895 and 15.24 mg/L) was recorded. The first isolated fraction (emodin) showed higher pupicidal activity against AeA (15.449 and 20.752 mg/L). Most emodin-treated larvae (ETL) showed variations in acetylcholine esterase,  $\alpha$  and  $\beta$ -carboxylesterases, and phosphatase activities in the 4<sup>th</sup> instar, indicating the intrinsic differences in their biochemical changes. ETL had numerous altered tissues, including muscle, gastric caeca, hindgut, midgut, nerve ganglia, and midgut epithelium. Acute toxicity of emodin on brine shrimp *Artemia nauplii* (54.0 and 84.5 mg/L) and the zebrafish *Danio rerio* (less toxicity observed) was recorded. In docking studies, Emodin interacted well with odorant-binding-proteins of AeA, AnS, and CuQ with docking scores of - 8.89, - 6.53, and - 8.09 kcal mol<sup>-1</sup>, respectively. Therefore, *A. terreus* is likely to be effective against mosquito larvicides.

### **Epidemic models and their use: Comment on "Mathematical models for dengue fever epidemiology: A 10-year systematic review" by Aguiar et al.**

**Codeço CT, Coelho FC.**

01-02-2023

*Phys Life Rev.*

<https://pubmed.ncbi.nlm.nih.gov/36933441/>

### **Negative regulation of type I interferon signaling by integrin-linked kinase permits dengue virus replication.**

**Kao YS, Wang LC, Chang PC, Lin HM, Lin YS, Yu CY, Chen CC, Lin CF, Yeh TM, Wan SW, Wang JR, Ho TS, Chu CC, Zhang BC, Chang CP.**

17-03-2023

*PLoS Pathog.*

<https://pubmed.ncbi.nlm.nih.gov/36930690/>

## Standardized evaluation of Zika nucleic acid tests used in clinical settings and blood screening.

Stone M, Bakkour S, Grebe E, Emperador DM, Escadafal C, Deng X, Dave H, Kelly-Cirino C, Lackritz E, Rojas DP, Simmons G, Rabe IB, Busch MP.

17-03-2023

*PLoS Negl Trop Dis.*

<https://pubmed.ncbi.nlm.nih.gov/36930653/>

## Repellent Screening of Selected Plant Essential Oils Against Dengue Fever Mosquitoes Using Behavior Bioassays.

Deng W, Li M, Liu S, Logan JG, Mo J.

16-03-2023

*Neotrop Entomol.*

<https://pubmed.ncbi.nlm.nih.gov/36928838/>

Among the efforts to reduce mosquito-transmitted diseases, such as malaria and dengue fever, essential oils (EOs) have become increasingly popular as natural replacements for the repellent DEET. In this study, seven commercially available plant EOs against *Aedes* species mosquitoes were evaluated for their complete protection time (CPT, min) in vivo using human-hand in cage tests (GB2009/China and WHO2009). Among the EOs with the highest efficacy in repelling mosquitoes, *Aedes albopictus* (Skuse) were clove bud oil and patchouli oil. Both were further assessed according to the in vivo method recommended by the WHO, to determine their minimum effective dose and CPT. A comparison of the ED<sub>50</sub> values (dose yielding a 50% repellent response) of these two EOs against *Aedes aegypti*(L.) showed that the ED<sub>50</sub> (2.496 µg/cm<sup>2</sup>) of patchouli oil was 1248 times higher than that of clove bud oil (0.002 µg/cm<sup>2</sup>), thus demonstrating their greater efficacy of the latter in repelling *Ae. aegypti* mosquitoes. For the 2 EOs, eugenol was the major component with higher than 80% in relative amount of the clove bud oil. The patchouli oil had more than 30% of characteristic chemical patchouli alcohol along with α-bulnesene (10.962%), α-guaiene (9.227%), and seychellene (7.566%). Clove bud oil was found to confer longer complete protection than patchouli oil against a common species of mosquito. These results suggest use of EOs as safe, highly potent repellents for use in daily life and against mosquito-transmitted diseases, such as malaria and dengue fever.

## Evolution of research funding for neglected tropical diseases in Brazil, 2004-2020.

Melo GBT, Angulo-Tuesta A, Silva END, Santos TDS, Uchimura LYT, Obara MT.

16-03-2023

*PLoS Negl Trop Dis.*

<https://pubmed.ncbi.nlm.nih.gov/36928796/>

Neglected tropical diseases are a global public health problem. Although Brazil is largely responsible for their occurrence in Latin America, research funding on the subject does not meet the population's health needs. The present study analyzed the evolution of research funding

for neglected tropical diseases by the Ministry of Health and its partners in Brazil, from 2004 to 2020. This is a retrospective study of data from investigations registered on Health Research (Pesquisa Saúde in Portuguese), a public repository for research funded by the Ministry of Health's Department of Science and Technology. The temporal trend of funding and the influence of federal government changes on funding were analyzed using Prais-Winsten generalized linear regression. From 2004 to 2020, 1,158 studies were financed (purchasing power parity (PPP\$) 230.9 million), with most funding aimed at biomedical research (81.6%) and topics involving dengue, leishmaniasis and tuberculosis (60.2%). Funding was stationary (annual percent change of -5.7%; 95%CI -54.0 to 45.0) and influenced by changes to the federal government. Research funding was lacking for chikungunya, Chagas disease, schistosomiasis, malaria and taeniasis/cysticercosis, diseases with a high prevalence, burden or mortality rates in Brazil. Although the Ministry of Health had several budgetary partners, it was the main funder, with 69.8% of investments. The study revealed that research funding for neglected tropical diseases has stagnated over the years and that diseases with a high prevalence, burden and mortality rate receive little funding. These findings demonstrate the need to strengthen the health research system by providing sustainable funding for research on neglected tropical diseases that is consistent with the population's health needs.

## Sociodemographic and environmental factors associated with dengue, Zika, and chikungunya among adolescents from two Brazilian capitals.

Dalvi APR, Gibson G, Ramos AN Jr, Bloch KV, Sousa GDS, Silva TLND, Braga JU, Castro MC, Werneck GL.

16-03-2023

*PLoS Negl Trop Dis.*

<https://pubmed.ncbi.nlm.nih.gov/36928657/>

## Notes From the Field: First Evidence of Locally Acquired Dengue Virus Infection - Maricopa County, Arizona, November 2022.

Kretschmer M, Collins J, Dale AP, Garrett B, Koski L, Zabel K, Staab RN, Turnbow K, Nativio J, Andrews K, Smith WE, Townsend J, Busser N, Will J, Burr K, Jones FK, Santiago GA, Fitzpatrick KA, Ruberto I, Fitzpatrick K, White JR, Adams L, Sunenshine RH.

17-03-2023

*MMWR Morb Mortal Wkly Rep.*

<https://pubmed.ncbi.nlm.nih.gov/36928186/>

## The rising cases of dengue amidst the prolonged monsoon in Pakistan: Challenges, efforts and recommendations.

Khan HA, Malik UU, Yousuf J, Shahzad A, Ur Rehman M, Tharwani ZH.

17-03-2023

*Int J Surg.*

<https://pubmed.ncbi.nlm.nih.gov/36928010/>

### Notes From the Field: Prevalence of Previous Dengue Virus Infection Among Children and Adolescents - U.S. Virgin Islands, 2022.

Mac VV, Wong JM, Volkman HR, Perez-Padilla J, Wakeman B, Delorey M, Biggerstaff BJ, Fagre A, Gumbs A, Drummond A, Zimmerman B, Lettsome B, Medina FA, Paz-Bailey G, Lawrence M, Ellis B, Rosenblum HG, Carroll J, Roth J, Rossington J, Meeker JR, Joseph J, Janssen J, Ekpo LL, Carrillo M, Hernandez N, Charles P, Tosado R, Soto R, Battle S, Bart SM, Wanga V, Valentin W, Powell W, Battiste Z, Ellis EM, Adams LE.

17-03-2023

*MMWR Morb Mortal Wkly Rep.*

<https://pubmed.ncbi.nlm.nih.gov/36927833/>

### Health seeking behaviours, dengue prevention behaviours and community capacity for sustainable dengue prevention in a highly dengue endemic area, Sri Lanka.

Rajapaksha RMNU, Abeysena C, Balasuriya A.

16-03-2023

*BMC Public Health.*

<https://pubmed.ncbi.nlm.nih.gov/36927487/>

**Introduction:** Dengue has become a major health problem in globally as well as locally. The delay in health-seeking is significantly associated with complications leading to severe dengue and active engagement of communities needs to minimize the delays in management to control epidemics. The aim of the study was to evaluate the relationship between sociodemographic characteristics and householders' Health-Seeking Behaviours (HSB), Dengue-Prevention Behaviours (DPB), and Community Capacities (CC) for sustained dengue prevention in Sri Lanka, a country with a high dengue endemicity. **Methods:** A cross-sectional analytical study was carried out in a district with the highest dengue endemicity from January to April 2019. Of the householders, 532 were chosen randomly. A pre-tested, validated, and interviewer-administered questionnaire was used to assess HSB and DPB. The HSB was assessed using three aspects, initial response for fever management, the duration of blood testing and initial response if suspected dengue. The DPB assessment was evaluated using 'waste, outdoor water container, indoor water container, roof gutter and water storage management'. 'Dengue Community Capacity Assessment Tool', with 14 key items was used to assess the level of community capacity for dengue prevention. Out of the total,  $\geq 50\%$  was considered as an "adequate" HSB, DPB and CC. Multiple logistic regression was performed to control confounding effects. The results were expressed as adjusted Odds-Ratios (aOR) and 95% Confidence Intervals (CI). **Results:** The response rate was 93.2% ( $n = 496$ ). Among them, 44.6% ( $n = 221$ ) had adequate overall HSB, and 19.2% ( $n = 95$ ) had adequate DPB. Householders who have  $\leq 4$  family members are 1.74 times (aOR = 1.74; 95% CI: 1.17 - 2.61) more likely to have adequate HSB and 1.85 times (aOR = 1.85; 95% CI: 1.11 - 3.09) more likely to have

adequate DPB. The age group of 46 to 70 years' individuals (aOR = 1.74; 95% CI: 1.12 - 2.92), and who engaged in employment (aOR = 1.68; 95% CI: 1.05 - 2.67) were more likely to have adequate DPB than the group of 18 to 45 years and the non-employed individuals respectively. Of them, 24.6% ( $n = 122$ ) perceived that they have adequate CC. The householders who have per-capita income < USD 50 are 1.95 times (aOR = 1.95; 95%CI: 1.11 - 3.40) more likely to have adequate CC. **Conclusion:** The HSB, DPB and CC need to be improved to change the behaviour for sustainable dengue prevention and community capacity-building programmes need to be conducted in the Kurunegala district, Sri Lanka.

### Maternal & perinatal outcome of fever in pregnancy in the context of dengue - A retrospective observational study.

Sagili H, Krishna RS, Dhodapkar R, Keepanasseri A.

Oct-Nov2022

*Indian J Med Res.*

<https://pubmed.ncbi.nlm.nih.gov/36926778/>

### A retrospective analysis of serological & molecular testing data on dengue fever in Kolkata & adjacent districts during 2016-2019.

Majumdar A, Gupta R, Chatterjee A, Banu H, Biswas M, Gupta R, Mukherjee S, Sadhukhan P, Dutta S.

Oct-Nov2022

*Indian J Med Res.*

<https://pubmed.ncbi.nlm.nih.gov/36926776/>

**Background & objectives:** Regional Virus Research and Diagnostic Laboratory established at ICMR-National Institute of Cholera and Enteric Diseases (NICED) regularly receives samples for dengue screening and serotyping from patients of acute febrile illness (AFI) from Kolkata and adjacent districts. In this study, data over a three year period (August 2016-July 2019) was retrospectively analyzed to provide insight into the epidemiological trends of dengue fever in this region. **Methods:** Serological screening of dengue was performed by detection of NS1 antigen and/or immunoglobulin M (IgM) antibody. Dengue serotyping was done by conventional or real-time reverse transcriptase-PCR. The data were analyzed to describe the distribution of dengue with respect to age of patient, duration of fever on the day of blood collection and month of the year. Zip codes were used for spatial plotting. **Results:** Out of the 24,474 samples received from Kolkata and its adjacent districts (Hooghly, Howrah, North and South 24 Parganas), 38.3 per cent (95% confidence interval: 37.7-38.9%) samples were screened positive for dengue. The correlation between age and dengue positivity was found to be weak. A combination of dengue NS1 antigen and dengue IgM antibody detection may be a better option for detecting dengue positivity compared to a single test. Most AFI cases were tested from August to November during the study period, with maximum dengue positivity noted during September (45.9%). The predominant serotype of 2016, dengue virus serotype 1 (DENV-1), was almost entirely replaced by DENV-2 in 2017 and 2018. **Interpretation & conclusions:** Dengue continues



to be an important cause of AFI in the region and round-the-year preventive measures are required for its control. Serotype switching is alarming and should be monitored routinely.

### **Successful treatment of acute liver failure secondary to dengue fever using low-volume plasma exchange.**

Jeyabalan SV, Tay TR, Tan SY, Kumar R.

13-03-2023

*Singapore Med J.*

<https://pubmed.ncbi.nlm.nih.gov/36926748/>

### **Phytofabrication and characterization of Alchornea cordifolia silver nanoparticles and evaluation of antiplasmodial, hemocompatibility and larvicidal potential.**

Kojom Foko LP, Hawadak J, Verma V, Belle Ebanga Kedi P, Eboumbou Moukoko CE, Kamaraju R, Pande V, Singh V.

28-02-2023

*Front Bioeng Biotechnol.*

<https://pubmed.ncbi.nlm.nih.gov/36926684/>

### **A phylogenetic study of dengue virus in urban Vietnam shows long-term persistence of endemic strains.**

Ashall J, Shah S, Biggs JR, Chang JR, Jafari Y, Brady OJ, Mai HK, Lien LT, Do Thai H, Nguyen HAT, Anh DD, Iwasaki C, Kitamura N, Van Look M, Herrera-Taracena G, Rasschaert F, Van Wesenbeeck L, Yoshida LM, Hafalla JCR, Hue S, Hibberd ML.

16-02-2023

*Virus Evol.*

<https://pubmed.ncbi.nlm.nih.gov/36926448/>

Dengue virus (DENV) causes repeated outbreaks of disease in endemic areas, with patterns of local transmission strongly influenced by seasonality, importation via human movement, immunity, and vector control efforts. An understanding of how each of these interacts to enable endemic transmission (continual circulation of local virus strains) is largely unknown. There are times of the year when no cases are reported, often for extended periods of time, perhaps wrongly implying the successful eradication of a local strain from that area. Individuals who presented at a clinic or hospital in four communes in Nha Trang, Vietnam, were initially tested for DENV antigen presence. Enrolled positive individuals then had their corresponding household members invited to participate, and those who enrolled were tested for DENV. The presence of viral nucleic acid in all samples was confirmed using quantitative polymerase chain reaction, and positive samples were then whole-genome sequenced using an amplicon and target enrichment library preparation techniques and Illumina MiSeq sequencing technology. Generated consensus genome sequences were then analysed using phylogenetic tree reconstruction to categorise sequences into clades with a common ancestor, enabling investigations of both viral clade persistence and introductions. Hypothetical

introduction dates were additionally assessed using a molecular clock model that calculated the time to the most recent common ancestor (TMRCA). We obtained 511 DENV whole-genome sequences covering four serotypes and more than ten distinct viral clades. For five of these clades, we had sufficient data to show that the same viral lineage persisted for at least several months. We noted that some clades persisted longer than others during the sampling time, and by comparison with other published sequences from elsewhere in Vietnam and around the world, we saw that at least two different viral lineages were introduced into the population during the study period (April 2017-2019). Next, by inferring the TMRCA from the construction of molecular clock phylogenies, we predicted that two of the viral lineages had been present in the study population for over a decade. We observed five viral lineages co-circulating in Nha Trang from three DENV serotypes, with two likely to have remained as uninterrupted transmission chains for a decade. This suggests clade cryptic persistence in the area, even during periods of low reported incidence.

### **Cellular T-cell immune response profiling by tetravalent dengue subunit vaccine (DSV4) candidate in mice.**

Aggarwal C, Ramasamy V, Garg A, Shukla R, Khanna N.

28-02-2023

*Front Immunol.*

<https://pubmed.ncbi.nlm.nih.gov/36926350/>

### **Dengue-chikungunya infection in the tertiary care hospital of northern India: Cross-sectional latent class cluster analysis in viral infection.**

Badoni G, Gupta PK, Gupta P, Kaistha N, Mathuria YP, Pai MO, Kant R.

23-02-2023

*Heliyon.*

<https://pubmed.ncbi.nlm.nih.gov/36925523/>

### **The sex pheromone heptacosane enhances the mating competitiveness of sterile Aedes aegypti males.**

Wang LM, Li N, Zhang M, Tang Q, Lu HZ, Zhou QY, Niu JX, Xiao L, Peng ZY, Zhang C, Liu M, Wang DQ, Deng SQ.

15-03-2023

*Parasit Vectors.*

<https://pubmed.ncbi.nlm.nih.gov/36922826/>

**Background:** Aedes aegypti is a vector that transmits various viral diseases, including dengue and Zika. The radiation-based sterile insect technique (SIT) has a limited effect on mosquito control because of the difficulty in irradiating males without reducing their mating competitiveness. In this study, the insect sex pheromone heptacosane was applied to Ae. aegypti males to investigate whether it could enhance the mating competitiveness of irradiated males. **Methods:** Heptacosane was smeared on the abdomens of Ae. aegypti males that were allowed to mate with untreated virgin females. The insemination rate was used to assess the attractiveness of heptacosane-treated males to

females. The pupae were irradiated with different doses of X-rays and γ-rays, and the emergence, survival time, egg number, and hatch rate were detected to find the optimal dose of X-ray and γ-ray radiation. The males irradiated at the optimal dose were smeared with heptacosane, released in different ratios with untreated males, and mated with females. The effect of heptacosane on the mating competitiveness of irradiated mosquitoes was then evaluated by the hatch rate, induced sterility, and mating competitiveness index. **Results:** Applying heptacosane to *Ae. aegypti* males significantly increased the insemination rate of females by 20%. Pupal radiation did not affect egg number but significantly reduced survival time and hatch rate. The emergence of the pupae was not affected by X-ray radiation but was affected by γ-ray radiation. Pupae exposed to 60 Gy X-rays and 40 Gy γ-rays were selected for subsequent experiments. After 60 Gy X-ray irradiation or 40 Gy γ-ray irradiation, the average hatch rate was less than 0.1%, and the average survival time was more than 15 days. Moreover, at the same release ratio, the hatch rate of the irradiated group perfumed with heptacosane was lower than that of the group without heptacosane. Conversely, the male sterility and male mating competitiveness index were significantly increased due to the use of heptacosane. **Conclusions:** The sex pheromone heptacosane enhanced the interaction between *Ae. aegypti* males and females. Perfuming males irradiated by X-rays or γ-rays with heptacosane led to a significant increase in mating competitiveness. This study provided a new idea for improving the application effect of SIT.

### **B-cell epitope discovery: The first protein flexibility-based algorithm-Zika virus conserved epitope demonstration.**

**Biner DW, Grosch JS, Ortoleva PJ.**  
15-03-2023

*PLoS One.*

<https://pubmed.ncbi.nlm.nih.gov/36920995/>

### **Pseudotyped Virus for Flaviviridae.**

**Zhang L, Wang X, Ming A, Tan W.**  
2023

*Adv Exp Med Biol.*

<https://pubmed.ncbi.nlm.nih.gov/36920705/>

### **Pseudotyped Viruses for the Alphavirus Chikungunya Virus.**

**Wu J, Huang W, Wang Y.**  
2023

*Adv Exp Med Biol.*

<https://pubmed.ncbi.nlm.nih.gov/36920704/>

Members of the genus Alphavirus are mostly mosquito-borne pathogens that cause disease in their vertebrate hosts. Chikungunya virus (CHIKV), which is one member of the genus Alphavirus [1], has been a major health problem in endemic areas since its re-emergence in 2006. CHIKV is transmitted to mammalian hosts by the *Aedes* mosquito, causing persistent debilitating symptoms in many cases. At present, there is no specific treatment or vaccine. Experiments involving live CHIKV need to be performed in

BSL-3 facilities, which limits vaccine and drug research. The emergence of pseudotyped virus technology offered the potential for the development of a safe and effective evaluation method. In this chapter, we review the construction and application of pseudotyped CHIKVs, the findings from which have enhanced our understanding of CHIKV. This will, in turn, enable the exploration of promising therapeutic strategies in animal models, with the ultimate aim of developing effective treatments and vaccines against CHIKV and other related viruses.

### **A systematic review of published literature on mosquito control action thresholds across the world.**

**Aryaprema VS, Steck MR, Peper ST, Xue RD, Qualls WA.**  
03-03-2023

*PLoS Negl Trop Dis.*

<https://pubmed.ncbi.nlm.nih.gov/36867651/>

### **Maternal and perinatal outcome in dengue and COVID-19 co-infected pregnancies.**

**Thakur P, Thakur V, Srivastava S.**  
Apr-2023

*Eur J Obstet Gynecol Reprod Biol.*

<https://pubmed.ncbi.nlm.nih.gov/36858873/>

### **Aedes albopictus invasion across Africa: the time is now for cross-country collaboration and control.**

**Longbottom J, Walekhwa AW, Mwingira V, Kijanga O, Mramba F, Lord JS.**

Apr-2023

*Lancet Glob Health.*

<https://pubmed.ncbi.nlm.nih.gov/36841255/>

The distribution of *Aedes albopictus* across west Africa is well documented. However, little has been done to synthesise data and establish the current distribution of this invasive vector in central and east Africa. In this Viewpoint, we show that *A. albopictus* is establishing across Africa, how this is potentially related to urbanisation, and how establishment poses risks of near-term increases in arbovirus transmission. We then use existing species distribution maps for *A. albopictus* and *Aedes aegypti* to produce consensus estimates of suitability and make these estimates accessible. Although urban development and increased trade have economic and other societal gains, the resulting potential changes in *Aedes*-borne virus epidemiology require a discussion of how cross-country collaboration and mitigation could be facilitated. Failure to respond to species invasion could result in increased transmission of *Aedes*-associated pathogens, including dengue, chikungunya, and Rift Valley fever viruses.

### **A quick prediction tool for Dengue fever: A timely response is essential!**

**Qureshi H, Khan MI, Bae SJ, Shah A.**  
Apr-2023

*J Infect Public Health.*

<https://pubmed.ncbi.nlm.nih.gov/36801635/>

### **Piperazine-derived small molecules as potential Flaviviridae NS3 protease inhibitors. In vitro antiviral activity evaluation against Zika and Dengue viruses.**

Del Rosario García-Lozano M, Dragoni F, Gallego P, Mazzotta S, López-Gómez A, Boccuto A, Martínez-Cortés C, Rodríguez-Martínez A, Pérez-Sánchez H, Manuel Vega-Pérez J, Antonio Del Campo J, Vicenti I, Vega-Holm M, Iglesias-Guerra F.

Apr-2023

*Bioorg Chem.*

<https://pubmed.ncbi.nlm.nih.gov/36801791/>

### **Why is Nicotiana tabacum leaf extract more effective than Piper betle leaf extract on mortality of Aedes aegypti larvae ?**

Destrianto PD, Wardani DPK, Hikmawati I, Mujahid I.

Apr-2023

*Exp Parasitol.*

<https://pubmed.ncbi.nlm.nih.gov/36754195/>

The control of the dengue vector is an important step in preventing dengue fever. The use of synthetic pesticides has been proven to cause environmental pollution, death of various living things and resistance. Therefore, research on innovative vegetable insecticides such as nicotiana tabacum leaf extract and piper betel leaf extract is urgently needed. This true experimental research to compare the effectiveness of nicotiana tabacum leaf extract and piper betel leaf extract on the *Aedes aegypti* larva using a post-test only design with a controlled-group design. The nicotiana tabacum leaf and piper betel leaf were extracted with 96% ethanol to be tested on the 600 third instar larvae. Then, the test was done with three concentrations of nicotiana tabacum leaf extract and piper betel leaf extract, including 0.1%, 0.2%, and 0.4%, with three repetitions in each concentration. The most effective concentration and time of nicotiana tabacum leaf extract and piper betel leaf extract on the larvae mortality were analyzed using the Freadman test as the alternative test since the data were not normally distributed. LC<sub>50</sub> and LC<sub>90</sub> of nicotiana tabacum leaf extract and piper betel leaf extract were tested using probit analysis. The results showed that the treatments of nicotiana tabacum leaf extract and piper betel leaf extract affected larvas mortality. The average mortality of larvae in nicotiana tabacum leaf extract was at concentrations of 0.1% (6 larvae), 0.2% (12 larvae), 0.4% (24 larvae) and occurred after 1 h exposure, whereas in piper betel leaf extract, only occurred after 4 h of exposure, with an average death ratio at a concentration of 0.1% in nicotiana tabacum leaf extract (29.33 larvae) and piper betel leaf extract (1.33 larvae). The results of the Probit analysis of nicotiana tabacum leaf extract and piper betel leaf extract at 8 h of exposure obtained LC<sub>50</sub> results of 1.2% nicotiana tabacum leaf extract and 9.036% piper betel leaf extract. The LC<sub>90</sub> yield of nicotiana tabacum leaf extract was 3.086% and piper betel leaf extract was 14.81%. The results of this

study indicated that there were differences in the mortality rates of the two extracts, and that nicotiana tabacum leaf extract had a higher mortality rate than piper betel leaf extract. LC<sub>50</sub> and LC<sub>90</sub> of piper betel leaf extract had lower values than nicotiana tabacum leaf extract. Piper betel leaf extract requires a higher extract concentration to kill 50% and 90% of test larvae compared to nicotiana tabacum leaf extract.

### **Informing COVID-19 Response and Health Equity Agenda: Collection of Public Health Reports Articles on Emerging Viral Epidemics in the United States, 1878-2021.**

Harada NM, Kuzmichev A, Dembek ZF, Ising AI, Dean HD.

Mar-Apr 2023

*Public Health Rep.*

<https://pubmed.ncbi.nlm.nih.gov/36752215/>

### **Antibody cross-reactivity and evidence of susceptibility to emerging Flaviviruses in the dengue-endemic Brazilian Amazon.**

Salgado BB, Maués FCJ, Jordão M, Pereira RL, Toledo-Teixeira DA, Parise PL, Granja F, Souza HFS, Yamamoto MM, Chiang JO, Martins LC, Boscardin SB, Lalwani JDB, Vasconcelos PFC, Proença-Modena JL, Lalwani P.

Apr-2023

*Int J Infect Dis.*

<https://pubmed.ncbi.nlm.nih.gov/36736575/>

### **Plasma transfusion-transmission of Zika virus in mice and macaques.**

Van Rompay KKA, Coffey LL, Yee JL, Singapuri A, Stuart J, Lanteri MC, Santa Maria F, Lu K, Singh I, Bakkour S, Stone M, Williamson PC, Muench MO, Busch MP, Simmons G.

Mar-2023

*Transfusion.*

<https://pubmed.ncbi.nlm.nih.gov/36621777/>

### **CRISPR Cas9 mediated knockout of sex determination pathway genes in Aedes aegypti.**

Zulhussnain M, Zahoor MK, Rania K, Ahmad A, Jabeen F.

Apr-2023

*Bull Entomol Res.*

<https://pubmed.ncbi.nlm.nih.gov/36259148/>

The vector role of *Aedes aegypti* for viral diseases including dengue and dengue hemorrhagic fever makes it imperative for its proper control. Despite various adopted control strategies, genetic control measures have been recently focused against this vector. CRISPR Cas9 system is a recent and most efficient gene editing tool to target the sex determination pathway genes in *Ae. aegypti*. In the present study, CRISPR Cas9 system was used to knockout *Ae. aegypti doublesex (Aaedsx)* and *Ae. aegypti sexlethal (AaeSxl)* genes in *Ae. aegypti* embryos. The injection mixes with Cas9 protein (333 ng  $\mu\text{l}^{-1}$ ) and gRNAs (each at 100 ng  $\mu\text{l}^{-1}$ ) were injected into eggs. Injected eggs were allowed to hatch at  $26 \pm 1^\circ\text{C}$ ,  $60 \pm 10\%$  RH. The survival and

mortality rate was recorded in knockout *Aaedsx* and *AaeSxl*. The results revealed that knockout produced low survival and high mortality. A significant percentage of eggs (38.33%) did not hatch as compared to control groups (*P* value 0.00). Highest larval mortality (11.66%) was found in the knockout of *Aaedsx* female isoform, whereas, the emergence of only male adults also showed that the knockout of *Aaedsx* (female isoform) does not produce male lethality. The survival (3.33%) of knockout for *AaeSxl* eggs to the normal adults suggested further study to investigate *AaeSxl* as an efficient upstream of *Aaedsx* to target for sex transformation in *Ae. aegypti* mosquitoes.

### **The association of obesity and dengue severity in hospitalized adult patients.**

Chiu YY, Lin CY, Yu LS, Wang WH, Huang CH, Chen YH.

Apr-2023

*J Microbiol Immunol Infect.*

<https://pubmed.ncbi.nlm.nih.gov/36055945/>

### **Oral alterations in children with microcephaly associated to congenital Zika syndrome: A systematic review and meta-analyses.**

Silva LVO, Hermont AP, Magnani IQ, Martins CC, Borges-Oliveira AC.

Mar-2023

*Spec Care Dentist.*

<https://pubmed.ncbi.nlm.nih.gov/35912588/>

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## **Rage**

### **Implementing a One Health Approach to Rabies Surveillance: Lessons From Integrated Bite Case Management.**

Swedberg C, Mazeri S, Mellanby RJ, Hampson K, Chng NR.

20-06-2022

*Front Trop Dis.*

<https://pubmed.ncbi.nlm.nih.gov/36945698/>

As part of the 'Zero by 30' strategy to end human deaths from dog-mediated rabies by 2030, international organizations recommend a One Health framework that includes Integrated Bite Case Management (IBCM). However, little is understood about the implementation of IBCM in practice. This study aims to understand how IBCM is conceptualized, exploring how IBCM has been operationalized in different contexts, as well as barriers and facilitators to implementation. Semi-structured interviews were conducted with seventeen practitioners and researchers with international, national, and local expertise across Africa, Asia, and the Americas. Thematic analysis was undertaken using both inductive and deductive approaches. Four main themes were identified: 1) stakeholders' and practitioners' conceptualization of IBCM and its role in rabies elimination; 2) variation in how IBCM operates across different contexts; 3) barriers and facilitators of IBCM implementation in relation to risk

assessment, PEP provisioning, animal investigation, One Health collaboration, and data reporting; and 4) the impact of the COVID-19 pandemic on IBCM programs. This study highlights the diversity within experts' conceptualization of IBCM, and its operationalization. The range of perspectives revealed that there are different ways of organizing IBCM within health systems and it is not a one-size-fits-all approach. The issue of sustainability remains the greatest challenge to implementation. Contextual features of each location influenced the delivery and the potential impact of IBCM. Programs spanned from highly endemic settings with limited access to PEP charged to the patient, to low endemicity settings with a large patient load associated with free PEP policies and sensitization. In practice, IBCM was tailored to meet the demands of the local context and level of rabies control. Thus, experts' experiences did not necessarily translate across contexts, affecting perceptions about the function, motivation for, and implementation of IBCM. To design and implement future and current programs, guidance should be provided for health workers receiving patients on assessing the history and signs of rabies in the biting animal. The study findings provide insights in relation to implementation of IBCM and how it can support programs aiming to reach the Zero by 30 goal.

### **Raccoon rabies control and elimination in the northeastern U.S. and southern Québec, Canada.**

Davis AJ, Gagnier M, Massé A, Nelson KM, Kirby JD, Wallace R, Ma X, Fehlner-Gardiner C, Chipman RB, Gilbert AT.

22-03-2023

*Epidemiol Infect.*

<https://pubmed.ncbi.nlm.nih.gov/36944589/>

### **BNST PKC $\delta$ neurons are activated by specific aversive conditions to promote anxiety-like behavior.**

Williford KM, Taylor A, Melchior JR, Yoon HJ, Sale E, Negasi MD, Adank DN, Brown JA, Bedenbaugh MN, Luchsinger JR, Centanni SW, Patel S, Calipari ES, Simerly RB, Winder DG.

20-03-2023

*Neuropsychopharmacology.*

<https://pubmed.ncbi.nlm.nih.gov/36941364/>

### **Evaluation of a real-time mobile PCR device (PCR 1100) for the detection of the rabies gene in field samples.**

Demetria C, Kimitsuki K, Yahiro T, Saito N, Hashimoto T, Khan S, Chu MYJ, Manalo D, Mananggit M, Quiambao B, Nishizono A.

17-03-2023

*Trop Med Health.*

<https://pubmed.ncbi.nlm.nih.gov/36932428/>

**Background:** The Philippines is ranked among the top countries with 200-300 annual deaths due to rabies. Most human rabies cases have been reported in remote areas, where dog surveillance is inadequate. Therefore, a strategy to effectively improve surveillance in remote



areas will increase the number of detections. Detecting pathogens using portable real-time reverse transcription-polymerase chain reaction (RT-PCR) has the potential to be accepted in these areas. Thus, we aimed to develop an assay to detect the rabies virus (RABV) genome by combining the robust primer system LN34 with the PicoGene PCR1100 portable rapid instrument targeting RABV RNA (PCR1100 assay). **Methods:** Procedures were optimised using an LN34 primer/probe set, KAPA3G Plant PCR Kit (KAPA Biosystems), FastGene Scriptase II (NIPPON Genetics), and an artificial positive control RNA. **Results:** Positive control RNA showed an analytical limit of detection of 10 copies/μL without false positivity, generating results in approximately 32 min. Compared to dFAT or RT-qPCR using field samples, the sensitivity and specificity of the PCR1100 assay were 100%, and even lower copy numbers (approximately 10 copies/μL) were detected. **Conclusions:** This study demonstrated that the developed assay can detect rabies RNA in field samples. Because dog-mediated rabies is endemic in remote areas, the rapidity, mobility, and practicality of the PCR1100 assay as well as the high sensitivity of the LN34 system make it an ideal tool for the confirmation of rabies in these areas.

### Case-control study of human anthrax outbreak investigation in farta woreda, South Gondar, Northwest Ethiopia.

Wondmnew T, Asrade B.

17-03-2023

*BMC Infect Dis.*

<https://pubmed.ncbi.nlm.nih.gov/36932357/>

### Evaluation of the efficacy of vitamin C on the immune response after rabies virus vaccine in BALB/c mice.

Sindi N.

Mar-2023

*Eur Rev Med Pharmacol Sci.*

<https://pubmed.ncbi.nlm.nih.gov/36930474/>

**Objective:** Rabies is a lethal zoonotic infection caused by the rabies virus. Interferon- (INF) and interleukins (ILs) are a cytokine that is primarily produced by cells of the immune system. Vitamin C is an essential micronutrient in various biological processes, especially immune responses, and plays an essential part. Vaccination can successfully activate immune responses to virus infection protection. This study aimed to investigate the effect of vitamin C administration on immune responses to an inactivated rabies vaccine. **Materials and methods:** Thirty male Balb/c mice weighing between 25-30 gm (8 weeks old) were used in the current experimental study and randomly equally divided into three groups. Group I: untreated healthy control group was inoculated with PBS as a negative control. Group II: vaccinated intradermally with rabies vaccine alone using a dose of 4 ml/animal at 0, 7, 21 days. Group III: In addition to the dose of vaccine, mice were injected single intraperitoneally with 10 mg of vitamin C with each dose of vaccine on days 0, 7, 21. At experimental end, serum levels of IFN-γ, IL-4, and IL-5 were measured. **Results:** The results revealed that vitamin

C supplementation significantly elevated IFN-γ, IL-4, and IL-5 levels in vaccinated mice and treated with vitamin C (group III) compared to vaccinated group II and healthy control group I. Similarly, vitamin C supplementation exhibited strong positive correlations between IFN-γ and both IL-4 and IL-5 level in all experimental group. Taken together, these results showed that vitamin C is an important stimulator of interferon, interleukin-4 and -5 during inactivated rabies vaccine vaccination in mice. **Conclusions:** Our results supported the hypothesis that indicated the immunological improvement of vitamin C to the effectiveness of the inactivated rabies virus vaccination. High dose of vitamin C increases the levels of interferon and interleukin-4 and interleukin-5.

### Strategies to interrupt Rabies Transmission for the Elimination Goal by 2030 In China (STRATEGIC): a modelling study.

Chen Q, Liu Q, Gong C, Yin W, Mu D, Li Y, Ding S, Liu Y, Yang H, Zhou S, Chen S, Tao Z, Zhang Y, Tang X.

16-03-2023

*BMC Med.*

<https://pubmed.ncbi.nlm.nih.gov/36927437/>

**Background:** A global plan has been set to end human deaths from dog-mediated rabies by 2030 ("Zero-by-30"), but whether it could be achieved in some countries, such as China, remains unclear. Although elimination strategies through post-exposure prophylaxis (PEP) use, dog vaccination, and patient risk assessments with integrated bite case management (IBCM) were proposed to be cost-effective, evidence is still lacking in China. We aim to evaluate the future burdens of dog-mediated human rabies deaths in the next decade and provide quantitative evidence on the cost-effectiveness of different rabies-control strategies in China. **Methods:** Based on data from China's national human rabies surveillance system, we used decision-analytic modelling to estimate dog-mediated human rabies death trends in China till 2035. We simulated and compared the expected consequences and costs of different combination strategies of the status quo, improved access to PEP, mass dog vaccination, and use of IBCM. **Results:** The predicted human rabies deaths in 2030 in China will be 308 (95%UI: 214-411) and remain stable in the next decade under the status quo. The strategy of improved PEP access alone could only decrease deaths to 212 (95%UI: 147-284) in 2028, remaining unchanged till 2035. In contrast, scaling up dog vaccination to coverage of 70% could eliminate rabies deaths by 2033 and prevent approximately 3,265 (95%UI: 2,477-3,687) extra deaths compared to the status quo during 2024-2035. Moreover, with the addition of IBCM, the "One Health" approach through mass dog vaccination could avoid unnecessary PEP use and substantially reduce total cost from 12.53 (95%UI: 11.71-13.34) to 8.73 (95%UI: 8.09-9.85) billion US dollars. Even if increasing the total costs of IBCM from 100 thousand to 652.10 million US dollars during 2024-2035, the combined strategy of mass dog vaccination and use of IBCM will still dominate, suggesting the robustness of our results. **Conclusions:** The combined strategy of mass dog vaccination and IBCM requires collaboration between health and livestock/veterinary sectors, and it could



eliminate Chinese rabies deaths as early as 2033, with more deaths averted and less cost, indicating that adding IBCM could reduce unnecessary use of PEP and make the "One Health" rabies-control strategy most cost-effective.

### **Towards dog-free hospital campuses in India.**

Rahi M, Joy S, Bhargava B.

Oct-Nov2022

*Indian J Med Res.*

<https://pubmed.ncbi.nlm.nih.gov/36510886/>

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## **Trachome**

### **Evolution of anti-malaria policies and measures in P.R. China for achieving and sustaining malaria-free.**

Yin JH, Zhang L, Feng XY, Xia ZG.

03-03-2023

*Front Public Health.*

<https://pubmed.ncbi.nlm.nih.gov/36935657/>

### **When the Neighboring Village is Not Treated: Role of Geographic Proximity to Communities Not Receiving Mass Antibiotics for Trachoma.**

Mosenia A, Haile BA, Shiferaw A, Gebresillasie S, Gebre T, Zerihun M, Tadesse Z, Emerson PM, Callahan EK, Zhou Z, Lietman TM, Keenan JD.

21-03-2023

*Clin Infect Dis.*

<https://pubmed.ncbi.nlm.nih.gov/36477547/>

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## **Lèpre**

### **Redefining tuberculosis: an interview with Lalita Ramakrishnan.**

Ramakrishnan L.

01-03-2023

*Dis Model Mech.*

<https://pubmed.ncbi.nlm.nih.gov/36951140/>

### **A systematic review of health care workers' knowledge and related factors towards burn first aid.**

Yarali M, Parvizi A, Ghorbani Vajargah P, Tamimi P, Mollaei A, Karkhah S, Firooz M, Hosseini SJ, Takasi P, Farzan R, Haddadi S.

23-03-2023

*Int Wound J.*

<https://pubmed.ncbi.nlm.nih.gov/36950866/>

### **JAK inhibitors in dermatology: the road travelled and path ahead, a narrative review.**

Muddebihal A, Khurana A, Sardana K.

22-03-2023

*Expert Rev Clin Pharmacol.*

<https://pubmed.ncbi.nlm.nih.gov/36946306/>

**Introduction:** Numerous cutaneous dermatoses mediated by cytokines depend on the JAK STAT pathway for intracellular signaling. JAK inhibitors form a useful therapeutic approach in treating these conditions. The literature on effectiveness of JAK inhibitors in treatment of alopecia areata, vitiligo, atopic dermatitis, psoriasis and several other inflammatory and autoimmune diseases is growing, although very few conditions have sufficiently well performed studies to their credit and barring a few indications, their use in rest remains empirical as yet.

**Areas covered:** A search of the PubMed database was made using the keywords Janus kinase inhibitors OR JAK inhibitors AND dermatology with the time duration limited to the last 5 years. Here, we review the JAK STAT pathway and the various conditions in which JAK inhibitors are currently used in dermatology and other conditions their use is being explored in. **Expert opinion:** The pathology of a large number of dermatological disorders is mediated via inflammatory cytokines which signal via the JAK STAT pathway. JAKinibs have shown great promise in treating cutaneous disorders refractory to conventional therapy. Their current clinical use in dermatology is based on robust evidence (for some), and anecdotal evidence for most other dermatoses.

### **Painful purpura on bilateral earlobes.**

Yumnam D, Paonam R, Moirangthem A.

20-03-2023

*Int J Dermatol.*

<https://pubmed.ncbi.nlm.nih.gov/36939091/>

### **SKINTED: an uncommon cutaneous complication of total knee replacement.**

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

25-02-2023

*Am J Neurodegener Dis.*

<https://pubmed.ncbi.nlm.nih.gov/36937110/>

### **Genotype Distribution and Antibiotic Susceptibility Pattern of Clinical Isolates of Group B Streptococcus in a Tertiary Care Hospital in Puducherry, South India.**

Sangeetha AV, Devi S, Subramanian A, Daniel M, Anandh P.

08-03-2023

*J Trop Med.*

<https://pubmed.ncbi.nlm.nih.gov/36935773/>

**Background:** *Streptococcus agalactiae* apart from being a colonizer in the genital region is also associated with several other invasive infections in all age groups. With the varied distribution of serotypes across different regions of the world, universal vaccination is also unattainable. However, in India, the knowledge of group B *Streptococcus* (GBS) genotype distribution is deficient. Thus, this study was initiated to add data on this aspect. **Methodology:** A cross-sectional study was conducted using isolates of

group B *Streptococcus* from all clinical specimens. Along with that, the clinical specimen type and the antibiotic resistance profile of the isolates were correlated with the genotypes recognized through a multiplex PCR assay. **Results:** Among the 86 isolates subjected to multiplex PCR for genotype identification, five genotypes were identified with genotype Ib as the predominant one (34.9%), followed by III (20.9%), II (16.3%), Ia (12.7%), and V (11.6%). **Conclusion:** The results demonstrated a correlation of types Ib and III with vaginal colonization and type II with urine specimens in the current study. This preliminary study exhibited the distribution of common genotypes and their antibiotic resistance profiles in various GBS isolates. However, multiple studies across the country with larger sample sizes are needed to validate these findings.

### Evolution of anti-malaria policies and measures in P.R. China for achieving and sustaining malaria-free.

Yin JH, Zhang L, Feng XY, Xia ZG.

03-03-2023

*Front Public Health.*

<https://pubmed.ncbi.nlm.nih.gov/36935657/>

### Treatment of recalcitrant cases of tinea corporis/cruris caused by *T. mentagrophytes* - interdigitale complex with mutations in ERG11 ERG 3, ERG4, MDR1 MFS genes & SQLE and their potential implications.

Bhattacharyya A, Sadhasivam S, Sinha M, Gupta S, Saini S, Singh H, Khurana A, Sachdeva S, Sardana K, Ghosh S.

17-03-2023

*Int J Dermatol.*

<https://pubmed.ncbi.nlm.nih.gov/36929499/>

**Background:** Recalcitrant dermatophyte infections are being reported from various parts of the world due to varied causes including strain variation, steroid misuse, SQLE mutations, and variable quality of itraconazole pellet formulations. The oral drug preferred in endemic areas is itraconazole, to which MIC levels remain low, and clinical failures to itraconazole reported defy a sound scientific explanation. **Objectives:** The objective of the study was to conduct a proteomic and genomic analysis on isolates from therapeutically recalcitrant case with isolation of gene mutations and enzymatic abnormalities to explain azole failures. **Methods:** *Trichophyton mentagrophytes* interdigitale complex strains were isolated from seven clinically non-responding tinea corporis/cruris patients, who had failed a sequential course of 6 weeks of terbinafine 250 mg QD and itraconazole 100 mg BID. After AFST 1 strain, KA01 with high MIC to most drugs was characterized using whole genome sequencing, comparative proteomic profiling, and total sterol quantification. **Results:** Sterol quantification showed that the standard strain of *Trichophyton mentagrophytes* (MTCC-7687) had half the ergosterol content than the resistant KA01 strain. Genomic analysis revealed mutations in SQLE, ERG4, ERG11, MDR1, MFS genes, and a novel ERG3 mutation. Proteomic analysis established the

aberrant expression of acetyl Co-A transferase in the resistant strain and upregulation of thioredoxin reductase and peroxiredoxin. **Conclusion:** Our findings demonstrate possible reasons for multidrug resistance in the prevalent strain with mutations in genes that predict terbinafine (SQLE) and azole actions (ERG4, ERG11, ERG3) apart from efflux pumps (MDR1, MFS) that can explain multidrug clinical failures.

### Trends in pediatric tuberculosis diagnosis utilizing xpert *Mycobacterium tuberculosis*/Rifampicin in a poor-resource, high-burden region: A retrospective, multicenter study.

Garba MA, Ogunbosi BO, Musa A, Ibraheem RM, Aloo MA, Jiya-Chitumu EN, Olorukooba AA, Makarfi HU, Tahir Y, Ibrahim H, Saidu AA, Bashir MF, Odimegwu CL, Ayuk A, Alkali NH.

Jan-Mar 2023

*Int J Mycobacteriol ;*

<https://pubmed.ncbi.nlm.nih.gov/36926767/>

### Obituary.

Khan AM.

16-03-2023

*Indian J Med Res.*

<https://pubmed.ncbi.nlm.nih.gov/36926754/>

### [Snakes as a source of drugs from the Han to the Song Dynasties].

Liu YZ, Wang YL.

28-01-2023

*Zhonghua Yi Shi Za Zhi.*

<https://pubmed.ncbi.nlm.nih.gov/36925147/>

### Where are the missing people affected by tuberculosis? A programme review of patient-pathway and cascade of care to optimise tuberculosis case-finding, treatment and prevention in Cambodia.

Teo AKJ, Morishita F, Prem K, Eng S, An Y, Huot CY, Khun KE, Tieng S, Deng S, Tuot S, Yi S.

Mar-2023

*BMJ Glob Health.*

<https://pubmed.ncbi.nlm.nih.gov/36921989/>

### Eruptive Hypomelanosis: An Under-Recognized Viral Exanthem.

Sil A, Khatua P.

Mar-2023

*J Pediatr.*

<https://pubmed.ncbi.nlm.nih.gov/36270393/>

### Induction of apoptosis by essential oil of *Dracocephalum kotschy* on *Trichomonas vaginalis*.

Chelgerdi Dehkordi B, Esmaeilifallah M, Kalantari R, Benchimol M, Khamesipour F.

Mar-2023

**Background:** *Trichomonas vaginalis* is a protist parasite that causes trichomoniasis, a sexually transmitted disease. Metronidazole is the current treatment for trichomoniasis. However, this drug can provoke severe side effects, and some strains present resistance, making the development of alternative treatments for trichomoniasis urgent. **Objectives:** We investigate the use of essential oil obtained from *Dracocephalum kotschy* on *T. vaginalis*. *D. kotschy* has antispasmodic and analgesic properties and is well known in Iran. **Methods:** The essential oil was obtained by hydrodistillation from 1000 g of the powdered plant. Gas chromatography-mass spectrometry analysis was used for the chemical composition of the essential oil, and 11 substances were identified, corresponding to 91.5% of the oil. Copaene (22.15%), Methyl geranate (16.31%), Geranial (13.78%) and Carvone (11.34%) were the main substances. A cell viability test was used to determine the percentage of growth inhibition (GI%) and the half-maximal inhibitory concentration (IC<sub>50</sub>) on *T. vaginalis* after incubation with the prepared essential oil. **Results:** The oil induced an IC<sub>50</sub> of 84.07 µg/ml after 24 h contact with trophozoites. Cytotoxicity was determined by MTT assay on the J774.A1 haematopoietic cell line. In addition, the initial stage of apoptosis was assayed using the fluorescein isothiocyanate Annexin V Apoptosis Detection Kit. Evaluation of the in vitro anti-trichomonal properties of *D. kotschy* essential oils showed that it effectively induces apoptosis on *T. vaginalis* between 100 and 700 µg/ml after 48 h without toxicity on haematopoietic cells, suggesting that *D. kotschy* essential oil can induce programmed death in *T. vaginalis*. **Conclusions:** The anti-trichomonal properties of *D. kotschy* essential oil indicate that they could be suitable for new pharmacologic studies after new tests with human vaginal epithelial cells.

## Mirror peripheral neuropathy and unilateral chronic neuropathic pain: insights from asymmetric neurological patterns in leprosy.

Raicher I, Zandonai AP, Anghinah IW, Frassetto M, Stump PRNAG, Trindade MAB, Harnik S, Oliveira RA, Macareno RSS, Doppler K, Üçeyler N, Mello ES, Sommer C, Teixeira MJ, Galhardoni R, de Andrade DC.

01-04-2023

Pain.

<https://pubmed.ncbi.nlm.nih.gov/35972460/>

## Trypanosomes (trypanosomiase et maladie de Chagas)

### Biochemical Fractionation of Trypanosomes for the Analysis of Glycosomal Protein Import Defects.

Chou SE, Kael VC, Erdmann R.

2023

Insect-transmitted trypanosomatid parasite infections cause life-threatening neglected tropical diseases (NTDs), including African sleeping sickness, Chagas disease and leishmaniasis. In these parasites, glycosomes are unique organelles that are essential for the parasite survival. Proper biogenesis of glycosomes is crucial to ensure correct compartmentation of the glycosomal metabolism. Genetic or chemical disruption of the glycosome biogenesis leads to a mislocalization of the glycosomal enzymes into the cytosol, which results in toxicity to the parasites. Here, we describe a detailed protocol for biochemical fractionation of *Trypanosoma brucei* parasites to detect mislocalization of glycosomal proteins to the cytosol. This approach utilizes increasing concentrations of digitonin that first permeabilizes the plasma membrane, followed by permeabilization of other organelles, depending on their cholesterol content. Fractionated samples can be further analyzed using immunoblotting for specific marker proteins or quantified by the specific enzyme activities.

### Isolation of Glycosomes from *Trypanosoma brucei*.

Krishna CK, Franke L, Erdmann R, Kael VC.

2023

Methods Mol Biol.

<https://pubmed.ncbi.nlm.nih.gov/36952176/>

### Vector competence of sterile male *Glossina fuscipes fuscipes* for *Trypanosoma brucei brucei*: implications for the implementation of the sterile insect technique in a sleeping sickness focus in Chad.

Mahamat MH, Ségard A, Rayaisse JB, Argiles-Herrero R, Parker AG, Solano P, Abd-Alla AMM, Bouyer J, Ravel S.

22-03-2023

Parasit Vectors.

<https://pubmed.ncbi.nlm.nih.gov/36949538/>

**Background:** Human African trypanosomiasis (HAT) is a neglected tropical disease caused by *Trypanosoma brucei* gambiense transmitted by tsetse flies in sub-Saharan West Africa. In southern Chad the most active and persistent focus is the Mandoul focus, with 98% of the reported human cases, and where African animal trypanosomiasis (AAT) is also present. Recently, a control project to eliminate tsetse flies (*Glossina fuscipes fuscipes*) in this focus using the sterile insect technique (SIT) was initiated. However, the release of large numbers of sterile males of *G. f. fuscipes* might result in a potential temporary increase in transmission of trypanosomes since male tsetse flies are also able to transmit the parasite. The objective of this work was therefore to experimentally assess the vector competence of sterile males treated with isometamidium for *Trypanosoma brucei brucei*. **Methods:** An experimental infection was set up in the laboratory, mimicking field conditions: the same tsetse species that is present in Mandoul was used. A *T. b. brucei* strain close to *T. b. gambiense* was used, and the ability of the sterile

male tsetse flies fed on blood with and without a trypanocide to acquire and transmit trypanosomes was measured. **Results:** Only 2% of the experimentally infected flies developed an immature infection (midgut) while none of the flies developed a metacyclic infection of *T. b. brucei* in the salivary glands. We did not observe any effect of the trypanocide used (isometamidium chloride at 100 mg/l) on the development of infection in the flies. **Conclusions:** Our results indicate that sterile males of the tested strain of *G. f. fuscipes* were unable to cyclically transmit *T. b. brucei* and might even be refractory to the infection. The data of the research indicate that the risk of cyclical transmission of *T. brucei* by sterile male *G. f. fuscipes* of the strain colonized at IAEA for almost 40 years appears to be small.

### Parasites as potential targets for cancer immunotherapy.

Yousefi M, Akbari M, Hadipour M, Dehkordi AB, Farahbakhsh Z, Darani HY.

22-03-2023

*J Cancer Res Clin Oncol.*

<https://pubmed.ncbi.nlm.nih.gov/36949175/>

### The RRM-mediated RNA binding activity in *T. brucei* RAP1 is essential for VSG monoallelic expression.

Gaurav AK, Afrin M, Yang X, Saha A, Sayeed SKA, Pan X, Ji Z, Wong KB, Zhang M, Zhao Y, Li B.

22-03-2023

*Nat Commun.*

<https://pubmed.ncbi.nlm.nih.gov/36949076/>

### Extensible membrane nanotubules mediate attachment of Trypanosoma cruzi epimastigotes under flow.

Perdomo-Gómez CD, Ruiz-Urbe NE, González JM, Forero-Shelton M.

22-03-2023

*PLoS One.*

<https://pubmed.ncbi.nlm.nih.gov/36947570/>

### CRK2 controls cytoskeleton morphogenesis in *Trypanosoma brucei* by phosphorylating $\beta$ -tubulin to regulate microtubule dynamics.

Lee KJ, Zhou Q, Li Z.

22-03-2023

*PLoS Pathog.*

<https://pubmed.ncbi.nlm.nih.gov/36947554/>

Microtubules constitute a vital part of the cytoskeleton in eukaryotes by mediating cell morphogenesis, cell motility, cell division, and intracellular transport. The cytoskeleton of the parasite *Trypanosoma brucei* contains an array of subpellicular microtubules with their plus-ends positioned toward the posterior cell tip, where extensive microtubule growth and cytoskeleton remodeling take place during early cell cycle stages. However, the control mechanism underlying microtubule dynamics at the posterior cell tip

remains elusive. Here, we report that the S-phase cyclin-dependent kinase-cyclin complex CRK2-CYC13 in *T. brucei* regulates microtubule dynamics by phosphorylating  $\beta$ -tubulin on multiple evolutionarily conserved serine and threonine residues to inhibit its incorporation into cytoskeletal microtubules and promote its degradation in the cytosol. Consequently, knockdown of CRK2 or CYC13 causes excessive microtubule extension and loss of microtubule convergence at the posterior cell tip, leading to cytoskeleton elongation and branching. These findings uncover a control mechanism for cytoskeletal microtubule dynamics by which CRK2 phosphorylates  $\beta$ -tubulin and fine-tunes cellular  $\beta$ -tubulin protein abundance to restrict excess microtubule extension for the maintenance of cytoskeleton architecture.

### Structure-Activity Relationships, Tolerability and Efficacy of Microtubule-Active 1,2,4-Triazolo[1,5- a ]pyrimidines as Potential Candidates to Treat Human African Trypanosomiasis.

Monti L, Liu LJ, Varricchio C, Lucero B, Alle T, Yang W, Bem-Shalom I, Gilson M, Brunden KR, Brancale A, Caffrey CR, Ballatore C.

11-03-2023

*bioRxiv.*

<https://pubmed.ncbi.nlm.nih.gov/36945407/>

### Bird Louse Flies *Ornithomya* spp. (Diptera: Hippoboscidae) as Potential Vectors of Mammalian *Babesia* and Other Pathogens.

Čisovská Bazsalovicsová E, Víchová B, Oboňa J, Radačovská A, Blažeková V, Králová-Hromadová I.

21-03-2023

*Vector Borne Zoonotic Dis.*

<https://pubmed.ncbi.nlm.nih.gov/36944122/>

### Performance of clinical signs and symptoms, rapid and reference laboratory diagnostic tests for diagnosis of human African trypanosomiasis by passive screening in Guinea: a prospective diagnostic accuracy study.

Camara O, Camara M, Falzon LC, Ilboudo H, Kaboré J, Compaoré CFA, Fèvre EM, Büscher P, Bucheton B, Lejon V.

20-03-2023

*Infect Dis Poverty.*

<https://pubmed.ncbi.nlm.nih.gov/36941656/>

### In silico evolutionary and structural analysis of cAMP response proteins (CARPs) from *Leishmania major*.

Bhakta S, Bhattacharya A.

20-03-2023

*Arch Microbiol.*

<https://pubmed.ncbi.nlm.nih.gov/36941487/>

With unidentified chemical triggers and novel-effectors, cAMP signaling is broadly noncanonical in kinetoplastida

parasites. Though novel protein kinase A regulatory subunits (PKAR) have been identified earlier, cAMP Response Proteins (CARPs) have been identified as a unique and definite cAMP effector of trypanosomatids. CARP1-CARP4 emerged as critical regulatory components of cAMP signaling pathway in *Trypanosoma* with evidences that CARP3 can directly interact with a flagellar adenylate cyclase (AC). CARP-mediated regulations, identified so far, reflects the mechanistic diversity of cAMP signaling. Albeit the function of the orthologous is not yet delineated, in kinetoplastids like *Leishmania*, presence of CARP1, 2 and 4 orthologues suggests existence of conserved effector mechanisms. Targeting CARP orthologues in *Leishmania*, a comprehensive evolutionary analysis of CARPs have been aimed in this study which revealed phylogenetic relationship, codon adaptation and structural heterogeneity among the orthologues, warranting functional analysis in future to explore their involvement in infectivity.

### **Collection of triatomines from sylvatic habitats by a *Trypanosoma cruzi*-infected scent detection dog in Texas, USA.**

**Christopher DM, Curtis-Robles R, Hamer GL, Bejcek J, Saunders AB, Roachell WD, Cropper TL, Hamer SA.**  
20-03-2023

*PLoS Negl Trop Dis.*

<https://pubmed.ncbi.nlm.nih.gov/36940217/>

### **In silico toxicologic profile and in vivo trypanocidal activity of estafietin, a sesquiterpene lactone isolated from *Stevia alpina* Griseb.**

**Elso OG, Cerny N, Laurella LC, Bivona AE, Sánchez Alberti A, Morales C, Catalán CAN, Malchiodi EL, Sülsen VP.**

20-03-2023

*Nat Prod Res.*

<https://pubmed.ncbi.nlm.nih.gov/36938813/>

### ***Trypanosoma cruzi* dysregulates expression profile of piRNAs in primary human cardiac fibroblasts during early infection phase.**

**Rayford KJ, Cooley A, Strode AW, Osi I, Arun A, Lima MF, Misra S, Pratap S, Nde PN.**

02-03-2023

*Front Cell Infect Microbiol.*

<https://pubmed.ncbi.nlm.nih.gov/36936778/>

*Trypanosoma cruzi*, the etiological agent of Chagas Disease, causes severe morbidity, mortality, and economic burden worldwide. Though originally endemic to Central and South America, globalization has led to increased parasite presence in most industrialized countries. About 40% of infected individuals will develop cardiovascular, neurological, and/or gastrointestinal pathologies. Accumulating evidence suggests that the parasite induces alterations in host gene expression profiles in order to facilitate infection and pathogenesis. The role of regulatory gene expression machinery during *T. cruzi* infection, particularly small noncoding RNAs, has yet to be

elucidated. In this study, we aim to evaluate dysregulation of a class of sncRNAs called piRNAs during early phase of *T. cruzi* infection in primary human cardiac fibroblasts by RNA-Seq. We subsequently performed *in silico* analysis to predict piRNA-mRNA interactions. We validated the expression of these selected piRNAs and their targets during early parasite infection phase by stem loop qPCR and qPCR, respectively. We found about 26,496,863 clean reads (92.72%) which mapped to the human reference genome. During parasite challenge, 441 unique piRNAs were differentially expressed. Of these differentially expressed piRNAs, 29 were known and 412 were novel. In silico analysis showed several of these piRNAs were computationally predicted to target and potentially regulate expression of genes including *SMAD2*, *EGR1*, *ICAM1*, *CX3CL1*, and *CXCR2*, which have been implicated in parasite infection, pathogenesis, and various cardiomyopathies. Further evaluation of the function of these individual piRNAs in gene regulation and expression will enhance our understanding of early molecular mechanisms contributing to infection and pathogenesis. Our findings here suggest that piRNAs play important roles in infectious disease pathogenesis and can serve as potential biomarkers and therapeutic targets.

### **Sec22b-dependent antigen cross-presentation is a significant contributor of T cell priming during infection with the parasite *Trypanosoma cruzi*.**

**Biscari L, Maza MC, Farré C, Kaufman CD, Amigorena S, Fresno M, Gironès N, Alloatti A.**

01-03-2023

*Front Cell Dev Biol.*

<https://pubmed.ncbi.nlm.nih.gov/36936692/>

Antigen cross-presentation is a vital mechanism of dendritic cells and other antigen presenting cells to orchestrate the priming of cytotoxic responses towards killing of infected or cancer cells. In this process, exogenous antigens are internalized by dendritic cells, processed, loaded onto MHC class I molecules and presented to CD8<sup>+</sup> T cells to activate them. Sec22b is an ER-Golgi Intermediate Compartment resident SNARE protein that, in partnership with syntaxin4, coordinates the recruitment of the transporter associated with antigen processing protein and the peptide loading complex to phagosomes, where antigenic peptides that have been proteolyzed in the cytosol are loaded in MHC class I molecules and transported to the cell membrane. The silencing of Sec22b in dendritic cells primary cultures and conditionally in dendritic cells of C57BL/6 mice, critically impairs antigen cross-presentation, but neither affects other antigen presentation routes nor cytokine production and secretion. Mice with Sec22b conditionally silenced in dendritic cells (Sec22b<sup>-/-</sup>) show deficient priming of CD8<sup>+</sup> T lymphocytes, fail to control tumor growth, and are resistant to anti-checkpoint immunotherapy. In this work, we show that Sec22b<sup>-/-</sup> mice elicit a deficient specific CD8<sup>+</sup> T cell response when challenged with sublethal doses of *Trypanosoma cruzi* trypomastigotes that is associated with increased blood parasitemia and diminished survival.



### **A multicenter comparative study of the performance of four rapid immunochromatographic tests for the detection of anti-*Trypanosoma cruzi* antibodies in Brazil.**

Iturra JAD, Leony LM, Medeiros FAC, de Souza Filho JA, Siriano LDR, Tavares SB, Luquetti AO, Belo VS, de Sousa AS, Santos FLN.

02-03-2023

*Front Med (Lausanne)*.

<https://pubmed.ncbi.nlm.nih.gov/36936214/>

### **Serosurvey of *Trypanosoma cruzi* in persons experiencing homelessness and shelter workers of Brazil.**

Kmetiuk LB, Gonçalves G, Chechia Do Couto A, Biondo AW, Figueiredo FB.

03-03-2023

*Front Public Health*.

<https://pubmed.ncbi.nlm.nih.gov/36935667/>

### **Extracellular vesicles in the context of Chagas Disease - A systematic review.**

Garcez EM, Gomes N, Moraes AS, Pogue R, Uenishi RH, Hecht M, Carvalho JL.

17-03-2023

*Acta Trop*.

<https://pubmed.ncbi.nlm.nih.gov/36935050/>

### **RNA-seq reveals that overexpression of TcUBP1 switches the gene expression pattern towards that of the infective form of *Trypanosoma cruzi*.**

Sabalette K, Sotelo-Silveira J, Smircich P, De Gaudenzi J.

17-03-2023

*J Biol Chem*.

<https://pubmed.ncbi.nlm.nih.gov/36935010/>

Trypanosomes regulate gene expression mainly by using post-transcriptional mechanisms. Key factors responsible for carrying out this regulation are RNA-binding proteins (RBPs), affecting subcellular localization, translation, and/or transcript stability. *Trypanosoma cruzi* U-rich RBP 1 (TcUBP1) is a small protein that modulates the expression of several surface glycoproteins of the trypomastigote infective stage of the parasite. Its mRNA targets are known but the impact of its overexpression at the transcriptome level in the insect-dwelling epimastigote cells has not yet been investigated. Thus, in the present study, by using a tetracycline-inducible system, we generated a population of TcUBP1-overexpressing parasites and analyzed its effect by RNA-seq methodology. This allowed us to identify 793 up- and 371 down-regulated genes with respect to the wild-type control sample. Among the up-regulated genes, it was possible to identify members coding for the TcS superfamily, MASP, MUCI/II, and protein kinases, whereas among the down-regulated transcripts, we found mainly genes coding for ribosomal, mitochondrial, and synthetic pathway proteins. RNA-seq comparison with two previously published datasets revealed that the expression profile of this TcUBP1-overexpressing replicative

epimastigote form resembles the transition to the infective metacyclic trypomastigote stage. We identified novel cis-regulatory elements in the 3'-untranslated region of the affected transcripts and confirmed that UB1m -a signature TcUBP1 binding element previously characterized in our lab- is enriched in the list of stabilized genes. We can conclude that the overall effect of TcUBP1 overexpression on the epimastigote transcriptome is mainly the stabilization of mRNAs coding for proteins that are important for parasite infection.

### **Cell-to-flagellum attachment and surface architecture in kinetoplastids.**

D Liz LV, Stoco PH, Sunter JD.

16-03-2023

*Trends Parasitol*.

<https://pubmed.ncbi.nlm.nih.gov/36933967/>

### **Emerging compounds and therapeutic strategies to treat infections from *Trypanosoma brucei*: an overhaul of the last 5-years patents.**

Melfi F, Carradori S, Campestre C, Haloci E, Ammazalorso A, Grande R, D'Agostino I.

18-03-2023

*Expert Opin Ther Pat*.

<https://pubmed.ncbi.nlm.nih.gov/36933190/>

**Introduction:** Human African Trypanosomiasis is a neglected disease caused by infection from parasites belonging to the *Trypanosoma brucei* species. Only six drugs are currently available and employed depending on the stage of the infection: pentamidine, suramin, melarsoprol, eflornithine, nifurtimox, and fexinidazole. Joint research projects were launched in an attempt to find new therapeutic options for this severe and often lethal disease. **Areas covered:** After a brief description of the recent literature on the parasite and the disease, we searched for patents dealing with the proposal of new antitrypanosomiasis agents and, following the PRISMA guidelines, we filtered the results to those published from 2018 onwards returning suitable entries, which represent the contemporary landscape of compounds/strategies against *Trypanosoma brucei*. In addition, some relevant publications from the overall scientific literature were also discussed. **Expert opinion:** This review comprehensively covers and analyzes the most recent advances not only in the discovery of new inhibitors and their structure-activity relationships but also in the assessment of innovative biological targets opening new scenarios in the MedChem field. Finally, also new vaccines and formulations recently patented were described. However, natural and synthetic compounds were analyzed in terms of inhibitory activity and selective toxicity against human cells.

### **Vector mapping and bloodmeal metabarcoding demonstrate risk of urban Chagas disease transmission in Caracas, Venezuela.**

Segovia M, Schwabl P, Sueto S, Nakad CC, Londoño JC, Rodriguez M, Paiva M, Llewellyn MS, Carrasco HJ.

17-03-2023

### **Tabanid-transmitted animal trypanosomiasis in Cameroon: Evidence from a study in the tsetse free pastoral zone of Galim.**

Lendzele SS, Abah S, Nguetoum C, Burinyuy KA, Koumba AA, Mavougou JF.

27-05-2022

*Parasite Epidemiol Control.*

<https://pubmed.ncbi.nlm.nih.gov/36926001/>

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## **Leishmaniose**

### **Leishmania donovani 6-phosphogluconolactonase: Crucial for growth and host infection?**

Paul A, Roy PK, Babu NK, Dhumal TT, Singh S.

21-03-2023

*Microb Pathog.*

<https://pubmed.ncbi.nlm.nih.gov/36958644/>

The hexose monophosphate shunt is a crucial pathway in a variety of microorganisms owing to its vital metabolic products and intermediates such as NADPH, ribose 5-phosphate etc. The enzyme 6-phosphogluconolactonase catalyses the second step of this pathway, converting 6-phosphogluconolactone to 6-phosphogluconic acid. This enzyme has been known to have a significant involvement in growth, pathogenesis and sensitivity to oxidative stress in bacterial and protozoal pathogens. However, the functional role of kinetoplastid *Leishmania donovani* 6-phosphogluconolactonase (Ld6PGL) remains unexplored. *L. donovani* is the second largest parasitic killer and causative organism of life threatening visceral leishmaniasis. To understand its possible functional role in the parasite, the alleles of Ld6PGL were sequentially knocked-out followed by gene complementation. The Ld6PGL mutant cell lines showed decrease in transcriptional and translational expression as well as in the enzyme activity. In case of Ld6PGL null mutants, approximately 2-fold reduction was observed in growth. The null mutants also showed ~38% decrease in infectivity, which recovered to ~15% on complementation. Scanning electron microscopy showed a marked decrease in flagellar length in the knockout parasites. When treated with the standard drug miltefosine, the mutant strains had no significant change in the drug sensitivity. However, the Ld6PGL mutants were more susceptible to oxidative stress. Our findings suggest that 6PGL is required for parasite growth and infection but it is not essential.

### **Editorial: Leishmania genome variability: Impacts on parasite evolution, parasitism and leishmaniases control.**

Tosi LRO, Denny PW, De Oliveira CI, Damasceno JD.

06-03-2023

*Front Cell Infect Microbiol.*

<https://pubmed.ncbi.nlm.nih.gov/36949811/>

### **T-cell activation, senescence, and exhaustion in asymptomatic HIV/Leishmania infantum co-infection.**

de Oliveira Mendes-Aguiar C, do Monte Alves M, Lopes Machado AA, de Góis Monteiro GR, Medeiros IM, Queiroz JW, Lima ID, Pearson RD, Wilson ME, Glesby MJ, do Nascimento ELT, Bezerra Jerônimo SM.

06-03-2023

*medRxiv.*

<https://pubmed.ncbi.nlm.nih.gov/36945413/>

### **Design, synthesis, and repurposing of O<sup>6</sup>-aminoalkyl-sulfuretin analogs towards discovery of potential lead compounds as antileishmanial agents.**

Hassan AHE, Phan TN, Moon S, Lee CH, Kim YJ, Cho SB, El-Sayed SM, Choi Y, No JH, Lee YS.

09-03-2023

*Eur J Med Chem.*

<https://pubmed.ncbi.nlm.nih.gov/36944273/>

Transmission of cutaneous leishmaniasis in Venezuela reveals diverse and changing epidemiological landscapes, as well as a spectrum of clinical phenotypes presumed to be linked to a variety of *Leishmania* species. Central-western Venezuela constitutes one of the highest endemic epicenters in the country, yet updated molecular epidemiological information is still lacking. Therefore, in this study we aimed to characterize the landscape of circulating *Leishmania* species across central-western Venezuela through the last two decades, performed comparisons of haplotype and nucleotide diversity, and built a geospatial map of parasite species distribution. A total of 120 clinical samples were collected from patients across the cutaneous disease spectrum, retrieving parasitic DNA, and further characterizing by PCR and sequencing of the HSP70 gene fragment. This data was later collated with further genetic, geospatial and epidemiological analyses. A peculiar pattern of species occurrence including *Leishmania* (*Leishmania*) *amazonensis* (77.63% N=59), *Leishmania* (*Leishmania*) *infantum* (14.47% N=11), *Leishmania* (*Viannia*) *panamensis* (5.26% N=4) and *Leishmania* (*Viannia*) *braziliensis* (2.63% N=2) was revealed, also highlighting a very low genetic diversity amongst all analyzed sequences. Geographical distribution showed that most cases are widely distributed across the greater urban-sub urban area of the Iribaren municipality. *L. (L.) amazonensis* appears to be widely dispersed throughout Lara state. Statistical analyses failed to reveal significance for any comparisons, leading to conclude a lack of association between the infective *Leishmania* species and clinical phenotypes. To the best of our knowledge, this is an unprecedented study which addresses comprehensively the geographical distribution of *Leishmania* species in central-western Venezuela throughout the last two decades, and the first to incriminate *L. (L.) infantum* as an etiologic agent of cutaneous leishmaniasis in this region. Our findings support that *Leishmania* endemism in central-western Venezuela is caused mainly by *L. (L.) amazonensis*.

Future studies are needed to unveil additional details on the ecological intricacies and transmission aspects of leishmaniasis (i.e. sampling phlebotomines and mammals) and to adopt adequate public health prevention and control strategies and mitigate disease impact in this endemic region.

### **In silico evolutionary and structural analysis of cAMP response proteins (CARPs) from *Leishmania major*.**

**Bhakta S, Bhattacharya A.**

20-03-2023

*Arch Microbiol.*

<https://pubmed.ncbi.nlm.nih.gov/36941487/>

### **Genome sequence of *Leishmania mexicana* MNYC/BZ/62/M379 expressing Cas9 and T7 RNA polymerase.**

**Beneke T, Dobramysl U, Catta-Preta CMC, Mottram JC, Gluenz E, Wheeler RJ.**

23-02-2023

*Wellcome Open Res.*

<https://pubmed.ncbi.nlm.nih.gov/36874584/>

We present the genome sequence of *Leishmania mexicana* MNYC/BZ/62/M379 modified to express Cas9 and T7 RNA-polymerase, revealing high similarity to the reference genome (MHOM/GT2001/U1103). Through RNAseq-based annotation of coding sequences and untranslated regions, we provide primer sequences for construct and sgRNA template generation for CRISPR-assisted gene deletion and endogenous tagging.

### **Diversity and geographical distribution of *Leishmania* species and the emergence of *Leishmania (Leishmania) infantum* and *L. (Viannia) panamensis* in Central-Western Venezuela.**

**LA LAD, Hernández-Pereira CE, Castillo-Castañeda AC, Patiño LH, Castañeda S, Herrera G, Mogollón E, Muñoz M, Duran A, Loyo D, Pacheco M, Arena L, Isquiel G, Yezpe L, Colmenarez B, Caviedes M, Mendez Y, Herrera S, Ramírez JD, Paniz-Mondolfi AE.**

18-03-2023

*Acta Trop.*

<https://pubmed.ncbi.nlm.nih.gov/36940857/>

### **Selective whole-genome amplification reveals population genetics of *Leishmania braziliensis* directly from patient skin biopsies.**

**Pilling OA, Reis-Cunha JL, Grace CA, Berry ASF, Mitchell MW, Yu JA, Malekshahi CR, Krespan E, Go CK, Lombana C, Song YS, Amorim CF, Lago AS, Carvalho LP, Carvalho EM, Brisson D, Scott P, Jeffares DC, Beiting DP.**

20-03-2023

*PLoS Pathog.*

<https://pubmed.ncbi.nlm.nih.gov/36940219/>

### **In vitro Anti-Leishmanial Activities of Methanol Extract of *Brucea***

### **antidysenterica J.F. Mill Seeds and Its Solvent Fractions.**

**Ketema T, Tadele M, Gebrie Z, Makonnen E, Hailu A, Abay SM.**

13-03-2023

*J Exp Pharmacol.*

<https://pubmed.ncbi.nlm.nih.gov/36937078/>

**Introduction:** Leishmaniasis is one of the neglected tropical diseases, threatening lives of about 350 million people globally. *Brucea antidysenterica* seeds are used for the treatment of cutaneous leishmaniasis in the traditional medicine in Ethiopia. **Objective:** This study aimed to evaluate *Brucea antidysenterica* seeds' anti-leishmanial activity in vitro. **Methods:** The crude (80% methanol) extract of *Brucea antidysenterica* seeds and its fractions were evaluated for their anti-leishmanial activities against promastigotes and intracellular amastigotes of *Leishmania donovani* and *Leishmania aethiopica*, and for their cytotoxic effects against mammalian cells. The quantitative estimations of total phenolic compounds (TPCs), flavonoids (TFCs) and alkaloids (TACs) were determined, spectrophotometrically. Median inhibitory concentration (IC<sub>50</sub>) and median cytotoxic concentration (CC<sub>50</sub>) of the extract and its solvent fractions were calculated using GraphPad Prism 9.1.0 computer software. Data was presented as mean ± standard error of the mean (SEM). **Results:** The crude extract and its hexane, ethyl acetate and butanol fractions showed anti-leishmanial activities, with IC<sub>50</sub> values of 4.14-60.12 µg/mL against promastigotes, and 6.16-40.12 µg/mL against amastigotes of both *Leishmania* species. They showed moderate cytotoxicity against Vero cell lines and peritoneal mice macrophages, with CC<sub>50</sub> values of 100-500 µg/mL, but >1600 µg/mL against red blood cells. Selectivity indices ranged from 7.97 to 30.97. The crude extract, and its ethyl acetate and hexane fractions possessed 54.78-127.72 mg of gallic acid equivalent TPC, 18.30-79.21 mg of quercetin equivalent TFC, and 27.62-97.22 mg of atropine equivalent TAC per gram of extracts. **Conclusion:** The seeds of the plant possessed anti-leishmanial activities against *L. aethiopica* and *L. donovani* that might provide a scientific justification for its use in the treatment of leishmaniasis by traditional healers. Future works are recommended to isolate, purify and identify the possible secondary metabolites attributed to the anti-leishmanial activity.

### **Corrigendum: *Leishmania infantum* infecting the carnivore *Nasua nasua* from urban forest fragments in an endemic area of visceral leishmaniasis in Brazilian Midwest.**

**de Macedo GC, Barreto WGT, de Oliveira CE, Santos FM, Porfirio GEO, Xavier SCDC, Alves FM, da Silva AR, de Andrade GB, Rucco AC, de Assis WO, Jansen AM, Roque ALR, Herrera HM.**

03-03-2023

*Front Cell Infect Microbiol.*

<https://pubmed.ncbi.nlm.nih.gov/36936769/>

### **Development of a microemulsion loaded with epoxy- $\alpha$ -lapachone against**

### **Leishmania (Leishmania) amazonensis murine infection.**

Figueiredo Peixoto J, Filipe Gonçalves-Oliveira L, Souza da Silva F, Monteiro de Castro Côrtes L, Dias-Lopes G, de Oliveira Cardoso F, de Oliveira Santos R, Ferreira de Carvalho Patricio B, Deckmann Nicoletti C, Guimarães de Souza Lima C, da Silva Calabrese K, de Lima Moreira D, Vinícius Antunes Rocha H, de Carvalho da Silva F, Francisco Ferreira V, Roberto Alves C.

17-03-2023

*Int J Pharm.*

<https://pubmed.ncbi.nlm.nih.gov/36934883/>

### **Leukoreduction as a control measure in transfusion transmission of visceral leishmaniasis.**

Pereira LQ, Tanaka SCSV, Ferreira-Silva MM, Gomes FVBAF, Santana MP, Aguiar PR, de Araújo Pereira G, Gómez-Hernández C, Junior VR, De Vito FB, Moraes-Souza H.

17-03-2023

*Transfusion.*

<https://pubmed.ncbi.nlm.nih.gov/36929836/>

**Background:** Asymptomatic visceral leishmaniasis (VL) infection is a risk for transfusion safety. Leukoreduction has been an alternative for the prevention of some blood-borne diseases, including VL. This study aimed to evaluate the role of leukoreduction of cellular blood components as a control measure for transfusional VL transmission.

**Research design and methods:** A total of 161 polytransfused patients with non-leukoreduced blood components (HNL), 95 polytransfused with leukoreduced blood components (LH), and 202 non-transfused (NT) from endemic regions for VL and with a similar epidemiological profile. The detection of antibodies against VL was performed by ELISA and the presence of the parasite was investigated by real-time PCR. Statistical significance was defined as  $p < .05$ . **Results:** When comparing three groups, ELISA results were statistically significant ( $p = .0065$ ). The residual analysis of ELISA showed statistically significant for the HNL group compared to the general group ( $p = .002$ ; OR: 5.6; CI: 1.7-25.8), demonstrating that individuals who received non-leukoreduced transfusions are five times more likely to acquire *Leishmania infantum* infection than the general.

**Discussion:** Higher prevalence in the group with HNL and low prevalence in those who received LH, similar to NT patients, highlight the risk of transfusional VL transmission and reinforce the role of leukoreduction in its prevention.

### **In silico designing of a novel polyvalent multi-subunit peptide vaccine leveraging cross-immunity against human visceral and cutaneous leishmaniasis: an immunoinformatics-based approach.**

Bhattacharjee M, Banerjee M, Mukherjee A.

16-03-2023

*J Mol Model.*

<https://pubmed.ncbi.nlm.nih.gov/36928431/>

### **Phlebotomine sandflies (Diptera: Psychodidae) of Ethiopia.**

Aklilu E, Yared S, Gebresilassie A, Legesse B, Hailu A.

09-03-2023

*Heliyon.*

<https://pubmed.ncbi.nlm.nih.gov/36925525/>

Phlebotomine sandflies have a long history of association with humans, which makes them the only proven natural vectors of *Leishmania* species, the parasitic protozoans that cause leishmaniasis in humans and animals. In Ethiopia, the three forms of leishmaniasis, viz., visceral, dermal and mucocutaneous are endemic in different parts of the country. Since the first report of phlebotomine sandflies in Ethiopia in 1936, the distribution of different species and their role in the transmission of leishmaniasis have been extensively studied. The objective of this review was to summarize the patchy information and give an updated list of phlebotomine sandfly species in Ethiopia and their known geographical distribution in the country. Peer-reviewed literature search was conducted using online databases. All articles published which focus on distribution and medical importance of *Phlebotomus* and *Sergentomyia* species of Ethiopia starting from 1936 up to 2022 were reviewed. Until July 2022, 65 phlebotomine sandfly species have been reported, belonging to the genus *Phlebotomus* and *Sergentomyia*. The genus *Phlebotomus* in Ethiopia is represented by six subgenera such as *Adlerius*, *Anaphlebotomus*, *Larrousius*, *Paraphlebotomus*, *Phlebotomus* and *Synphlebotomus*, whereas the genus *Sergentomyia* is represented by six subgenera, namely *Grassomyia*, *Parrotomyia*, *Parvidens*, *Rondanomyia*, *Sergentomyia*, and *Sintonius*.

### **Detection of asymptomatic Leishmania infection in blood donors at two blood banks in Ethiopia.**

Mohammed R, Melkamu R, Pareyn M, Abdellati S, Bogale T, Engidaw A, Kinfu A, Girma T, van Griensven J.

09-03-2023

*PLoS Negl Trop Dis.*

<https://pubmed.ncbi.nlm.nih.gov/36893183/>

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## **Cysticercose**

### **Food- and vector-borne parasitic zoonoses: Global burden and impacts.**

Anisuzzaman, Hossain MS, Hatta T, Labony SS, Kwofie KD, Kawada H, Tsuji N, Alim MA.

2023

*Adv Parasitol.*

<https://pubmed.ncbi.nlm.nih.gov/36948728/>

### **Evolution of research funding for neglected tropical diseases in Brazil, 2004-2020.**

Melo GBT, Angulo-Tuesta A, Silva END, Santos TDS, Uchimura LYT, Obara MT.

16-03-2023

*PLoS Negl Trop Dis.*



<https://pubmed.ncbi.nlm.nih.gov/36928796/>

### **Spatial and temporal distribution of *Taenia solium* and its risk factors in Uganda.**

Ngwili N, Sentamu DN, Korir M, Adriko M, Beinamaryo P, Dione MM, Kaducu JM, Mubangizi A, Mwinzi PN, Thomas LF, Dixon MA.

Apr-2023

*Int J Infect Dis.*

<https://pubmed.ncbi.nlm.nih.gov/36805327/>

### **Neurocysticercosis: challenges in pediatric neurosurgery practice.**

Yamaki VN, Telles JPM, Yamashita RHG, Matushita H.

Mar-2023

*Childs Nerv Syst.*

<https://pubmed.ncbi.nlm.nih.gov/36689000/>

**Purpose:** Neurocysticercosis (NCC) is considered a neglected infectious disease, but the most common parasitic disease of the central nervous system (CNS). Due to oral tendencies in childhood, it is hypothesized that individuals are infected around this age and develop symptoms as late as during young adulthood. Although it is considered a benign disease, it may cause great impact in the patient's quality of life due to epilepsy, visual symptoms, and hydrocephalus, which eventually requires frequent hospitalizations. The treatment of hydrocephalus is the main challenge for neurosurgeons. **Methods:** We performed a concise review on neurocysticercosis in children and the main presentations of NCC in the neurosurgery practice and a systematic review on hydrocephalus secondary to extraparenchymal NCC.

**Results:** Our review showed a rate of complete resolution of hydrocephalus secondary to NCC of around 80% with the first attempt of surgical treatment combined with medication therapy. Endoscopic removal of the intraventricular cysts with third ventriculostomy was the most common treatment modality. Patients previously managed with ventricular shunts are likely to have worse outcomes and complications. **Conclusion:** Endoscopic approach is the gold standard surgical treatment for hydrocephalus secondary to neurocysticercosis.

### **Metastatic neuroendocrine tumor masquerading as orbital cysticercosis.**

Wirth MA, Khan HM, Sabiq F, Agoumi M, Neufeld A.

Apr-2023

*Neuroradiol J.*

<https://pubmed.ncbi.nlm.nih.gov/36044662/>

Orbital metastases secondary to neuroendocrine tumors are exceedingly rare. We present a unique case of a 30-year-old female initially presenting with fever, chills, periorbital swelling, and painful proptosis. CT orbits revealed two ovoid-shaped ring-enhancing lesions in the right lateral and superior rectus muscles and clear sinuses, atypical for infectious post-septal cellulitis. Further work-up included serologic analysis, auto-immune panel, and MRI. Further imaging showed pseudocystic orbital lesions mimicking orbital cysticercosis. Additionally, given the

bilateral nature of the lesions and patient's country of origin, this parasitic process was highly suspected. A course of albendazole and steroids led to resolution of symptoms. With a presentation at age 30, this is by far the youngest case reported in literature to date.

## **Dracunculose**

### **Modulation of MRSA virulence gene expression by the wall teichoic acid enzyme TarO.**

Lu Y, Chen F, Zhao Q, Cao Q, Chen R, Pan H, Wang Y, Huang H, Huang R, Liu Q, Li M, Bae T, Liang H, Lan L.

22-03-2023

*Nat Commun.*

<https://pubmed.ncbi.nlm.nih.gov/36949052/>

Phenol-soluble modulins (PSMs) and Staphylococcal protein A (SpA) are key virulence determinants for community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA), an important human pathogen that causes a wide range of diseases. Here, using chemical and genetic approaches, we show that inhibition of TarO, the first enzyme in the wall teichoic acid (WTA) biosynthetic pathway, decreases the expression of genes encoding PSMs and SpA in the prototypical CA-MRSA strain USA300 LAC. Mechanistically, these effects are linked to the activation of *VraRS* two-component system that directly represses the expression of accessory gene regulator (*agr*) locus and *spa*. The activation of *VraRS* was due in part to the loss of the functional integrity of penicillin-binding protein 2 (PBP2) in a PBP2a-dependent manner. TarO inhibition can also activate *VraRS* in a manner independent of PBP2a. We provide multiple lines of evidence that accumulation of lipid-linked peptidoglycan precursors is a trigger for the activation of *VraRS*. In sum, our results reveal that WTA biosynthesis plays an important role in the regulation of virulence gene expression in CA-MRSA, underlining TarO as an attractive target for anti-virulence therapy. Our data also suggest that acquisition of PBP2a-encoding *mecA* gene can impart an additional regulatory layer for the modulation of key signaling pathways in *S. aureus*.

### **First report of *Dickeya dadantii* causing bacterial soft rot of *Scindapsus pictus* in Taiwan.**

Chang CY, Tang WC, Chu CC.

22-03-2023

*Plant Dis.*

<https://pubmed.ncbi.nlm.nih.gov/36947837/>

*Scindapsus pictus* (satin pothos or silver vine) is an evergreen climbing plant belonging to the Araceae family, subfamily Monstereae (Bown, 2000), which is also cultivated as a foliage ornamental (Masnira et al. 2019). In September of 2022, soft rot symptoms were observed on potted *S. pictus* plants grown in a greenhouse in Nantun District, Taichung, Taiwan, in which soft rot of another aroid (philodendron) has also been reported (Wu et al. 2023). The symptoms appeared on the petioles and most of them tended to extend to the leaf blades; the colors of leaf lesions ranged from dark brown to gray (Fig. S1). Some



70% of the plants in the greenhouse showed similar symptoms and losses were estimated to be 15-30%. Four symptomatic plants were sampled. Macerated tissues from rotting petioles were soaked in 10 mM MgCl<sub>2</sub> and observed under a light microscope (Nikon, Japan) at 400 x magnification. Motile, rod-shaped bacteria were observed, and 1-2 loopfuls of undiluted sample suspension were streaked onto nutrient agar (NA; Gibco, USA). After culturing at 28°C for 1 day, all samples yielded round, creamy-white colonies (0.9 mm in diameter) and from each of the four samples a pure culture was obtained (Spi1-Spi4). All isolates exhibited oxidative and fermentative metabolism of glucose (Schaad et al. 2001). They caused pitting on crystal violet pectate agar, induced maceration on potato tuber and were tested positive for phosphatase activity and indigoidine production (Lee and Yu 2006; Schaad et al. 2001). Polymerase chain reaction tests using *Dickeya*-specific primers 5A and 5B (Chao et al. 2006) amplified the expected amplicon (0.5 kb) in extracted DNA samples of all isolates. Identification of the strains was achieved by amplifying and sequencing fragments of the housekeeping genes *gyrB*, *recN*, *dnaA*, *dnaJ*, and *dnaX* (Marrero et al. 2013); the lengths of the five gene fragments analyzed were 822, 762, 720, 672, and 450 bp, respectively (accession nos. OP985528-OP985532). The five sequences were concatenated for every isolate; the resulting 3,426 bp sequences were aligned with ClustalW and found to be identical. A maximum-likelihood analysis was conducted using the 3,426-bp sequences and those of known *Dickeya* species' type strains. Spi1 to Spi4 clustered with *D. dadantii* subsp. *dieffenbachiae* NCPPB 2976<sup>T</sup> and *D. dadantii* subsp. *dadantii* CFBP 1269<sup>T</sup> (Fig. S2) with sequence identities of 98.4 and 98%, respectively. To fulfil Koch's Postulates, stab inoculations of the four isolates into the petioles of cutting propagated, 38-day-old *S. pictus* plants (3 plants per isolate) were conducted using sterile toothpicks. The amounts of bacteria used was approximately 10<sup>6</sup> cfu per toothpick; the bacterial loads were estimated by suspending the cells in 10 mM MgCl<sub>2</sub> and spread-plating diluted suspensions on NA. Sterile toothpicks were used as control. All tested plants were sealed in plastic bags (containing wet paper towel) and kept in a growth chamber (28°C; 12-h photoperiod). After 1 day, all isolates induced soft rot symptoms resembling those observed under natural conditions in the greenhouse. Bacteria were re-isolated, and they all shared the same *dnaX* sequence with strains Spi1 to Spi4. This is the first report of *S. pictus* affected by *D. dadantii* in Taiwan. Further investigation is needed to determine whether Spi1-Spi4 belong to *D. dadantii* subsp. *dieffenbachiae*. *Dickeya dadantii* has been found infecting different aroids (Lee and Chen 2021; Lin et al. 2012). The species has also been reported in Taiwan on poinsettia (Wei et al., 2019) and philodendron (Wu et al. 2023). Because these plants are often grown closely in the same facilities, growers should be wary of *D. dadantii*'s spread among these plants. Reduction of environmental humidity and avoiding overhead irrigation may be effective in preventing the pathogen's transmission.

### **The complete chloroplast genome sequence of *Anthurium andraeanum* Linden (Araceae; Pothoideae).**

**Wan X, Ge Y, Pan G, Tian D.**

08-03-2023

*Mitochondrial DNA B Resour.*

<https://pubmed.ncbi.nlm.nih.gov/36926637/>

### **Joint effects of gamma radiation and zinc on duckweed *Lemna minor* L.**

**Bodnar IS, Cheban EV.**

Apr-2023

*Aquat Toxicol.*

<https://pubmed.ncbi.nlm.nih.gov/36889126/>

When assessing the consequences of combined chemical and radiation pollution on bodies of water, it is important to take into account the interaction of different factors, especially the possible synergistic increase in the toxic effect on growth, biochemical and physiological processes of living organisms. In this work, we studied the combined effect of γ-radiation and zinc on freshwater duckweed *Lemna minor* L. Irradiated plants (doses were 18, 42, and 63 Gy) were placed on a medium with an excess of zinc (3.15, 6.3, 12.6 μmol/L) for 7 days. Our results showed that the accumulation of zinc in tissues increased in irradiated plants when compared to non-irradiated plants. The interaction of factors in assessing their effect on the growth rate of plants was most often additive, but there was also a synergistic increase in the toxic effect at a zinc concentration of 12.6 μmol/L and irradiation at doses of 42 and 63 Gy. When comparing the combined and separate effects of gamma radiation and zinc, it was found that a reduction in the area of fronds (leaf-like plates) was caused exclusively due to the effects of radiation. Zinc and γ-radiation contributed to the enhancement of membrane lipid peroxidation. Irradiation stimulated the production of chlorophylls a and b, as well as carotenoids.

### **Genomic analysis of *Leishmania turanica* strains from different regions of Central Asia.**

**Novozhilova TS, Chistyakov DS, Akhmadishina LV, Lukashev AN, Gerasimov ES, Yurchenko V.**

06-03-2023

*PLoS Negl Trop Dis.*

<https://pubmed.ncbi.nlm.nih.gov/36877735/>

### **Drug resistance in *Leishmania*: does it really matter?**

**Domagalska MA, Barrett MP, Dujardin JC.**

Apr-2023

*Trends Parasitol.*

<https://pubmed.ncbi.nlm.nih.gov/36803859/>

Treatment failure (TF) jeopardizes the management of parasitic diseases, including leishmaniasis. From the parasite's point of view, drug resistance (DR) is generally considered as central to TF. However, the link between TF and DR, as measured by in vitro drug susceptibility assays, is unclear, some studies revealing an association between treatment outcome and drug susceptibility, others not. Here we address three fundamental questions aiming to shed light on these ambiguities. First, are the right assays being used to measure DR? Second, are the parasites

studied, which are generally those that adapt to in vitro culture, actually appropriate? Finally, are other parasite factors - such as the development of quiescent forms that are recalcitrant to drugs - responsible for TF without DR?

### **CD38<sup>high</sup>/HLA-DR<sup>+</sup> CD8<sup>+</sup> T cells as potential biomarker of hemophagocytic lymphohistiocytosis secondary to visceral Leishmania infection.**

**Mastrolia MV, Boscia S, Galli L, Lodi L, Pisano L, Maccora I, Ricci S, Pagnini I, Marrani E, Azzari C, Simonini G.**

Mar-2023

*Eur J Pediatr.*

<https://pubmed.ncbi.nlm.nih.gov/36631689/>

### **The glycoprotein gp63- a potential pan drug target for developing new antileishmanial agents.**

**Devsani N, Vemula D, Bhandari V.**

Apr-2023

*Biochimie.*

<https://pubmed.ncbi.nlm.nih.gov/36473603/>

Leishmaniasis is a tropical parasitic disease caused by *Leishmania* spp. They cause several presentations of illness ranging from cutaneous leishmaniasis to visceral leishmaniasis. The current arsenal of drugs to treat leishmaniasis is limited, and drug resistance further impedes the problem. Therefore, it is necessary to revisit the available information to identify an alternative or new target for treatment. The glycoprotein 63 (gp63), is a potential anti-leishmanial target that plays a significant role in host-pathogen interaction and virulence. Many studies are ongoing to develop gp63 inhibitors or use it as a vaccine target. In this review, we will discuss the potential of gp63 as a drug target. This review summarises the studies focusing on gp63 as a drug target and its inhibitors identified using in silico approaches.

### **Study of ocular manifestations and humoral immune response in eyes of dogs with leishmaniasis.**

**El Goulli AF, Zribi L, Sanhaji R, Chabchoub A, Bouratbine A, Gharbi M, Abdelmelek H.**

Mar-2023

*Vet Med Sci.*

<https://pubmed.ncbi.nlm.nih.gov/36253884/>

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## **Echinococcosis**

### **Complete excision of giant clavicular hydatid cyst: a case report.**

**Wang X, Huang J, Su L, Ma Q, Ma C, Xie Z.**

22-03-2023

*BMC Infect Dis.*

<https://pubmed.ncbi.nlm.nih.gov/36949399/>

**Background:** Echinococcosis, also known as hydatid disease, is a zoonotic parasitic disease prevalent in pastoral areas, mainly involving the liver and lungs, and less frequently the bones and surrounding soft tissues.

Diagnosis and treatment of bone hydatid disease is a challenge, and because of the insidious course of the disease, the lesions are often widely disseminated by the time patients seek medical attention. **Case presentation:** A 29-year-old woman presented with a painless mass that was gradually increasing in size in the cervical thorax. Imaging revealed an enlarged clavicle with multiple bone cortical defects and the existence of cysts in the soft tissues surrounding the clavicle, for which complete excision of the clavicle and the attached cysts was performed. There was no recurrence of the cyst within one year after the operation, and the patient felt well and had normal shoulder joint movement. **Conclusions:** Bone hydatid may appear in bones throughout the body, and cysts that leak from the bone into the surrounding soft tissues may spread at a relatively rapid rate. Prompt surgical removal of the affected bone and surrounding cysts is necessary for treatment.

### **Parasites as potential targets for cancer immunotherapy.**

**Yousefi M, Akbari M, Hadipour M, Dehkordi AB, Farahbakhsh Z, Darani HY.**

22-03-2023

*J Cancer Res Clin Oncol.*

<https://pubmed.ncbi.nlm.nih.gov/36949175/>

Parasites and cancers have some common antigens. Much scientific evidence in the human population, animal models, and in vitro experiments exhibit that parasites have significant anti-cancer effects. The larval stage of the tapeworm *Echinococcus granulosus*, *Toxoplasma gondii*, *Trypanosoma cruzi*, *Plasmodium*'s, and *Trichinella spiralis* are among the parasites that have been subjects of anti-cancer research in the last decades. Anti-tumor effects of parasites may be due to the direct impact of the parasites per se or indirectly due to the immune response raised against common antigens between malignant cells and parasites. This manuscript reviews the anti-cancer effects of parasites and possible mechanisms of these effects. Options for using parasites or their antigens for cancer treatment in the future have been discussed.

### **Design and functional preliminary investigation of recombinant antigen EgG1Y162-EgG1Y162 against *Echinococcus granulosus*.**

**Zhou Y, Zhao S, Li Y, Yu M, Zheng J, Gong Q, Cao C, Ding J, Zhou X.**

14-03-2023

*Open Life Sci.*

<https://pubmed.ncbi.nlm.nih.gov/36941829/>

### **Acute pancreatitis revealing an isolated hydatid pancreatic cyst simulating a pseudocyst: A case report.**

**Afilal I, Abbou W, Oukrid K, Aichouni N, Nasri S, Kamaoui I, Skiker I.**

07-03-2023

*Radiol Case Rep.*

<https://pubmed.ncbi.nlm.nih.gov/36936800/>

### **Rapid detection of alveolar echinococcosis in hepatic nodules of horses by recombinase polymerase amplification assay.**

Hifumi T, Tanaka T, Sato M, Akioka K, Fujimata C, Miyoshi N.

02-03-2023

*Vet Anim Sci.*

<https://pubmed.ncbi.nlm.nih.gov/36936549/>

Alveolar echinococcosis in slaughtered horses remains a public health issue. This study aimed to develop a Recombinase polymerase amplification (RPA) assay targeting the mitochondrial NADH dehydrogenase subunit 5 (*Nad5*) gene of *Echinococcus multilocularis* for the rapid detection of equine alveolar echinococcosis. Thirty-six hepatic solid nodules obtained from each horse ( $n = 36$ ) were evaluated based on histopathological examination and *Nad5*-targeted PCR and then submitted to the RPA assay. The results of the developed RPA assay were 94.4% consistent with those of *Nad5* PCR and Cohen's kappa coefficient value was 0.89 statistically, indicating high agreement. In addition, the RPA assay using the plasmid samples was one hundredfold more sensitive than PCR testing. Consequently, these results suggest that the performance of the RPA assay developed in this study is equal to that of conventional PCR testing.

### **Update on the genetic diversity and population structure of *Echinococcus granulosus* in Gansu Province, Tibet Autonomous Region, and Xinjiang Uygur Autonomous Region, Western China, inferred from mitochondrial *cox1*, *nad1*, and *nad5* sequences.**

Shumuye NA, Li L, Ohiolei JA, Qurishi SA, Li WH, Zhang NZ, Wu YT, Wu YD, Gao SZ, Zhang FH, Tian XQ, Tian WJ, Fu Y, Wang XZ, Pan YH, Zhan F, Zhang LS, Guo MK, Li WD, Fu BQ, Yan HB, Jia WZ.

18-03-2023

*Parasitol Res.*

<https://pubmed.ncbi.nlm.nih.gov/36933066/>

### **Inhibition of mouse colon cancer growth following immunotherapy with a fraction of hydatid cyst fluid.**

Rostamirad S, Daneshpour S, Mofid MR, Andalib A, Eskandariyan A, Mousavi S, Yousofi Darani H.

15-03-2023

*Exp Parasitol.*

<https://pubmed.ncbi.nlm.nih.gov/36931383/>

### **Immunology of a unique biological structure: the *Echinococcus* laminated layer.**

Díaz Á, Barrios AA, Grezzi L, Mouhape C, Jenkins SJ, Allen JE, Casaravilla C.

16-03-2023

*Protein Cell.*

<https://pubmed.ncbi.nlm.nih.gov/36929004/>

The larval stages of the cestode parasites belonging to the genus *Echinococcus* grow within internal organs of humans and a range of animal species. The resulting diseases, collectively termed echinococcoses, include major neglected tropical diseases of humans and livestock. *Echinococcus* larvae are outwardly protected by the laminated layer (LL), an acellular structure that is unique to this genus. The LL is based on a fibrillar meshwork made up of mucins, which are decorated by galactose-rich O-glycans. In addition, in the species cluster termed *E. granulosus sensu lato*, the LL features nano-deposits of the calcium salt of myo-inositol hexakisphosphate (Insp6). The main purpose of our article is to update the immunobiology of the LL. Major recent advances in this area are (i) the demonstration of LL "debris" at the infection site and draining lymph nodes, (ii) the characterization of the decoy activity of calcium Insp6 with respect to complement, (iii) the evidence that the LL mucin carbohydrates interact specifically with a lectin receptor expressed in Kupffer cells (Clec4F), and (iv) the characterization of what appear to be receptor-independent effects of LL particles on dendritic cells and macrophages. Much information is missing on the immunology of this intriguing structure: we discuss gaps in knowledge and propose possible avenues for research.

### **[Evaluation of the knowledge on alveolar echinococcosis among general practitioners in the province of Liege : impact of a formative intervention].**

Boulanger M, Léonard P, Egrek S, Detry O, Hayette MP.

Mar-2023

*Rev Med Liege.*

<https://pubmed.ncbi.nlm.nih.gov/36924153/>

### **MicroRNA-Transcription factor regulatory networks in the early strobilar development of *Echinococcus granulosus* protoscoleces.**

Mohammadi MA, Mansouri M, Derakhshani A, Rezaie M, Borhani M, Nasibi S, Mousavi SM, Afgar A, Macchiaroli N, Rosenzvit MC, Harandi MF.

15-03-2023

*BMC Genomics.*

<https://pubmed.ncbi.nlm.nih.gov/36922762/>

**Background:** *Echinococcus granulosus sensu lato* has a complex developmental biology with a variety of factors relating to both intermediate and final hosts. To achieve maximum parasite adaptability, the development of the cestode is dependent on essential changes in transcript regulation. Transcription factors (TFs) and miRNAs are known as master regulators that affect the expression of downstream genes through a wide range of metabolic and signaling pathways. In this study, we aimed to develop a regulatory miRNA-Transcription factor (miRNA-TF) network across early developmental stages of *E. granulosus* protoscoleces by performing in silico analysis, and to experimentally validate TFs expression in protoscoleces obtained from in vitro culture, and from in vivo experiments. **Results:** We obtained list of 394 unique *E. granulosus* TFs and matched them with 818

differentially expressed genes which identified 41 predicted TFs with differential expression. These TFs were used to predict the potential targets of 31 differentially expressed miRNAs. As a result, eight miRNAs and eight TFs were found, and the predicted network was constructed using Cytoscape. At least four miRNAs (egr-miR-124a, egr-miR-124b-3p, egr-miR-745-3p, and egr-miR-87-3p) and their corresponding differentially expressed TFs (Zinc finger protein 45, Early growth response protein 3, Ecdysone induced protein 78c and ETS transcription factor elf 2) were highlighted in this investigation. The expression of predicted differentially expressed TFs obtained from in vitro and in vivo experiments, were experimentally validated by quantitative polymerase chain reaction. This confirmed findings of RNA-seq data. **Conclusion:** miRNA-TF networks presented in this study control some of the most important metabolic and signaling pathways in the development and life cycle of *E. granulosus*, providing a potential approach for disrupting the early hours of dog infection and preventing the development of the helminth in the final host.

### Optimization of single-tube nested PCR for the detection of *Echinococcus* spp.

Zhang X, Jian Y, Li Z, Duo H, Guo Z, Fu Y.

Aor-2023

*Exp Parasitol.*

<https://pubmed.ncbi.nlm.nih.gov/36849051/>

Echinococcosis is a serious zoonotic life-threatening parasitic disease caused by metacestodes of *Echinococcus* spp., and appropriate sensitive diagnosis and genotyping techniques are required to detect infections and study the genetic characterization of *Echinococcus* spp. isolates. In this study, a single-tube nested PCR (STNPCR) method was developed and evaluated for the detection of *Echinococcus* spp. DNA based on the COI gene. STNPCR was 100 times more sensitive than conventional PCR and showed the same sensitivity to common nested PCR (NPCR); but with a lower risk of cross-contamination. The limit of detection of the developed STNPCR method was estimated to be 10 copies/ $\mu$ L of the recombinant standard plasmids of *Echinococcus* spp. COI gene. In clinical application, 8 cyst tissue samples and 12 calcification tissue samples were analysed by conventional PCR with outer and inner primers and resulted in 100.00% (8/8) and 8.33% (1/12), 100.00% (8/8) and 16.67% (2/12) positive reactions, respectively, while STNPCR and NPCR were all able to identify the presence of genomic DNA in 100.00% (8/8) and 83.33% (10/12) of the same samples. Due to its high sensitivity combined with the potential for the elimination of cross-contamination, the STNPCR method was suitable for epidemiological investigations and characteristic genetic studies of *Echinococcus* spp. tissue samples. The STNPCR method can effectively amplify low concentrations of genomic DNA from calcification samples and cyst residues infected with *Echinococcus* spp. Subsequently, the sequences of positive PCR products were obtained, which were useful for haplotype analysis, genetic diversity, and evolution studies of *Echinococcus* spp., and understanding of *Echinococcus* spp. dissemination and transmission among the hosts.

### Killing Two Birds with One Stone: Discovery of Dual Inhibitors of Oxygen and Fumarate Respiration in Zoonotic Parasite, *Echinococcus multilocularis*.

Enkai S, Kouguchi H, Inaoka DK, Shiba T, Hidaka M, Matsuyama H, Sakura T, Yagi K, Kita K.

16-03-2023

*Antimicrob Agents Chemother.*

<https://pubmed.ncbi.nlm.nih.gov/36840588/>

### Hydatid disease of the brain and spine.

Padayachy LC, Ozek MM.

Mar-2023

*Childs Nerv Syst.*

<https://pubmed.ncbi.nlm.nih.gov/36443475/>

Hydatid disease of the central nervous system is relatively rare and comprises about 2-3% of all the hydatid cyst cases reported in the world. Spinal hydatid disease is an even rarer entity. It is endemic in sheep and cattle-raising regions, seen mainly in Mediterranean countries including Turkey and Syria. Pediatric neurosurgeons in non-endemic countries face a challenge when they encounter children with hydatid cysts of the central nervous system, mostly due to lack of awareness and the ensuing diagnostic dilemmas. It is also a significant socioeconomic problem in developing countries, due to improper hygiene and lack of dedicated veterinary practice. The clinical features are largely nonspecific and very according to location and severity of disease. However, with the advent of advances in MR imaging, the diagnostic accuracy of hydatid disease involving the brain and spine has increased. Intact removal of the cyst/s, without causing any spillage, and appropriate antihelminthic therapy is the goal and key to cure and prevention of recurrence. In this manuscript, the current literature on hydatid cyst of the brain and spine is reviewed to better understand the epidemiology, pathophysiology, diagnostic accuracy, and advances in therapeutic options. A heightened clinical suspicion, awareness of MR imaging features, improved surgical strategies, and options for prevention are discussed.

### Trématodoses d'origine alimentaire (clonorchiose, opisthorchiase, fasciolase et paragonimose

### Urinary Metabolic Profiling of Liver Fluke-Induced Cholangiocarcinoma-A Follow-Up Study.

Alsaleh M, Sithithaworn P, Khuntikeo N, Loilome W, Yongvanit P, Hughes T, O'Connor T, Andrews RH, Wadsworth CA, Williams R, Koomson L, Cox IJ, Holmes E, Taylor-Robinson SD.

Mar-Apr 2023

*J Clin Exp Hepatol.*



<https://pubmed.ncbi.nlm.nih.gov/36950498/>

**Background/aims:** Global liquid chromatography mass spectrometry (LC-MS) profiling in a Thai population has previously identified a urinary metabolic signature in *Opisthorchis viverrini*-induced cholangiocarcinoma (CCA), primarily characterised by disturbance in acylcarnitine, bile acid, steroid, and purine metabolism. However, the detection of thousands of analytes by LC-MS in a biological sample in a single experiment potentially introduces false discovery errors. To verify these observed metabolic perturbations, a second validation dataset from the same population was profiled in a similar fashion. **Methods:** Reverse-phase ultra-performance liquid-chromatography mass spectrometry was utilised to acquire the global spectral profile of 98 spot urine samples (from 46 healthy volunteers and 52 CCA patients) recruited from Khon Kaen, northeast Thailand (the highest incidence of CCA globally). **Results:** Metabolites were differentially expressed in the urinary profiles from CCA patients. High urinary elimination of bile acids was affected by the presence of obstructive jaundice. The urine metabolome associated with non-jaundiced CCA patients showed a distinctive pattern, similar but not identical to published studies. A panel of 10 metabolites achieved a diagnostic accuracy of 93.4% and area under the curve value of 98.8% (CI = 96.3%-100%) for the presence of CCA. **Conclusions:** Global characterisation of the CCA urinary metabolome identified several metabolites of biological interest in this validation study. Analyses of the diagnostic utility of the discriminant metabolites showed excellent diagnostic potential. Further larger scale studies are required to confirm these findings internationally, particularly in comparison to sporadic CCA, not associated with liver fluke infestation.

### A case of a dog with paragonimiasis after consumption of raw deer meat.

**Yoshimura A, Azakami D, Kishimoto M, Ohmori T, Hirao D, Morita S, Hasegawa S, Morita T, Fukushima R.**

21-03-2023

*J Vet Med Sci.*

<https://pubmed.ncbi.nlm.nih.gov/36948633/>

### Development of an enzyme linked immunosorbent assay using recombinant cathepsin B5 antigen for sero-surveillance of bovine tropical fasciolosis.

**Jacob SS, Sengupta PP, Pavithra BS, Chandu AGS, Raina OK.**

Apr-2023

*Vet Parasitol.*

<https://pubmed.ncbi.nlm.nih.gov/36857937/>

Bovine tropical fasciolosis, caused by *Fasciola gigantica*, is a major parasitic disease in tropical countries responsible for significant production losses in animal husbandry practices. The disease is transmitted by the Radix sp. snails. In the early developmental stage of the parasite, the juveniles and immature flukes cause considerable damage to the liver parenchyma of the bovine host while migrating through the liver. The cathepsin (cat) B5 is a cysteine

protease that is present in the excretory-secretory product of the fluke both in immature and adult stages. The early detection of fasciolosis is very critical in effective disease management. In this study, the cathepsin B5 gene from newly excysted juveniles were cloned, sequenced and analyzed. The phylogenetic analysis revealed existence of two distinct clades. The clade I includes cat B 1 to B3 whereas clade II consist of cat B4 to B7. Further, the present study was aimed to develop an enzyme linked immuno sorbent assay (ELISA) using recombinant cat B5 antigen. The developed enzyme immuno assay showed 95.3 % sensitivity and 92.4 % specificity with a cut-off of 60 % percent positive. It revealed weighted Kappa value as 0.768 (95 % CI 0.648-0.889) when compared with ELISA using native cathepsin protein. Hence, the developed assay can be exploited as a potent tool in the diagnosis and sero-surveillance of bovine tropical fasciolosis.

### Assessment of genetic markers for multilocus sequence typing (MLST) of Fasciola isolates from Iran.

**Nazari N, Rokni MB, Ichikawa-Seki M, Raeghi S, Hajjaran H, Falahi S, Hamzavi Y, Heydarian P, Davari A, Ghadiri K, Bozorgomid A.**

Mar-2023

*Vet Med Sci.*

<https://pubmed.ncbi.nlm.nih.gov/36343016/>

**Background:** Several markers have been described to characterise the population structure and genetic diversity of *Fasciola* species (*Fasciola hepatica* (F. hepatica) and *Fasciola gigantica* (F. gigantica)). However, sequence analysis of a single genomic locus cannot provide sufficient resolution for the genetic diversity of the *Fasciola* parasite whose genomes are ~1.3 GB in size. **Objectives:** To gain a better understanding of the gene diversity of *Fasciola* isolates from western Iran and to identify the most informative markers as candidates for epidemiological studies, five housekeeping genes were evaluated using a multilocus sequence typing (MLST) approach. **Methods:** MLST analysis was developed based on five genes (ND1, Pepck, Pold, Cyt b and HSP70) after genomic DNA extraction, amplification and sequencing. Nucleotide diversity and phylogeny analysis were conducted on both concatenated MLST loci and each individual locus. A median joining haplotype network was created to examine the haplotypes relationship among *Fasciola* isolates. **Results:** Thirty-three *Fasciola* isolates (19 F. hepatica and 14 F. gigantica) were included in the study. A total of 2971 bp was analysed for each isolate and 31 sequence types (STs) were identified among the 33 isolates (19 for F. hepatica and 14 for F. gigantica isolates). The STs produced 44 and 42 polymorphic sites and 17 and 14 haplotypes for F. hepatica and F. gigantica, respectively. Haplotype diversity was  $0.982 \pm 0.026$  and  $1.000 \pm 0.027$  and nucleotide diversity was  $0.00200$  and  $0.00353 \pm 0.00088$  for F. hepatica and F. gigantica, respectively. There was a high degree of genetic diversity with a Simpson's index of diversity of 0.98 and 1 for F. hepatica and F. gigantica, respectively. While HSP70 and Pold haplotypes from *Fasciola* species were separated by one to three mutational steps, the haplotype networks of ND1 and Cyt



b were more complex and numerous mutational steps were found, likely due to recombination.

**Conclusions:** Although HSP70 and Pold genes from *F. gigantica* were invariant over the entire region of sequence coverage, MLST was useful for investigating the phylogenetic relationship of *Fasciola* species. The present study also provided insight into markers more suitable for phylogenetic studies and the genetic structure of *Fasciola* parasites.

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## Mycétome

### The estimated burden of fungal diseases in Mali.

Doumbo SN, Cissoko Y, Dama S, Niangaly A, Garango A, Konaté A, Koné A, Traoré B, Thera M, Djimde A, Denning DW.

Mar-2023

*J Mycol Med.*

<https://pubmed.ncbi.nlm.nih.gov/36270216/>

### Wako $\beta$ -D-glucan assay can be used to measure serum $\beta$ -D-glucan in Sudanese patients to aid with diagnosis of eumycetoma caused by *Madurella mycetomatis*.

Nyuykonge B, Siddig E, Mhmoud NA, Bakhiat S, Zijlstra E, Verbon A, Fahal AH, van de Sande WWJ.

Apr-2023

*J Eur Acad Dermatol Venereol.*

<https://pubmed.ncbi.nlm.nih.gov/36201367/>

**Background:** Eumycetoma is a neglected tropical infection of the subcutaneous tissue commonly caused by the fungus *Madurella mycetomatis*. Previously, we demonstrated that  $\beta$ -D-glucan was present in the serum of eumycetoma patients. **Objective:** To compare the performance of the recently approved easy-to-use Wako  $\beta$ -D-glucan assay to that of the Fungitell assay in eumycetoma patients. **Methods:** Using sera obtained from 41 eumycetoma, 12 actinomycetoma and 29 healthy endemic controls, we measured the  $\beta$ -glucan serum concentrations using the Wako assay and compared the performance to that of the Fungitell assay. **Results:** With the Fungitell assay, median  $\beta$ -glucan serum concentrations of 208, 70 and 27 pg/ml were obtained for the 41 eumycetoma patients, the 12 actinomycetoma patients and the 29 healthy endemic controls, respectively. With the Wako assay these concentrations were 14.45, 11.57 and 2.5 pg/ml, respectively. We demonstrated that when using the optimized cut-off value (5.5 pg/ml) for the Wako assay, the Wako and Fungitell assays had comparable performance in terms of sensitivity and specificity. **Conclusion:** The Wako assay is comparable to the Fungitell assay for measurement of serum  $\beta$ -glucan in mycetoma patients and hence can be used in combination with current diagnostic tools. However, this test should be used in combination with other tests to differentiate actinomycetoma from eumycetoma.

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## Onchocercose

### Unraveling cross-reactivity of anti-glycan IgG responses in filarial nematode infections.

Petralia LMC, van Diepen A, Nguyen DL, Lokker LA, Sartono E, Bennuru S, Nutman TB, Pfarr K, Hoerauf A, Wanji S, Foster JM, Hokke CH.

06-03-2023

*Front Immunol.*

<https://pubmed.ncbi.nlm.nih.gov/36949937/>

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## Schistosomiasis

### Identification and characterisation of the tegument-expressed aldehyde dehydrogenase SmALDH\_312 of *Schistosoma mansoni*, a target of disulfiram.

Beutler M, Harnischfeger J, Weber MHW, Hahnel SR, Quack T, Blohm A, Ueberall ME, Timm T, Lochnit G, Rennar GA, Gallinger TL, Houhou H, Rahlfs S, Falcone FH, Becker K, Schlitzer M, Haeblerlein S, Czermak P, Salz D, Greveling CG.

10-02-2023

*Eur J Med Chem.*

<https://pubmed.ncbi.nlm.nih.gov/36948075/>

Schistosomiasis is an infectious disease caused by blood flukes of the genus *Schistosoma* and affects approximately 200 million people worldwide. Since Praziquantel (PZQ) is the only drug for schistosomiasis, alternatives are needed. By a biochemical approach, we identified a tegumentally expressed aldehyde dehydrogenase (ALDH) of *S. mansoni*, SmALDH\_312. Molecular analyses of adult parasites showed Smaldh\_312 transcripts in both genders and different tissues. Physiological and cell-biological experiments exhibited detrimental effects of the drug disulfiram (DSF), a known ALDH inhibitor, on larval and adult schistosomes in vitro. DSF also reduced stem-cell proliferation and caused severe tegument damage in treated worms. In silico-modelling of SmALDH\_312 and docking analyses predicted DSF binding, which we finally confirmed by enzyme assays with recombinant SmALDH\_312. Furthermore, we identified compounds of the Medicine for Malaria Venture (MMV) pathogen box inhibiting SmALDH\_312 activity. Our findings represent a promising starting point for further development towards new drugs for schistosomiasis.

### Subclinical vascular damage in *Schistosoma* spp. endemic regions.

Silvestri V, Mshana MI, Mushi V, Bonaventura WM, Justine NC, Kinabo C, Zacharia A, La Torre G, Ngasala B.

22-03-2023

*Vasa.*

<https://pubmed.ncbi.nlm.nih.gov/36946126/>

### The balance between gasdermin D and STING signaling shapes the severity of schistosome immunopathology.

Kalantari P, Shecter I, Hopkins J, Pilotta Gois A, Morales Y, Harandi BF, Sharma S, Stadecker MJ.

28-03-2023

*Proc Natl Acad Sci U S A.*

<https://pubmed.ncbi.nlm.nih.gov/36943884/>

There is significant disease heterogeneity among mouse strains infected with the helminth *Schistosoma mansoni*. Here, we uncover a unique balance in two critical innate pathways governing the severity of disease. In the low-pathology setting, parasite egg-stimulated dendritic cells (DCs) induce robust interferon (IFN) $\beta$  production, which is dependent on the cyclic GMP-AMP synthase (cGAS)/stimulator of interferon genes (STING) cytosolic DNA sensing pathway and results in a Th2 response with suppression of proinflammatory cytokine production and Th17 cell activation. IFN $\beta$  induces signal transducer and activator of transcription (STAT)1, which suppresses CD209a, a C-type lectin receptor associated with severe disease. In contrast, in the high-pathology setting, enhanced DC expression of the pore-forming protein gasdermin D (Gsdmd) results in reduced expression of cGAS/STING, impaired IFN $\beta$ , and enhanced pyroptosis. Our findings demonstrate that cGAS/STING signaling represents a unique mechanism inducing protective type I IFN, which is counteracted by Gsdmd.

### Urogenital schistosomiasis outbreak in a basic school, Volta Region, Ghana: a case-control study.

Dsane-Aidoo PH, Odikro MA, Alomatu H, Ametepi D, Akwensy PS, Ameme DK, Kenu E.

13-12-2022

*Pan Afr Med J.*

<https://pubmed.ncbi.nlm.nih.gov/36942139/>

### Efficacy and safety of praziquantel preventive chemotherapy in *Schistosoma mansoni* infected school children in Southern Ethiopia: A prospective cohort study.

Gebreyesus TD, Makonnen E, Tadele T, Mekete K, Gashaw H, Gerba H, Aklillu E.

01-03-2023

*Front Pharmacol.*

<https://pubmed.ncbi.nlm.nih.gov/36937860/>

### Inhibition of signal peptidase complex expression affects the development and survival of *Schistosoma japonicum*.

Yang WB, Luo F, Zhang W, Sun CS, Tan C, Zhou A, Hu W.

03-03-2023

*Front Cell Infect Microbiol.*

<https://pubmed.ncbi.nlm.nih.gov/36936776/>

**Background:** Schistosomiasis, the second most neglected tropical disease defined by the WHO, is a significant zoonotic parasitic disease infecting approximately 250 million people globally. This debilitating disease has

seriously threatened public health, while only one drug, praziquantel, is used to control it. Because of this, it highlights the significance of identifying more satisfactory target genes for drug development. Protein translocation into the endoplasmic reticulum (ER) is vital to the subsequent localization of secretory and transmembrane proteins. The signal peptidase complex (SPC) is an essential component of the translocation machinery and functions to cleave the signal peptide sequence (SP) of secretory and membrane proteins entering the ER. Inhibiting the expression of SPC can lead to the abolishment or weaker cleavage of the signal peptide, and the accumulation of uncleaved protein in the ER would affect the survival of organisms. Despite the evident importance of SPC, *in vivo* studies exploring its function have yet to be reported in *S. japonicum*. **Methods:** The *S. japonicum* SPC consists of four proteins: *SPC12*, *SPC18*, *SPC22* and *SPC25*. RNA interference was used to investigate the impact of SPC components on schistosome growth and development *in vivo*. qPCR and *in situ* hybridization were applied to localize the *SPC25* expression. Mayer's carmalum and Fast Blue B staining were used to observe morphological changes in the reproductive organs of dsRNA-treated worms. The effect of inhibitor treatment on the worm's viability and pairing was also examined *in vitro*. **Results:** Our results showed that RNAi-SPC delayed the worm's normal development and was even lethal for schistosomula *in vivo*. Among them, the expression of *SPC25* was significantly higher in the developmental stages of the reproductive organs in schistosomes. Moreover, *SPC25* possessed high expression in the worm tegument, testes of male worms and the ovaries and vitellarium of female worms. The *SPC25* knockdown led to the degeneration of reproductive organs, such as the ovaries and vitellarium of female worms. The *SPC25* exhaustion also reduced egg production while reducing the pathological damage of the eggs to the host. Additionally, the SPC-related inhibitor AEBSF or suppressing the expression of *SPC25* also impacted cultured worms' pairing and viability *in vitro*. **Conclusions:** These data demonstrate that SPC is necessary to maintain the development and reproduction of *S. japonicum*. This research provides a promising anti-schistosomiasis drug target and discovers a new perspective on preventing worm fecundity and maturation.

### Prevalence of malaria-helminth co-infections among children living in a setting of high coverage of standard interventions for malaria and helminths: Two population-based studies in Senegal.

Afolabi MO, Sow D, Mbaye I, Diouf MP, Loum MA, Fall EB, Seck A, Manga IA, Cissé C, Camara B, Diouf A, Gaye NA, Colle Lo A, Greenwood B, Ndiaye JLA.

02-03-2023

*Front Public Health.*

<https://pubmed.ncbi.nlm.nih.gov/36935683/>

### **Inhibition of hepatic natural killer cell function via the TIGIT receptor in schistosomiasis-induced liver fibrosis.**

Gao Y, Zhang X, Jiang T, Zhou H, Liu H, Hu Y, Cao J.  
17-03-2023

*PLoS Negl Trop Dis.*

<https://pubmed.ncbi.nlm.nih.gov/36930687/>

Schistosomiasis is a zoonotic parasitic disease. *Schistosoma japonicum* eggs deposited in the liver tissue induce egg granuloma formation and liver fibrosis, seriously threatening human health. Natural killer (NK) cells kill activated hepatic stellate cells (HSCs) or induce HSC apoptosis and inhibit the progression of liver fibrosis. However, the function of NK cells in liver fibrosis caused by *S. japonicum* infection is significantly inhibited. The mechanism of this inhibition remains unclear. Twenty mice were percutaneously infected with *S. japonicum* cercariae. Before infection and 2, 4, 6, and 8 weeks after infection, five mice were euthanized and dissected at each time point. Hepatic NK cells were isolated and transcriptome sequenced. The sequencing results showed that Tigit expression was high at 4-6 weeks post infection. This phenomenon was verified by reverse transcription quantitative PCR (RT-qPCR) and flow cytometry. NK cells derived from Tigit<sup>-/-</sup> and wild-type (WT) mice were co-cultured with HSCs. It was found that Tigit<sup>-/-</sup> NK cells induced apoptosis in a higher proportion of HSCs than WT NK cells. Schistosomiasis infection models of Tigit<sup>-/-</sup> and WT mice were established. The proportion and killing activity of hepatic NK cells were significantly higher in Tigit<sup>-/-</sup> mice than in WT mice. The degree of liver fibrosis in Tigit<sup>-/-</sup> mice was significantly lower than that in WT mice. NK cells were isolated from Tigit<sup>-/-</sup> and WT mice and injected via the tail vein into WT mice infected with *S. japonicum*. The degree of liver fibrosis in mice that received NK cell infusion reduced significantly, but there was no significant difference between mice that received NK cells from Tigit<sup>-/-</sup> and WT mice, respectively. Our findings indicate that Tigit knockout enhanced the function of NK cells and reduced the degree of liver fibrosis in schistosomiasis, thus providing a novel strategy for treating hepatic fibrosis induced by schistosomiasis.

### **Unisexual infection with *Schistosoma mansoni* in mice has the potential to boost the immune response against eggs after challenge infection.**

Reinholdt C, Winkelmann F, Koslowski N, Reisinger EC, Sombetzki M.

24-02-2023

*Front Immunol.*

<https://pubmed.ncbi.nlm.nih.gov/36923416/>

### **First report of *Biomphalaria tenagophila* (d'Orbigny, 1835) (Gastropoda/Planorbidae) in Pará State, Amazon region of Brazil.**

Goveia CO, Caldeira RL, Barata RR, Lemos PDS, Teixeira Nunes MR, Dias IHL, Enk MJ.

Apr-2023

*Exp Parasitol.*

<https://pubmed.ncbi.nlm.nih.gov/36801395/>

### **First bovine vaccine to prevent human schistosomiasis - a cluster randomised Phase 3 clinical trial.**

Ross AG, Harn DA, Chy D, Inobaya M, Guevarra JR, Shollenberger L, Li Y, McManus DP, Gray DJ, Williams GM.

Apr-2023

*Int J Infect Dis.*

<https://pubmed.ncbi.nlm.nih.gov/36736992/>

**Objective:** Schistosomiasis is a neglected tropical parasitic disease caused by blood flukes of the genus *Schistosoma*. *Schistosoma japonicum* is zoonotic in China, the Philippines, and Indonesia, with bovines acting as major reservoirs of human infection. The primary objective of the trial was to examine the impact of a combination of human mass chemotherapy, snail control through mollusciciding, and SJCPTI bovine vaccination on the rate of human infection. **Methods:** A 5-year phase IIIa cluster randomized control trial was conducted among 18 schistosomiasis-endemic villages comprising 18,221 residents in Northern Samar, The Philippines. **Results:** Overall, bovine vaccination resulted in a statistically significant decrease in human infection (relative risk [RR] = 0.75; 95% confidence interval [CI] = 0.69 to 0.82) across all trial follow-ups. The best outcome of the trial was when bovine vaccination was combined with snail mollusciciding. This combination resulted in a 31% reduction (RR = 0.69; 95% CI = 0.61 to 0.78) in human infection. **Conclusion:** This is the first trial to demonstrate the effectiveness of a bovine vaccine for schistosomiasis in reducing human schistosome infection. The trial is registered with Australian New Zealand Clinical Trials Registry (ACTRN12619001048178).

### **The role of the host gut microbiome in the pathophysiology of schistosomiasis.**

Stark KA, Rinaldi G, Cortés A, Costain A, MacDonald AS, Cantacessi C.

*Parasite Immunol.* 2023 Apr

<https://pubmed.ncbi.nlm.nih.gov/36655799/>

The pathophysiology of schistosomiasis is linked to the formation of fibrous granulomas around eggs that become trapped in host tissues, particularly the intestines and liver, during their migration to reach the lumen of the vertebrate gut. While the development of *Schistosoma* egg-induced granulomas is the result of finely regulated crosstalk between egg-secreted antigens and host immunity, evidence has started to emerge of the likely contribution of an additional player-the host gut microbiota-to pathological processes that culminate with the formation of these tissue lesions. Uncovering the role(s) of schistosome-mediated changes in gut microbiome composition and function in granuloma formation and, more broadly, in the pathophysiology of schistosomiasis, will shed light on the mechanisms underlying this three-way parasite-host-microbiome interplay. Such knowledge may, in turn, pave the way towards the discovery of novel therapeutic targets and control strategies.

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

### Emergence of *Ancylostoma caninum* parasites with the benzimidazole resistance F167Y polymorphism in the US dog population.

Leutenegger CM, Lozoya CE, Tereski J, Savard C, Ogeer J, Lallier R.

14-03-2023

*Int J Parasitol Drugs Drug Resist.*

<https://pubmed.ncbi.nlm.nih.gov/36958067/>

**Background:** Anthelmintic resistance to benzimidazole has been detected in the canine hookworm, *Ancylostoma caninum*. Benzimidazole resistance is believed to have developed originally in greyhounds, but has also been detected in non-greyhound pet dogs. The aim of this study was to validate a probe-based allele-specific real-time PCR tests for the F167Y polymorphism on the  $\beta$ -tubulin isotype-1 gene and to determine the geographic distribution. **Methods:** Allele-specific real-time PCR tests were established and validated to detect the codon 167 polymorphism in the *Ancylostoma caninum*  $\beta$ -tubulin isotype-1 gene. Additionally, real-time PCR tests were validated for *Ancylostoma* spp. and *Uncinaria stenocephala*. Two nucleic acid extraction protocols were validated including mechanical disruption of parasite structures in stool. The frequency of the F167Y single nucleotide polymorphism (SNP) was determined in hookworm confirmed stool samples. Samples with the resistant 167Y genotype were confirmed by  $\beta$ -tubulin gene sequencing and allele frequencies were determined. **Results:** The *Ancylostoma* spp. and *A. caninum* F167Y allele-specific real-time PCR tests were highly sensitive and specific when tested against synthetic DNA, spiked samples, and characterized parasites. Using an optimized total nucleic acid extraction protocol, 54 of 511 (10.6%) were found to contain the benzimidazole resistance allele. All 55 samples containing hookworms with the resistance mutation were confirmed by  $\beta$ -tubulin gene sequencing. The majority of resistant hookworms (44 resistant, 183 tested; 24.4%) originated from Florida, five from California (103 tested, 4.9%), three from Idaho (40 tested, 7.5%), two from Nevada (22 tested, 9.1%), and one sample from Hawaii (13 tested, 7.7%). Resistant genotypes were found in 14 different dog breeds including eight in Greyhounds. Allele-frequency determination revealed resistance allele frequencies between 1 and 100% with 58% above 50%. **Conclusions:** This data strongly supports recent findings of benzimidazole resistant canine hookworms present throughout the general US pet dog population.

### Continuity in intestinal parasite infection in Aalst (Belgium) from the medieval to the early modern period (12th-17th centuries).

Rabinow S, Deforce K, Mitchell PD.

20-03-2023

*Int J Paleopathol.*

<https://pubmed.ncbi.nlm.nih.gov/36947954/>

**Objective:** To characterize patterns in the taxonomic diversity of parasites infecting the population of Aalst, Belgium, between the 12th and 17th centuries. **Materials:** 14 sediment samples from seven cesspits dated 1100-1700 CE. **Methods:** Digital light microscopy and Enzyme-linked immunosorbent assay (ELISA). **Results:** We identified eggs of four species of helminths: whipworm (*Trichuris trichiura*), roundworm (*Ascaris lumbricoides*), *Echinostoma* fluke and *Dicrocoelium* fluke. ELISA results for protozoal parasites were negative. **Conclusions:** Taxonomic diversity of parasite infections remained constant from the 12th to the 17th centuries. Roundworm and whipworm, spread by poor sanitation, were dominant. Two species of zoonotic parasites were also identified, including for the first time ever in the Low Countries the *Echinostoma* fluke, which may have been spread by eating uncooked freshwater animal foods. **Significance:** Analysis of sediment samples spanning such a broad chronology (six centuries) from a single city offers the opportunity to track diachronic change, which is rare in paleoparasitological studies. **Limitations:** We were unable to acquire samples from cesspits dating to the 14th century. **Suggestions for further research:** Additional data from other Low Countries towns may strengthen the patterns identified in this paper. A similar approach can be used to investigate towns in different regions of the world.

### Predisposition to soil-transmitted helminth reinfection after four rounds of mass drug administration: results from a longitudinal cohort in the Geshiyaro project, a transmission elimination feasibility study in the Wolaita zone of southern Ethiopia.

Rayment Gomez S, Maddren R, Liyew EF, Chernet M, Anjulo U, Tamiru A, Mengitsu B, Forbes K, Collyer B, Salasibew M, Anderson R.

20-03-2023

*Trans R Soc Trop Med Hyg.*

<https://pubmed.ncbi.nlm.nih.gov/36939014/>

### Malarial and intestinal parasitic co-infections in indigenous populations of the Brazilian Amazon rainforest.

Vasconcelos MPA, Sánchez-Arcila JC, Peres L, de Sousa PSF, Dos Santos Alvarenga MA, Castro-Alves J, de Fatima Ferreira-da-Cruz M, Maia-Herzog M, Oliveira-Ferreira J.

Apr-2023

*J Infect Public Health*

<https://pubmed.ncbi.nlm.nih.gov/36842196/>

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## Gale

### Human ectoparasitosis by mites of the genus *Pyemotes* Amerling 1861 (Acarina: Pyemotidae).



**Stingeni L, Hansel K, Casciola G, Bianchi L, Tramontana M, Marietti R, Zampetti S, Napoli F, Miñón Llera G, Biancolini F, Romani R, Sevarika M, Masini P.**  
Feb-2023

*Ital J Dermatol Venerol.*

<https://pubmed.ncbi.nlm.nih.gov/36598397/>

The mites of the family Pyemotidae Berlese (1897) are a large family of ectoparasitoid arthropods, known as pathogen for humans since the 18<sup>th</sup> century and responsible for the so-called "straw itch" or "grain itch" in granary and dock workers. The identified species of the genus *Pyemotes* are divided into two groups: the scolyti group (*P. scolyti*, *P. parviscolyti* and *P. dimorphus*) and the ventricosus group (*P. tritici* and *P. ventricosus*). The first group is characterized by nonvenomous mites usually parasitizing bark beetles; the ventricosus group includes species associated with a large number of hosts (Coleoptera, Lepidoptera, Hymenoptera, Diptera and Rhynchota), parasitizing all host stages, often highly poisonous and responsible for itchy skin lesions for humans. Several species of *Pyemotes* mites can be pathogenic to humans, especially in spring and summer and in indoor environments, where worm-eaten wood or infested foodstuffs are present. The most frequent clinical feature is the "strophulus," characterized by small erythematous, edematous, and papular lesions centered by a tiny vesicle evolving into a small erosion covered by crust, or by a central hemorrhagic punctum. Other less frequently observed clinical features are urticaria-like lesions, erythematous excoriated papular and pustular lesions, and rarely scabies-like eruptions. The parasitological diagnosis together with the environmental disinfection and removing of each substrate infested by insects parasitized by Pyemotidae is mandatory to definitely solve *Pyemotes* dermatitis.

### Scabies and Fairyfly: more than meets the eye.

**Ranjan E, Arora S, Radhakrishnan S, Rameshkumar A.**  
17-03-2023

*Clin Exp Dermatol.*

<https://pubmed.ncbi.nlm.nih.gov/36928356/>

### One versus two doses of ivermectin-based mass drug administration for the control of scabies: A cluster randomised non-inferiority trial.

**Lake SJ, Engelman D, Zinihite J, Sokana O, Boara D, Nasi T, Gorae C, Osti MH, Phelan S, Parnaby M, Grobler AC, Schuster T, Andrews R, Whitfield MJ, Marks M, Romani L, Steer AC, Kaldor JM.**  
17-03-2023

*PLoS Negl Trop Dis.*

<https://pubmed.ncbi.nlm.nih.gov/36930667/>

**Background:** Mass drug administration (MDA) based on two doses of ivermectin, one week apart, substantially reduces prevalence of both scabies and impetigo. The Regimens of Ivermectin for Scabies Elimination (RISE) trial assessed whether one-dose ivermectin-based MDA would be as effective. **Methods:** RISE was a cluster-randomised trial in Solomon Islands. We assigned 20 villages in a 1:1

ratio to one- or two-dose ivermectin-based MDA. We planned to test whether the impact of one dose on scabies prevalence at 12 and 24 months was non-inferior to two, at a 5% non-inferiority margin. **Results:** We deferred endpoint assessment to 21 months due to COVID-19. We enrolled 5239 participants in 20 villages at baseline and 3369 at 21 months from an estimated population of 5500. At baseline scabies prevalence was similar in the two arms (one-dose 17.2%; two-dose 13.2%). At 21 months, there was no reduction in scabies prevalence (one-dose 18.7%; two-dose 13.4%), and the confidence interval around the difference included values substantially greater than 5%. There was however a reduction in prevalence among those who had been present at the baseline assessment (one-dose 15.9%; two-dose 10.8%). Additionally, we found a reduction in both scabies severity and impetigo prevalence in both arms, to a similar degree. **Conclusions:** There was no indication of an overall decline in scabies prevalence in either arm. The reduction in scabies prevalence in those present at baseline suggests that the unexpectedly high influx of people into the trial villages, likely related to the COVID-19 pandemic, may have compromised the effectiveness of the MDA. Despite the lack of effect there are important lessons to be learnt from this trial about conducting MDA for scabies in high prevalence settings.

### Combination of Crusted Scabies with Bullous Scabies: A Rare Case.

**Asnawi V, Maulida M, Hidayati A, Gunawan H, Dwiyanara RF, Hindritiani R.**

11-03-2023

*Int Med Case Rep J.*

<https://pubmed.ncbi.nlm.nih.gov/36936186/>

### A horse or a zebra? Unusual manifestations of common cutaneous infections in primary immunodeficiency pediatric patients.

**Ollech A, Simon AJ, Lev A, Stauber T, Sherman G, Solomon M, Barzilai A, Somech R, Greenberger S.**

06-03-2023

*Front Pediatr.*

<https://pubmed.ncbi.nlm.nih.gov/36950172/>

**Background:** Patients with primary immunodeficiency disorders (PIDs) often suffer from recurrent infections because of their inappropriate immune response to both common and less common pathogens. These patients may present with unique and severe cutaneous infectious manifestations that are not common in healthy individuals and may be more challenging to diagnose and treat.

**Objective:** To describe a cohort of patients with PIDs with atypical presentations of skin infections, who posed a diagnostic and/or therapeutic challenge. **Methods:** This is a retrospective study of pediatric patients with PID with atypical presentations of infections, who were treated at the immunodeficiency specialty clinic and the pediatric dermatology clinic at the Sheba Medical Center between September 2012 and August 2022. Epidemiologic data, PID diagnosis, infectious etiology, presentation, course, and treatment were recorded. **Results:** Eight children with



a diagnosis of PID were included, five of whom were boys. The average age at PID diagnosis was 1.7 ( $\pm$ SD 3.2) years. The average age of cutaneous infection was 6.9 ( $\pm$ SD 5.9) years. Three patients were born to consanguineous parents. The PIDs included the following: common variable immunodeficiency, severe combined immunodeficiency, DOCK8 deficiency, ataxia telangiectasia, CARD11 deficiency, MALT1 deficiency, chronic granulomatous disease, and a combined cellular and humoral immunodeficiency syndrome of unknown etiology. The infections included the following: ulcerative-hemorrhagic varicella-zoster virus (two cases) atypical fungal and bacterial infections, resistant Norwegian scabies, giant perianal verrucae (two cases), and diffuse molluscum contagiosum. **Conclusions:** In this case series, we present unusual manifestations of infectious skin diseases in pediatric patients with PID. In some of the cases, recognition of the infectious process prompted life-saving treatment. Increasing familiarity with these dermatological manifestations, as well as keeping a high index of suspicion, is important to enabling early diagnosis of cutaneous infections in PIDs and initiation of prompt suitable treatment.

## Morsures de serpent

### The clinical efficacy of Zuqing Xu "Wuduling" powder for snake injury on the swelling of the affected limb bitten by *Agkistrodon halys*.

Ye J, Qian W, Chen N, Hu Z, Ye S, Li M, Zhang L, Wang H, Lu Y.

22-03-2023

*Biotechnol Genet Eng Rev.*

<https://pubmed.ncbi.nlm.nih.gov/36946536/>

To determine the clinical efficacy of Zuqing Xu 'Wuduling' powder for snake injury on the swelling of the affected limb bitten by *Agkistrodon halys*. Sixty-five patients with *Agkistrodon halys* bite were assigned to a treatment group ( $n = 35$ ) or control group ( $n = 30$ ). The treatment group was additionally given 'Wuduling' powder dressing locally based on the therapy to the control group with conventional Western medicine. Clinical efficacy and improvement of traditional Chinese medicine symptoms and signs in the two groups were evaluated. The treatment group showed a notably higher cure rate than the control group. After 3 days of therapy, the swelling and pain of the affected limb in the treatment group were greatly alleviated. Additionally, after 7 days of therapy, the swelling and pain of the affected limb in the treatment group were more greatly alleviated, and those in the control group were also alleviated. The comparison of the two groups during the same period showed more obvious alleviation of swelling and pain in the treatment group than that in the other. Moreover, the treatment group experienced notably shorter disappearing time of swelling and pain than the control group. After treatment, the levels of CRP, TBIL, Cr, ALT, AST, BUN, CK, LDH and CK-MB in both groups declined notably, with notably lower levels of them in the treatment group than those in the other. Zuqing Xu 'Wuduling' powder for snake injury can

substantially alleviate the swelling and local pain of affected limbs bitten by *Agkistrodon halys*.

### Clinical predictors of early surgical intervention in patients with venomous snakebites.

Lu HY, Mao YC, Liu PY, Lai KL, Wu CY, Tsai YC, Yen JH, Chen IC, Lai CS.

21-03-2023

*Eur J Med Res.*

<https://pubmed.ncbi.nlm.nih.gov/36945006/>

### Clinical aspects of snakebite envenoming and its treatment in low-resource settings.

Warrell DA, Williams DJ.

14-03-2023

*Lancet.*

<https://pubmed.ncbi.nlm.nih.gov/36931290/>

There is increasing recognition of the public health importance of snakebite envenoming. Worldwide annual incidence is likely to be 5 million bites, with mortality exceeding 150 000 deaths, and the resulting physical and psychological morbidity leads to substantial social and economic repercussions. Prevention through community education by trained health workers is the most effective and economically viable strategy for reducing risk of bites and envenoming. Clinical challenges to effective treatment are most substantial in rural areas of low-resource settings, where snakebites are most common. Classic skills of history taking, physical examination, and use of affordable point-of-care tests should be followed by monitoring of evolving local and systemic envenoming. Despite the profusion of new ideas for interventions, hyperimmune equine or ovine plasma-derived antivenoms remain the only specific treatment for snakebite envenoming. The enormous interspecies and intraspecies complexity and diversity of snake venoms, revealed by modern venomomics, demands a radical redesign of many current antivenoms.

### Epidemiology of secondary infection after snakebites in center-west Brazil.

Soares Coriolano Coutinho JV, Fraga Guimarães T, Borges Valente B, Gomes Martins de Moura Tomich L.

06-03-2023

*PLoS Negl Trop Dis.*

<https://pubmed.ncbi.nlm.nih.gov/36877732/>

**Background:** Snakebites represent a significant health problem in tropical countries, with an annual incidence of 2.7 million cases worldwide. The incidence of secondary infections after snake bites is also high and is usually caused by bacteria from the oral cavity of snakes. *Morganella morganii* has been identified as an important cause of infections and has been guiding antibiotic therapy in several regions of Brazil and the world.

**Methodology/principal findings:** We performed a retrospective cross-sectional evaluation of snakebites in hospitalized patients between January 2018 and November 2019 and selected those with secondary

infection in their medical records. During the period, 326 cases of snakebites were treated, and 155 (47.5%) of them eventually had secondary infections. However, only seven patients underwent culture of soft tissue fragments, in which three cases were negative culture results, while *Aeromonas hydrophila* was identified in four cases. Of these, 75% were resistant to ampicillin/sulbactam, 50% had intermediate sensitivity to imipenem, and 25% had intermediate sensitivity to piperacillin/tazobactam. Trimethoprim/sulfamethoxazole (TMP-SMX) was not tested on any strain. Of the 155 cases that progressed to secondary infections, 48.4% (75) were empirically treated with amoxicillin/clavulanate, 41.9% (65) with TMP-SMX, and 32 (22%) of these 144 cases required a change to a second regimen, and 10 of these 32 patients required a third therapeutic regimen. **Conclusion:** Wild animals act as reservoirs of resistant bacteria because their oral cavity favors biofilm formation, which explains the finding of *A. hydrophila* with a reduced sensitivity profile in this study. This fact is essential for the appropriate choice of empirical antibiotic therapy.

### **Case of small eyed snake envenoming.**

**Young R, Little M.**

Apr-2023

*Emerg Med Australas.*

<https://pubmed.ncbi.nlm.nih.gov/36574962/>