# Veille scientifique
# Maladies tropicales négligées

**Semaine 07**
*13 au 19 février 2022*

# Dengue, chikungunya et maladie à virus Zika

## Understanding "Hybrid Immunity": Comparison and Predictors of Humoral Immune Responses to Severe Acute Respiratory Syndrome Coronavirus 2 Infection (SARS-CoV-2) and Coronavirus Disease 2019 (COVID-19) Vaccines.

Epsi NJ, Richard SA, Lindholm DA, Mende K, Ganesan A, Huprikar N, Lalani T, Fries AC, Maves RC, Colombo RE, Larson DT, Smith A, Chi SW, Maldonado CJ, Ewers EC, Jones MU, Berjohn CM, Libraty DH, Edwards MS, English C, Rozman JS, Mody RM, Colombo CJ, Samuels EC, Nwachukwu P, Tso MS, Scher AI, Byrne C, Rusiecki J, Simons MP, Tribble D, Broder CC, Agan BK, Burgess TH, Laing ED, Pollett SD; Epidemiology, Immunology, and Clinical Characteristics of Emerging Infectious Diseases with Pandemic Potential COVID-19 Cohort Study Group.

**Background:** Comparison of humoral responses in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccinees, those with SARS-CoV-2 infection, or combinations of vaccine/ infection ("hybrid immunity") may clarify predictors of vaccine immunogenicity. **Methods:** We studied 2660 US Military Health System beneficiaries with a history of SARS-CoV-2 infection-alone (n = 705), vaccination-alone (n = 932), vaccine-after-infection (n = 869), and vaccine-breakthrough-infection (n = 154). Peak anti-spike-immunoglobulin G (IgG) responses through 183 days were compared, with adjustment for vaccine product, demography, and comorbidities. We excluded those with evidence of clinical or subclinical SARS-CoV-2 reinfection from all groups. **Results:** Multivariable regression results indicated that vaccine-after-infection anti-spike-IgG responses were higher than infection-alone (P < .01), regardless of prior infection severity. An increased time between infection and vaccination was associated with greater post-vaccination IgG response (P < .01). Vaccination-alone elicited a greater IgG response but more rapid waning of IgG (P < .01) compared with infection-alone (P < .01). BNT162b2 and mRNA-1273 vaccine-receipt was associated with greater IgG responses compared with JNJ-78436735 vaccine-receipt (P < .01), regardless of infection history. Those with vaccine-after-infection or vaccine-breakthrough-infection had a more durable anti-spike-IgG response compared to infection-alone (P < .01). **Conclusions:** Vaccine-receipt elicited higher anti-spike-IgG responses than infection-alone, although IgG levels waned faster in those vaccinated (compared to infection-alone). Vaccine-after-infection elicits a greater humoral response compared with vaccine or infection alone; and the timing, but not disease severity, of prior infection predicted these post-vaccination IgG responses. While differences between groups were small in magnitude, these results offer insights into vaccine immunogenicity variations that may help inform vaccination timing strategies.

## Clinical Safety Experience of TAK-003 for Dengue Fever: A New Tetravalent Live Attenuated Vaccine Candidate.

Patel SS, Rauscher M, Kudela M, Pang H.

## Neurodevelopmental outcomes in a cohort of children with congenital Zika syndrome at 12 and 24 months of age.

Marques FJP, Amarante C, Elias MAC, Klein R, Nascimento OJM, Leyser M.

**Background:** Early child development is a critical stage of life that influences social, educational and health outcomes worldwide. A few years after Zika epidemic, families of children born with congenital Zika syndrome (CZS) continue to face uncertainties when it comes to the development of their children. The present study sought to analyse the developmental trajectories of a subset of children born with CZS in the first 24 months of life. **Methods:** Thirty-five children with CZS were assessed with the Bayley-III Scales at 12 and 24 months of age from November 2016 to December 2018 in a rehabilitation centre in Brazil. Inclusion criteria included children with established diagnosis of CZS. Exclusion criteria included the presence of arthrogryposis, prematurity, irregular follow-up, clinical complications or other causes of microcephaly. Children born with CZS who evolved with cerebral palsy (CP) were classified according to the Gross Motor Function Classification System (GMFCS) at 2 years of age. **Results:** At 12 months of age mean composite scores on the Bayley cognitive, communication and motor scores were 57.71 (SD 7.11), 57.94 (SD 14.34) and 49.26 (7.20), respectively. At 24 months of age, composite scores were 57.43 (SD 7.11), 53.60 (SD 12.29) and 48.83 (7.76). In addition, 31 (88.57%) out of 34 children diagnosed with CP were classified as GMFCS levels IV and V. **Conclusion:** Zika virus congenital infection is a risk factor for functional impairments across all developmental domains having a direct and substantial negative impact in early child development.

## Satellite observation to assess dengue risk due to Aedes aegypti and Aedes albopictus in a subtropical city of Argentina.

Martín ME, Alonso AC, Faraone J, Stein M, Estallo EL.

## Arbovirus detection in synanthropic mosquitoes from the Brazilian Amazon and in mosquito saliva using Flinders Technology Associates cards.

**Rios FGF, Alves do Nascimento V, Naveca FG, Vieira DS, Julião GR.**
Mar-Apr 2023
*Microbes Infect.*
https://pubmed.ncbi.nlm.nih.gov/36167274/

## Two for the price of one: itaconate and its derivatives as an anti-infective and anti-inflammatory immunometabolite.

**McGettrick AF, O'Neill LA.**
Feb-2023
*Curr Opin Immunol.*
https://pubmed.ncbi.nlm.nih.gov/36446152/

The metabolite itaconate (ITA) and its derivatives, both chemically synthesized and endogenous, have emerged as immunoregulators, with roles in limiting inflammation but also having effects on bacterial and viral infection. Some members of the ITA family have been shown to target and inhibit multiple processes in macrophages with recently identified targets, including NLRP3, JAK1, ten-eleven translocation-2 dioxygenases, and TFEB, a key transcription factor for lysosomal biogenesis. They have also been shown to target multiple bacteria, inhibiting their replication, as well as having antiviral effects against viruses such as SARS-CoV2, Zika virus, and Influenza virus. The importance of ITA is highlighted by the fact that several pathogens have developed mechanisms to evade ITA and can manipulate ITA for their own gain. Two newly discovered isomers of ITA, mesaconate and citraconate, are also discussed, which also have immunomodulatory effects. ITA continues to be a fascination, both in terms of inflammation but also as an antibacterial and antiviral agent, with therapeutic potential in immune and inflammatory diseases.

## Rhodanine derivatives: An insight into the synthetic and medicinal perspectives as antimicrobial and antiviral agents.

**Chaurasyia A, Chawla P, Monga V, Singh G.**
Mar-2023
*Chem Biol Drug Des.*
https://pubmed.ncbi.nlm.nih.gov/36447391/

## Discrepant Activation Pattern of Inflammation and Pyroptosis Induced in Dermal Fibroblasts in Response to Dengue Virus Serotypes 1 and 2 and Nonstructural Protein 1.

**Wei KC, Wei WJ, Liao CL, Chang TH.**
14-02-2023
*Microbiol Spectr.*
https://pubmed.ncbi.nlm.nih.gov/36629424/

## Influence of Dosing Regimen and Adjuvant Type on the Immunogenicity of Novel Recombinant Zika Virus-Like Particles.

**Brzuska G, Szewczyk B, Krol E.**
14-02-2023
*Microbiol Spectr.*

https://pubmed.ncbi.nlm.nih.gov/36541807/
Zika virus (ZIKV) is a reemerging mosquito-borne flavivirus that causes febrile illness and is also linked to Guillain-Barré syndrome as well as to microcephaly in newborns. Due to the risk of fetuses developing microcephaly, ZIKV is a serious problem for pregnant women. Although different types of vaccine antigens have been investigated, there is still no approved vaccine that prevents ZIKV. The aim of this study was to produce a potential anti-Zika virus vaccine candidate based on virus-like particles (VLPs) in mammalian cells and to analyze the role of dosing regimen and adjuvant type on the immunogenicity of the obtained antigen. Novel recombinant VLPs (F2A) were designed by introducing the optimized signal sequence of prM protein and by adding a self-cleavage peptide 2A between proteins prM and E. These modifications improved the formation of the glycoprotein E dimer. It has been shown that the increasing dosing regimen generates a significantly higher titer of antibodies; however, the adjuvant type does not affect this process. Sera from mice immunized using an increasing dosing schedule also showed higher neutralization activity against both Zika strains (H/PAN/2016/BEI-259634, a pandemic strain belonging to Asian lineage, and MR766, a reference strain from African lineage). In summary, this is the first report showing the influence of vaccination schedules and adjuvants on the immunogenicity of ZIKV virus-like particles. **IMPORTANCE** Considering the transmission of ZIKV and the risk of another epidemic as well as the neurological complications that follow ZIKV infection, the virus remains a serious problem for the human population, especially pregnant women. Therefore, there is a great need to develop new effective vaccine candidates. Although different types of vaccine antigens have been used in preclinical studies worldwide, there is still no approved vaccine to prevent ZIKV. VLPs are among the most potent antigens, but to use VLPs, adjuvants must be added to the formulation and appropriate administration must be performed. In this study, we show for the first time the influence of vaccination schedules and adjuvants on the immunogenicity of recombinant ZIKV VLPs. The obtained results can be used in new vaccine designs not only against ZIKV but also against other important viral pathogens.

## OTU7B Modulates the Mosquito Immune Response to Beauveria bassiana Infection via Deubiquitination of the Toll Adaptor TRAF4.

**Wang Y, Chang M, Wang M, Ji Y, Sun X, Raikhel AS, Zou Z.**
14-02-2023
*Microbiol Spectr.*
https://pubmed.ncbi.nlm.nih.gov/36537797/

The Aedes aegypti mosquito transmits devastating flaviviruses, such as Zika, dengue, and yellow fever viruses. For more effective control of the vector, the pathogenicity of Beauveria bassiana, a fungus commonly used for biological control of pest insects, may be enhanced based on in-depth knowledge of molecular interactions between the pathogen and its host. Here, we identified a mechanism employed by B. bassiana, which efficiently

blocks the Ae. aegypti antifungal immune response by a protease that contains an ovarian tumor (OTU) domain. RNA-sequencing analysis showed that the depletion of OTU7B significantly upregulates the mRNA level of immunity-related genes after a challenge of the fungus. CRISPR-Cas9 knockout of OTU7B conferred a higher resistance of mosquitoes to the fungus B. bassiana. OTU7B suppressed activation of the immune response by preventing nuclear translocation of the NF-κB transcription factor Rel1, a mosquito orthologue of *Drosophila* Dorsal. Further studies identified tumor necrosis factor receptor-associated factor 4 (TRAF4) as an interacting protein of OTU7B. TRAF4-deficient mosquitoes were more sensitive to fungal infection, indicating TRAF4 to be the adaptor protein that activates the Toll pathway. TRAF4 is K63-link polyubiquitinated at K338 residue upon immune challenge. However, OTU7B inhibited the immune signaling by enzymatically removing the polyubiquitin chains of mosquito TRAF4. Thus, this study has uncovered a novel mechanism of fungal action against the host innate immunity, providing a platform for further improvement of fungal pathogen effectiveness. IMPORTANCE Insects use innate immunity to defend against microbial infection. The Toll pathway is a major immune signaling pathway that is associated with the antifungal immune response in mosquitoes. Our study identified a fungal-induced deubiquitinase, OTU7B, which, when knocked out, promotes the translocation of the NF-κB factor Rel1 into the nucleus and confers enhanced resistance to fungal infection. We further found the counterpart of OTU7B, TRAF4, which is a component of the Toll pathway and acts as an adaptor protein. OTU7B enzymatically removes K63-linked polyubiquitin chains from TRAF4. The immune response is suppressed, and mosquitoes become much more sensitive to the Beauveria bassiana infection. Our findings reveal a novel mechanism of fungal action against the host innate immunity.

### Insect-Specific Chimeric Viruses Potentiated Antiviral Responses and Inhibited Pathogenic Alphavirus Growth in Mosquito Cells.

**Tan L, Zhang Y, Kim DY, Li R.**
14-02-2023
*Microbiol Spectr*.
https://pubmed.ncbi.nlm.nih.gov/36511715/

### Environmental emissions and pollution characteristics of mosquitocides for the control of dengue fever in a typical urban area.

**Zhang B, Zhang QQ, Cai YY, Yan XT, Zhai YQ, Guo Z, Ying GG.**
01-04-2023
*Sci Total Environ*.
https://pubmed.ncbi.nlm.nih.gov/36634776/

### A randomized phase 3 trial of the immunogenicity and safety of coadministration of a live-attenuated tetravalent dengue vaccine (TAK-003)

### and an inactivated hepatitis a (HAV) virus vaccine in a dengue non-endemic country.

**Tricou V, Eyre S, Ramjee M, Collini P, Mojares Z, Loeliger E, Mandaric S, Rauscher M, Brose M, Lefevre I, Folschweiller N, Wallace D.**
10-02-2023
*Vaccine*.
https://pubmed.ncbi.nlm.nih.gov/36681529/

### Rapid Diagnostic Tests for the Detection of the Four Dengue Virus Serotypes in Clinically Relevant Matrices.

**Pollak NM, Olsson M, Ahmed M, Tan J, Lim G, Setoh YX, Wong JCC, Lai YL, Hobson-Peters J, Macdonald J, McMillan D.**
14-02-2023
*Microbiol Spectr*.
https://pubmed.ncbi.nlm.nih.gov/36682882/

The efficient and accurate diagnosis of dengue, a major mosquito-borne disease, is of primary importance for clinical care, surveillance, and outbreak control. The identification of specific dengue virus serotype 1 (DENV-1) to DENV-4 can help in understanding the transmission dynamics and spread of dengue disease. The four rapid low-resource serotype-specific dengue tests use a simple sample preparation reagent followed by reverse transcription-isothermal recombinase polymerase amplification (RT-RPA) combined with lateral flow detection (LFD) technology. Results are obtained directly from clinical sample matrices in 35 min, requiring only a heating block and pipettes for liquid handling. In addition, we demonstrate that the rapid sample preparation step inactivates DENV, improving laboratory safety. Human plasma and serum were spiked with DENV, and DENV was detected with analytical sensitivities of 333 to 22,500 median tissue culture infectious doses ($TCID_{50}$)/mL. The analytical sensitivities in blood were 94,000 to 333,000 $TCID_{50}$/mL. Analytical specificity testing confirmed that each test could detect multiple serotype-specific strains but did not respond to strains of other serotypes, closely related flaviviruses, or chikungunya virus. Clinical testing on 80 human serum samples demonstrated test specificities of between 94 and 100%, with a DENV-2 test sensitivity of 100%, detecting down to 0.004 PFU/μL, similar to the sensitivity of the PCR test; the other DENV tests detected down to 0.03 to 10.9 PFU/μL. Collectively, our data suggest that some of our rapid dengue serotyping tests provide a potential alternative to conventional labor-intensive RT-quantitative PCR (RT-qPCR) detection, which requires expensive thermal cycling instrumentation, technical expertise, and prolonged testing times. Our tests provide performance and speed without compromising specificity in human plasma and serum and could become promising tools for the detection of high DENV loads in resource-limited settings. IMPORTANCE The efficient and accurate diagnosis of dengue, a major mosquito-borne disease, is of primary importance for clinical care, surveillance, and outbreak control. This study describes the evaluation of four rapid low-resource serotype-specific dengue tests for the detection of specific DENV

serotypes in clinical sample matrices. The tests use a simple sample preparation reagent followed by reverse transcription-isothermal recombinase polymerase amplification (RT-RPA) combined with lateral flow detection (LFD) technology. These tests have several advantages compared to RT-qPCR detection, such as a simple workflow, rapid sample processing and turnaround times (35 min from sample preparation to detection), minimal equipment needs, and improved laboratory safety through the inactivation of the virus during the sample preparation step. The low-resource formats of these rapid dengue serotyping tests have the potential to support effective dengue disease surveillance and enhance the diagnostic testing capacity in resource-limited countries with both endemic dengue and intense coronavirus disease 2019 (COVID-19) transmission.

## A concerted mechanism involving ACAT and SREBPs by which oxysterols deplete accessible cholesterol to restrict microbial infection.

Heisler DB, Johnson KA, Ma DH, Ohlson MB, Zhang L, Tran M, Corley CD, Abrams ME, McDonald JG, Schoggins JW, Alto NM, Radhakrishnan A.
25-01-2023
*Elife*.
https://pubmed.ncbi.nlm.nih.gov/36695568/

## Developing Wolbachia-based disease interventions for an extreme environment.

Ross PA, Elfekih S, Collier S, Klein MJ, Lee SS, Dunn M, Jackson S, Zhang Y, Axford JK, Gu X, Home JL, Nassar MS, Paradkar PN, Tawfik EA, Jiggins FM, Almalik AM, Al-Fageeh MB, Hoffmann AA.
31-01-2023
*PLoS Pathog.*
https://pubmed.ncbi.nlm.nih.gov/36719928/

## Recombinant Protein Mimicking the Antigenic Structure of the Viral Surface Envelope Protein Reinforces Induction of an Antigen-Specific and Virus-Neutralizing Immune Response Against Dengue Virus.

Kim J, Lim TY, Park J, Jang YS.
Jan-2023
*J Microbiol*.
https://pubmed.ncbi.nlm.nih.gov/36723792/

Dengue virus (DENV), belonging to the family Flaviviridae, is the causative agent of dengue and comprises four serotypes. A second heterologous DENV infection is a critical risk factor for severe dengue, and no effective vaccine is available to prevent infection by all four DENV serotypes. Recombinant DENV vaccines are primarily based on the envelope proteins, prM and E. The E protein and its envelope domain III (EDIII) have been investigated as candidate antigens (Ags) for recombinant subunit vaccines. However, most EDIII-based Ags are monomers that do not display the cognate antigenic structure of E protein, which is essential for induction of virus-

neutralizing immunity. Here, we developed recombinant DENV-2 envelope domain (r2ED) protein as an Ag that mimics the quaternary structure of E protein on the DENV surface. We confirmed that r2ED retained the conformational epitope displayed at the E-dimer interface, which reportedly exhibits broad virus-neutralizing capacity, without displaying the fusion loop epitope that causes antibody (Ab)-dependent enhancement. Furthermore, compared with EDIII alone, r2ED elicited stronger Ag-specific and cross-reactive neutralizing Ab and T cell-mediated immune responses in mice. This Ag-specific immunity was maintained at an elevated level 6 months after the last immunization, suggesting sustained Ag-specific immune memory. Taken together, these observations suggest that r2ED could be used to develop an improved subunit vaccine capable of inducing a broadly cross-reactive and long-lasting immune response against DENV infection.

## Features of the urban environment associated with Aedes aegypti abundance in high-rise public apartments in Singapore: An environmental case-control study.

Fernandez SA, Sun H, Dickens BL, Ng LC, Cook AR, Lim JT.
02-02-2023
*PLoS Negl Trop Dis*.
https://pubmed.ncbi.nlm.nih.gov/36730440/

## Antiviral effects of the fused tricyclic derivatives of indoline and imidazolidinone on ZIKV infection and RdRp activities of ZIKV and DENV.

Zhou GF, Li F, Xue JX, Qian W, Gu XR, Zheng CB, Li C, Yang LM, Xiong SD, Zhou GC, Zheng YT.
Mar-2023
*Virus Res*.
https://pubmed.ncbi.nlm.nih.gov/36746341/

The prevalence and ravages of Zika virus (ZIKV) seriously endanger human health, especially causing significant neurological defects in both neonates as pediatric microcephaly and adults as Guillain-Barré syndrome. In this work, we studied anti-ZIKV effects of the fused tricyclic derivatives of indoline and imidazolidinone and discovered that some of them are valuable leads for drug discovery of anti-ZIKV agents. The current results show that certain compounds are broad-spectrum inhibitors of ZIKV- and dengue virus (DENV)-infection while distinctive compounds are selective ZIKV inhibitors or selective DENV inhibitors. Compounds of 12, 17 and 28 are more active against Asian ZIKV SZ-VIV01 strain than African ZIKV MR766 strain. It is valued that silylation makes six TBS compounds of 4-nitrophenyl hydrazine series and phenyl hydrazine series more active against ZIKV infection than their phenols. Time-of-addition and withdrawal studies indicate that compound 12 majorly acts on post-infection of RNA synthesis stage of ZIKV life cycle. Moreover, compounds of 12, 17 and 18 are anti-ZIKV agents with the inhibitory activities to ZIKV NS5 RdRp while 12 doesn't inhibit DENV infection even though it is a DENV RdRp inhibitor, 17 is an active agent against DENV infection but

is only a weak DENV NS5 RdRp inhibitor, and 28 is inactive against DENV infection and not a DENV NS5 RdRp inhibitor. As a result, a compound's antiviral difference between ZIKV and DENV is not always related to anti-RdRp difference between ZIKV RdRp and DENV RdRp, and structural features of a compound play important roles in executing antiviral and anti-RdRp functions. Further discovery of highly potent broad-spectrum or selective agents against infection by ZIKV and DENV will be facilitated.

## Disturbance gradient and mosquito diversity pattern in areas surrounding Chini Lake - the second largest freshwater lake in Peninsular Malaysia.

**Pathy TS, Lee JM, Yek SH.**

Malaysia is a tropical country that has consistently been facing a prevalent threat of mosquito-borne diseases. Amongst the plethora of diseases, the most common mosquito-borne disease in the country is dengue fever, transmitted by *Aedes* spp. mosquitoes. This study aims to examine the effects of human activity associated with different land use on mosquito population composition and diversity. Our study site is Chini Lake, a naturally occurring lake and the second-largest freshwater body in Malaysia. The areas surrounding the Lake have been subjected to various human activities, such as economic development and conversion into rubber plantations, while some areas remain pristine, making Chini Lake an ideal location to examine the gradient of human disturbances on mosquito composition and diversity. We sampled adult mosquitoes and larvae across a range of sites with different levels of human disturbance. As expected, in areas with high disturbance scores, the species richness of adult and larval mosquitoes were reduced while the abundance was higher. The results also revealed minimal overlap between species captured for adult and larval samplings, suggesting that land-use changes affect both life stages differently. Different resource requirements of adult and larval mosquitoes likely led to the observed diversity pattern in this small survey. We suggest future work to look into how habitat heterogeneity affects both life stages and sexes of mosquito diversity patterns and distribution.

## Enteric fever masquerading as Crohn's disease in a child with abdominal tuberculosis.

**Sahoo B, Kumar K, Malhotra S, Sibal A.**

## Genomic and phenotypic analyses suggest moderate fitness differences among Zika virus lineages.

**Oliveira G, Vogels CBF, Zolfaghari A, Saraf S, Klitting R, Weger-Lucarelli J, P Leon K, Ontiveros CO, Agarwal R,**

**Tsetsarkin KA, Harris E, Ebel GD, Wohl S, Grubaugh ND, Andersen KG.**

## [Dengue during pregnancy, less incidence of thrombocytopenia than in general population].

**Gutiérrez-Aguirre CH, Palomares-Leal A, Soto-Flores L, Colunga-Pedraza P, Jaime-Pérez JC, Zambrano-Velarde M, Vega-Cortes D, Flores-Jiménez JA, Gómez-Almaguer D.**

**Objective**: Dengue is a generally self-limited viral disease, considered a public health problem in Mexico. It can be accompanied by laboratory alterations such as neutropenia, lymphopenia and thrombocytopenia. The objective of the study was to evaluate the incidence of hematological alterations in patients with dengue. **Methods**: We retrospectively included 64 patients, including 14 pregnant women, with a diagnosis of dengue at the Hospital Universitario de Monterrey and Civil Nuevo de Guadalajara from January 2014 to December 2017. **Results**: The most common clinical symptom in the general group was headache and retro-ocular pain in 53 patients (83%), while in pregnant patients it was fever in 12 patients (86%). The median platelet count in the general group was $51.4 \times 10^3/\mu!$, with thrombocytopenia in 88% of patients, while in pregnant patients it was $141.1 \times 10^3/$ with thrombocytopenia in 57% of patients (p=0.002). Platelet recovery was achieved in 7 days in the general group and 4.5 days in pregnant patients. **Conclusions**: Contrary to that reported in the literature, pregnant patients had a lower incidence of thrombocytopenia and a higher platelet count at time of diagnosis without impact on maternal mortality or in the course of pregnancy.

## [Epidemiological surveillance system for the acute febrile syndrome in Villeta, Colombia].

**Yaya-Lancheros N, Polo-Terán LJ, Faccini-Martínez ÁA, Hidalgo-Díaz M.**

## [Barriers and negative behaviors that prevail in the prevention and control of dengue in Cartagena, Colombia].

**Pasos-Simancas ES, Archibold-Suárez R.**

**Objective:** To investigate the negative risk barriers for the prevention and control of dengue that prevail in the population and in the institutional and sectoral responsible of the city of Cartagena. **Materials and**

**methods:** A qualitative, narrative-ethnographic design approach supported by the COMBI methodology was used. The population was 90 people residing in the three localities belonging to the District of Cartagena de Indias (Colombia) and registered in the Administrative Department of District Health (hereinafter DADIS), specifically in the National System of Public Health Surveillance (Sivigilia), with high incidences or probabilities of suspected cases of dengue fever and cases of dengue. **Results:** People reside in houses made of cardboard, wood, zinc, block, cement, eternity shelters. Although they are aware of the problem of dengue, they relate it to other diseases such as the cold and the flu. They give more importance to other social problems, such as violence and insecurity in the area. The educational and preventive messages in the press, radio and television made by DADIS and other dengue control entities do not cover all the measures that must be implemented for the prevention and control of the disease. **Conclusion:** The transmission of dengue can be related to socio-economic factors such as: little knowledge the com-munity has about the health consequences that Dengue transmission can cause; the attitude and practices indifferent to this pathology, as well as the insufficient educational and preventive communication carried out by DADIS through communication channels and social networks, among others.

## mRNA vaccines: The future of prevention of viral infections?

**Rzymski P, Szuster-Ciesielska A, Dzieciątkowski T, Gwenzi W, Fal A.**
10-02-2023
*J Med Virol.*
https://pubmed.ncbi.nlm.nih.gov/36762592/

Messenger RNA (mRNA) vaccines against COVID-19 are the first authorized biological preparations developed using this platform. During the pandemic, their administration has been proven to be a life-saving intervention. Here, we review the main advantages of using mRNA vaccines, identify further technological challenges to be met during the development of the mRNA platform, and provide an update on the clinical progress on leading mRNA vaccine candidates against different viruses that include influenza viruses, human immunodeficiency virus 1, respiratory syncytial virus, Nipah virus, Zika virus, human cytomegalovirus, and Epstein-Barr virus. The prospects and challenges of manufacturing mRNA vaccines in low-income countries are also discussed. The ongoing interest and research in mRNA technology are likely to overcome some existing challenges for this technology (e.g., related to storage conditions and immunogenicity of some components of lipid nanoparticles) and enhance the portfolio of vaccines against diseases for which classical formulations are already authorized. It may also open novel pathways of protection against infections and their consequences for which no safe and efficient immunization methods are currently available.

## Cryo-EM reveals binding of linoleic acid to SARS-CoV-2 spike glycoprotein, suggesting an antiviral treatment strategy.

**Toelzer C, Gupta K, Berger I, Schaffitzel C.**
01-02-2023
*Acta Crystallogr D Struct Biol.*
https://pubmed.ncbi.nlm.nih.gov/36762857/

## Synthesis and biological evaluation of new β-D-N4-hydroxycytidine analogs against SARS-CoV-2, influenza viruses and DENV-2.

**Jin An Y, Myeong Choi S, Rang Choi E, Eun Nam Y, Woo Seo E, Bin Ahn S, Jang Y, Kim M, Hyun Cho J.**
08-02-2023
*Bioorg Med Chem Lett.*
https://pubmed.ncbi.nlm.nih.gov/36764470/

Drug repurposing approach was applied to find a potent antiviral agent against RNA viruses such as SARS-CoV-2, influenza viruses and dengue virus with a concise strategy of small change in parent molecular structure. For this purpose, β-D-N4-hydroxycytidine (NHC, 1) with a broad spectrum of antiviral activity was chosen as the parent molecule. Among the prepared NHC analogs (8a-g, and 9) from uridine, β-D-N4-O-isobutyrylcytidine (8a) showed potent activity against SARS-CoV-2 ($EC_{50}$ 3.50 μM), Flu A (H1N1) ($EC_{50}$ 5.80 μM), Flu A (H3N2) ($EC_{50}$ 7.30 μM), Flu B ($EC_{50}$ 3.40 μM) and DENV-2 ($EC_{50}$ 3.95 μM) in vitro. Furthermore, its potency against SARS-CoV-2 was >5-fold, 3.4-fold, and 3-fold compared to that of NHC (1), MK-4482 (2), and remdesivir (RDV) in vitro, respectively. Ultimately, compound 8a was expected to be a potent inhibitor toward RNA viruses as a viral mutagenic agent like MK-4482.

## The Lesser of Two Evils: Application of Maslahah-Mafsadah Criteria in Islamic Ethical-Legal Assessment of Genetically Modified Mosquitoes in Malaysia.

**Arham AF, Hasim NA, Mokhtar MI, Zainal N, Rusly NS, Amin L, Saifuddeen SM, Mustapa MAC, Mahadi Z.**
Dec-2022
*J Bioeth Inq.*
https://pubmed.ncbi.nlm.nih.gov/36350531/

## Fetuses and infants with Amyoplasia congenita in congenital Zika syndrome: The evidence of a viral cause. A narrative review of 144 cases.

**Hageman G, Nihom J.**
Jan-2022
*Eur J Paediatr Neurol.*
https://pubmed.ncbi.nlm.nih.gov/36442412/

## Genome sequencing of dengue virus serotype 4 in a bat brain sample (Platyrrhinus helleri) from the Brazilian Amazon.

**Franco Filho LC, Barata RR, Coelho MS, Cardoso JF, Lemos PDS, Dos Reis HS, Favacho JDFR, Faria NR, Nunes MRT.**
09-02-2023
*Infect Genet Evol.*
https://pubmed.ncbi.nlm.nih.gov/36764633/

The existence of sylvatic transmission of dengue virus in communities of neotropical bats remains uncertain. In this work we present a near-complete genome of dengue virus serotype 4 obtained from the brain sample of a bat from Platyrrhinus helleri specie collected in the Brazilian Amazon region. The presence of the virus in the brain sample may indicate a possible tropism for the central nervous system in bats, which may justify negative results in previous studies that focused on analysis of other tissues, such as liver and spleen. Besides the duration of dengue virus circulation in the Americas (circa 40 years) may be too short for an implementation of a sylvatic dengue virus cycle. Our findings suggest that continued monitoring is needed to confirm with the neotropical bats could potentially act as a natural reservoir of dengue in the region.

## Use of Envelope Domain III Protein for the Detection of IgG Type Antibodies Specific to Zika Virus by Indirect ELISA.

**Ndiaye O, Diagne CT, Abd El Wahed A, Dia F, Dia M, Faye A, Leal SDV, Dos Santos M, Lima Mendonça MDL, da Silva Leite CC, Bouh Boye CS, Bryant JE, Desprès P, Faye O, Sall AA, Faye O.**
26-01-2023
*Diagnostics (Basel).*
https://pubmed.ncbi.nlm.nih.gov/36766567/

## Identification of Potent Zika Virus NS5 RNA-Dependent RNA Polymerase Inhibitors Combining Virtual Screening and Biological Assays.

**Chen Y, Chi X, Zhang H, Zhang Y, Qiao L, Ding J, Han Y, Lin Y, Jiang J.**
18-01-2023
*Int J Mol Sci.*
https://pubmed.ncbi.nlm.nih.gov/36768218/

The Zika virus (ZIKV) epidemic poses a significant threat to human health globally. Thus, there is an urgent need for developing effective anti-ZIKV agents. ZIKV non-structural protein 5 RNA-dependent RNA polymerase (RdRp), a viral enzyme for viral replication, has been considered an attractive drug target. In this work, we screened an anti-infection compound library and a natural product library by virtual screening to identify potential candidates targeting RdRp. Then, five selected candidates were further applied for RdRp enzymatic analysis, cytotoxicity, and binding examination by SPR. Finally, posaconazole (POS) was confirmed to effectively inhibit both RdRp activity with an $IC_{50}$ of 4.29 μM and the ZIKV replication with an $EC_{50}$ of 0.59 μM. Moreover, POS was shown to reduce RdRp activity by binding with the key amino acid D666 through molecular docking and site-directed mutation analysis. For the first time, our work found that POS could inhibit ZIKV replication with a stronger inhibitory activity than chloroquine. This work also demonstrated fast anti-ZIKV screening for inhibitors of RdRp and provided POS as a potential anti-ZIKV agent.

## The Immunogenicity of DENV1-4 ED3s Strongly Differ despite Their Almost Identical Three-Dimensional Structures and High Sequence Similarities.

**Islam MD, Sharmin T, Tipo IH, Saha A, Yesmin S, Roy MG, Brindha S, Kuroda Y, Islam MM.**
25-01-2023
*Int J Mol Sci.*
https://pubmed.ncbi.nlm.nih.gov/36768719/

## Evolution of Antiretroviral Drug Rilpivirine and Approach to Oncology.

**Pereira M, Vale N.**
02-02-2023
*Int J Mol Sci.*
https://pubmed.ncbi.nlm.nih.gov/36769210/

## Quercetin: A Functional Food-Flavonoid Incredibly Attenuates Emerging and Re-Emerging Viral Infections through Immunomodulatory Actions.

**Shorobi FM, Nisa FY, Saha S, Chowdhury MAH, Srisuphanunt M, Hossain KH, Rahman MA.**
17-01-2023
*Molecules*.
https://pubmed.ncbi.nlm.nih.gov/36770606/

Many of the medicinally active molecules in the flavonoid class of phytochemicals are being researched for their potential antiviral activity against various DNA and RNA viruses. Quercetin is a flavonoid that can be found in a variety of foods, including fruits and vegetables. It has been reported to be effective against a variety of viruses. This review, therefore, deciphered the mechanistic of how Quercetin works against some of the deadliest viruses, such as influenza A, Hepatitis C, Dengue type 2 and Ebola virus, which cause frequent outbreaks worldwide and result in significant morbidity and mortality in humans through epidemics or pandemics. All those have an alarming impact on both human health and the global and national economies. The review extended computing the Quercetin-contained natural recourse and its modes of action in different experimental approaches leading to antiviral actions. The gap in effective treatment emphasizes the necessity of a search for new effective antiviral compounds. Quercetin shows potential antiviral activity and inhibits it by targeting viral infections at multiple stages. The suppression of viral neuraminidase, proteases and DNA/RNA polymerases and the alteration of many viral proteins as well as their immunomodulation are the main molecular mechanisms of Quercetin's antiviral activities. Nonetheless, the huge potential of Quercetin and its extensive use is inadequately approached as a therapeutic for emerging and re-emerging viral infections. Therefore, this review enumerated the food-functioned Quercetin source, the modes of action of Quercetin for antiviral effects and made insights on the mechanism-based antiviral action of Quercetin.

## Lichen-Derived Diffractaic Acid Inhibited Dengue Virus Replication in a Cell-Based System.

**Loeanurit N, Tuong TL, Nguyen VK, Vibulakhaophan V, Hengphasatporn K, Shigeta Y, Ho SX, Chu JJH, Rungrotmongkol T, Chavasiri W, Boonyasuppayakorn S.**

Dengue is a mosquito-borne flavivirus that causes 21,000 deaths annually. Depsides and depsidones of lichens have previously been reported to be antimicrobials. In this study, our objective was to identify lichen-derived depsides and depsidones as dengue virus inhibitors. The 18 depsides and depsidones of *Usnea baileyi*, *Usnea aciculifera*, *Parmotrema dilatatum*, and *Parmotrema tsavoense* were tested against dengue virus serotype 2. Two depsides and one depsidone inhibited dengue virus serotype 2 without any apparent cytotoxicity. Diffractaic acid, barbatic acid, and Parmosidone C were three active compounds further characterized for their efficacies ($EC_{50}$), cytotoxicities ($CC_{50}$), and selectivity index (SI; $CC_{50}/EC_{50}$). Their $EC_{50}$ (SI) values were 2.43 ± 0.19 (20.59), 0.91 ± 0.15 (13.33), and 17.42 ± 3.21 (8.95) µM, respectively. Diffractaic acid showed the highest selectivity index, and similar efficacies were also found in dengue serotypes 1-4, Zika, and chikungunya viruses. Cell-based studies revealed that the target was mainly in the late stage with replication and the formation of infectious particles. This report highlights that a lichen-derived diffractaic acid could become a mosquito-borne antiviral lead as its selectivity indices ranged from 8.07 to 20.59 with a proposed target at viral replication.

## Prolonged Repellent Activity of Plant Essential Oils against Dengue Vector, Aedes aegypti.

**Haris A, Azeem M, Abbas MG, Mumtaz M, Mozūratis R, Binyameen M.**

## Anti-Dengue Activity of Lipophilic Fraction of Ocimum basilicum L. Stem.

**Joshi RK, Agarwal S, Patil P, Alagarasu K, Panda K, Cherian S, Parashar D, Roy S.**

*Ocimum basilicum* L. is used to cure many types of fever in traditional medicine. This study aims to explore the antiviral activity of the lipophilic fraction of the stem of *O. basilicum* (LFOB) against dengue virus (DENV) and chikungunya virus (CHIKV). The LFOB was analyzed using GC-FID and GC-MS. The antiviral activity of LFOB was studied using the Vero CCL-81 cell line. The cytotoxicity assay was performed using 3-(4,5-dimethythiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT). In vitro antiviral activity and FFU assay were used to determine and confirm antiviral activity against DENV and CHIKV. Twenty-six compounds were identified in LFOB using GC/MS. The most abundant compounds were $\beta$-sitosterol (22.9%), stigmasterol (18.7%), and campesterol (12.9%). Significant reduction in DENV titre was observed under pre- and post-infection treatment conditions at a concentration of 3.125 µg/mL, but no anti-CHIKV activity was observed. Our earlier and the present AutoDock-Vina-based in silico docking study revealed that $\beta$-sitosterol and stigmasterol could form strong interactions with the DENV E glycoprotein and DENV RdRp domain, respectively. Our findings suggest that LFOB can inhibit DENV infection and might act as a potent prophylactic/therapeutic agent against DENV-2. In silico results suggested that $\beta$-sitosterol and stigmasterol may block the viral entry by inhibiting the fusion process and viral replication respectively.

## Data-rich modeling helps answer increasingly complex questions on variant and disease interactions: Comment on "Mathematical models for dengue fever epidemiology: A 10-year systematic review" by Aguiar et al.

**Roster KO.**

## The evolution of chikungunya virus circulating in Indonesia: Sequence analysis of the orf2 gene encoding the viral structural proteins.

**Hakim MS, Annisa L, Aman AT.**

Chikungunya virus (CHIKV) is an arthropod-borne virus that has caused several major epidemics globally, including in Indonesia. Although significant progress has been achieved in understanding the epidemiology and genotype circulation of CHIKV in Indonesia, the evolution of Indonesian CHIKV isolates is poorly understood. Thus, our study aimed to perform phylogenetic and mutation analyses of the orf2 gene encoding its viral structural protein to improve our understanding of CHIKV evolution in Indonesia. Complete orf2 gene sequences encoding the viral structural proteins of Indonesian-derived CHIKV were downloaded from GenBank until August 31, 2022. Various bioinformatics tools were employed to perform phylogenetic and mutation analyses of the orf2 gene. We identified 76 complete sequences of orf2 gene of CHIKV isolates originally derived from Indonesia. Maximum likelihood trees demonstrated that the majority (69/76, 90.8%) of Indonesian-derived CHIKV isolates belonged to the Asian genotype, while seven isolates (9.2%) belonged to the East/Central/South African (ECSA) genotype. The Indonesian-derived CHIKV isolates were calculated to be originated in Indonesia around 95 years ago (1927), with 95% highest posterior density (HPD) ranging from 1910 to 1942 and a nucleotide substitution rate of $5.07 \times 10^{-4}$ (95% HPD: $3.59 \times 10^{-4}$ to $6.67 \times 10^{-4}$). Various synonymous and

non-synonymous substitutions were identified in the C, E3, E2, 6K, and E1 genes. Most importantly, the E1-A226V mutation, which has been reported to increase viral adaptation in Aedes albopictus mosquitoes, was present in all ECSA isolates. To our knowledge, our study is the first comprehensive research analyzing the mutation and evolution of Indonesian-derived CHIKV based on complete sequences of the orf2 genes encoding its viral structural proteins. Our results clearly showed a dynamic evolution of CHIKV circulating in Indonesia.

## [Argentine hemorrhagic fever: report of two cases in a non-endemic area].

**García Gili MI, Zampetti A, Asencio MD, Leone CS, Gutiérrez M, Mindlin PE.**
2023
*Medicina (B Aires).*
https://pubmed.ncbi.nlm.nih.gov/36774608/

We present the case of a 38-year-old woman with no relevant medical history, resident of the City of Buenos Aires, who was admitted in hospital for presenting fever, retroocular headache, myalgia, arthralgia, and maculopapular pruritic rash on the back of the hands and feet of 6 days of evolution. Laboratory tests revealed lymphopenia, severe thrombocytopenia, and anicteric hepatitis. Her husband had been hospitalized three weeks earlier for a condition of similar characteristics without etiological diagnosis. Subsequently, it evolved with metrorrhagia and axillary petechiae associated with photophobia, drowsiness, and fine tremor of the tongue with normal cerebrospinal fluid, treated with intravenous ceftriaxone 2 g/day for 7 days. Computed tomography of abdomen and pelvis showed a left abdominal wall hematoma. Serological samples were sent to the National Institute of Human Viral Diseases Dr. Julio I. Maiztegui for dengue virus, leptospirosis and hantavirus with non-reactive results, and RT-PCR of Junín virus that was positive. Retrospectively, the spouse was diagnosed by detection of IgG antibodies to Junin virus by ELISA and neutralization tests. Neither of the two cases had a clear epidemiological link. Our aim is to highlight the importance of clinical suspicion outside of endemic areas.

## Recent updates on correlates of vaccine-induced protection.

**Plotkin SA.**
27-01-2023
*Front Immunol.*
https://pubmed.ncbi.nlm.nih.gov/36776392/

## NS1 from Two Zika Virus Strains Differently Interact with a Membrane: Insights to Understand Their Differential Virulence.

**Poveda Cuevas SA, Barroso da Silva FL, Etchebest C.**
13-02-2023
*J Chem Inf Model.*
https://pubmed.ncbi.nlm.nih.gov/36780300/

Zika virus (ZIKV) from Uganda (UG) expresses a phenotype related to fetal loss, whereas the variant from Brazil (BR) induces microcephaly in neonates. The differential virulence has a direct relation to biomolecular mechanisms that make one strain more aggressive than the other. The nonstructural protein 1 (NS1) is a key viral toxin to comprehend these viral discrepancies because of its versatility in many processes of the virus life cycle. Here, we aim to examine through coarse-grained models and molecular dynamics simulations the protein-membrane interactions for both $NS1_{ZIKV-UG}$ and $NS1_{ZIKV-BR}$ dimers. A first evaluation allowed us to establish that the NS1 proteins, in the membrane presence, explore new conformational spaces when compared to systems simulated without a lipid bilayer. These events derive from both differential coupling patterns and discrepant binding affinities to the membrane. The N-terminal domain, intertwined loop, and greasy finger proposed previously as binding membrane regions were also computationally confirmed by us. The anchoring sites have aromatic and ionizable residues that manage the assembly of NS1 toward the membrane, especially for the Ugandan variant. Furthermore, in the presence of the membrane, the difference in the dynamic cross-correlation of residues between the two strains is particularly pronounced in the putative epitope regions. This suggests that the protein-membrane interaction induces changes in the distal part related to putative epitopes. Taken together, these results open up new strategies for the treatment of flaviviruses that would specifically target these *dynamic* differences.

## A systematic review of dengue outbreak prediction models: Current scenario and future directions.

**Leung XY, Islam RM, Adhami M, Ilic D, McDonald L, Palawaththa S, Diug B, Munshi SU, Karim MN.**
13-02-2023
*PLoS Negl Trop Dis.*
https://pubmed.ncbi.nlm.nih.gov/36780568/

## The Aedes aegypti peritrophic matrix controls arbovirus vector competence through HPx1, a heme-induced peroxidase.

**Talyuli OAC, Oliveira JHM, Bottino-Rojas V, Silveira GO, Alvarenga PH, Barletta ABF, Kantor AM, Paiva-Silva GO, Barillas-Mury C, Oliveira PL.**
13-02-2023
*PLoS Pathog.*
https://pubmed.ncbi.nlm.nih.gov/36780872/

## Cost-effectiveness of sub-national geographically targeted vaccination programs: A systematic review.

**Getchell M, Mantaring EJ, Yee K, Pronyk P.**
11-02-2023
*Vaccine*.

Immunization is an essential component of national health plans. However, the growing number of new vaccine introductions, vaccination campaigns and increasing administrative costs create logistic and financial challenges, especially in resource-limited settings. Sub-national geographic targeting of vaccination programs is a potential strategy for governments to reduce the impact of infectious disease outbreaks while optimizing resource allocation and reducing costs, promoting sustainability of critically important national immunization plans. We conducted a systematic review of peer-reviewed literature to identify studies that investigated the cost-effectiveness of geographically targeted sub-national vaccination programs, either through routine immunization or supplementary immunization activities. A total of 16 studies were included in our review, covering nine diseases of interest: cholera, dengue, enterotoxigenic Escherichia coli (ETEC), hepatitis A, Japanese encephalitis, measles, rotavirus, Shigella and typhoid fever. All studies modelled cost-effectiveness of geographically targeted vaccination. Despite the variation in study design, disease focus and country context, studies generally found that in countries where a heterogenous burden of disease exists, sub-national geographic targeting of vaccination programs in areas of high disease burden was more cost-effective than a non-targeted strategy. Sensitivity analysis revealed that cost-effectiveness was most sensitive to variations in vaccine price, vaccine efficacy, mortality rate, administrative and operational costs, discount rate, and treatment costs. This systematic review identified several key characteristics related to geographic targeting of vaccination, including the vaccination strategy used, variations in modelling parameters and their impact on cost-effectiveness. Additional research and guidance is needed to support the appropriateness and feasibility of geographically targeted vaccination and to determine what country context would make this a viable complement to routine immunization programs.

## Hesitancy for Adult Vaccines Among Healthcare Providers and their Family Members in Delhi, India: A Cross-Sectional Study.

**Kalra N, Kalra T, Mishra S, Basu S, Bhatnagar N.**
Dec-2022
*Dialogues Health*.

**Objectives:** Adult immunisation has recently emerged as an area of emphasis in research and policy. Increasing life expectancy, outbreaks like COVID-19, and the endemic nature of diseases like dengue, malaria have underscored its importance. Therefore, this study was carried out to assess hesitancy and the factors influencing the uptake of vaccines in adults.

**Methods:** A descriptive cross-sectional study was conducted among the medical students and doctors affiliated to a medical college and tertiary care hospital in Delhi, India and their immediate family members in January 2021. Online data collection was done using the Google Form platforms. Data on awareness and perceptions regarding adult vaccination and immunisation status of participants was collected. The dataset was exported in the Microsoft Excel format and analysed with IBM SPSS Version 25 (Armonk, NY: IBM Corp). **Results:** A total of 461 adults responded to the survey. The most common reasons for vaccine hesitancy were fear of side effects (51.41%), lack of awareness of vaccines (49.46%), and the lack of national guidelines on adult vaccination (32.97%). Hesitancy for vaccines among those who were informed by healthcare workers of vaccine availability was highest for zoster vaccine (97.80%) and least for tetanus toxoid (57.62%). Significant hesitancy was also observed for pneumococcal, human papillomavirus, influenza and varicella vaccines. **Conclusions:** Reduced vaccine uptake due to vaccine hesitancy in adulthood is a major health concern. Framing national guidelines for adult vaccination in India and awareness generation to create a public demand for adult vaccination warrants prioritization.

## A molecular surveillance-guided vector control response to concurrent dengue and West Nile virus outbreaks in a COVID-19 hotspot of Florida.

**Coatsworth H, Lippi CA, Vasquez C, Ayers JB, Stephenson CJ, Waits C, Florez M, Wilke ABB, Unlu I, Medina J, Ryan SJ, Lednicky JA, Beier JC, Petrie W, Dinglasan RR.**
19-02-2023
*Lancet Reg Health Am*.

## Validation of a Reporter Cell Line for Flavivirus Inhibition Assays.

**Rezende TMT, Macera G, Heyndrickx L, Michiels J, Coppens S, Thibaut HJ, Dallmeier K, Van Esbroeck M, Neyts J, Ariën KK, Bartholomeeusen K.**
14-02-2023
*Microbiol Spectr*.

Here, we report the validation of a new reporter cell line, Hec1a-IFNB-Luc, for use in inhibition studies of various flaviviruses relevant to human pathology. The reporter system allows the detection of viral replication after luciferase gene activation driven by an interferon beta (IFN-β) promoter. We found the reporter cell line to be highly responsive to all 10 flaviviruses tested, including the 4 dengue virus serotypes. The applicability of the Hec1a-IFNB-Luc reporter cell line for serodiagnostic purposes in neutralizing antibody assays was confirmed by comparison of its sensitivity and specificity to those of "gold-standard," clinically applied, cytopathic effect-based assays, showing comparable performances. The reporter cell line used for the assessment of viral inhibition by small-molecule antiviral compounds was also confirmed, and the sensitivity of the Hec1a-IFNB-Luc reporter cell line was compared to those from published data reporting on the activity of the antivirals in various other assays, indicating that the Hec1a-IFNB-Luc reporter cell line allowed the determination of the inhibitory capacity at least as

sensitive as alternative assays. By measuring luciferase activity as a proxy for viral replication, the reporter cell line allows early detection, reducing the time to results from often 5 to 7 days to 3 days, without the need for optical inspection of cytopathic effects, which often differ between viruses and cell lines, streamlining the development of flavivirus assays. **IMPORTANCE** The Hec1a-IFNB-Luc reporter cell line allows the detection of all 10 flaviviruses tested, including the 4 dengue virus serotypes. Its use for serodiagnostic purposes, measuring neutralizing antibody activity in sera, and the assessment of the antiviral activities of small-molecule compounds was confirmed, and it was found to be comparable to clinically applied assays. The Hec1a-IFNB-Luc reporter cell line allows the rapid and quantitative determination of antiviral effects on multiple human pathological flaviviruses using a single protocol.

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

**Nie Y, Deng D, Mou L, Long Q, Chen J, Wu J.**
15-02-2023
*J Microbiol Biotechnol*.
https://pubmed.ncbi.nlm.nih.gov/36788451/

### Dengue, chikungunya, and Zika virus infections in Latin America and the Caribbean: a systematic review.

**Santos LLM, de Aquino EC, Fernandes SM, Ternes YMF, Feres VCR.**
10-02-2023
*Rev Panam Salud Publica*.
https://pubmed.ncbi.nlm.nih.gov/36788963/

### Rising cases of Dengue and Malaria in Flood Affected Areas of Pakistan: A Major Threat to the Country's Healthcare System.

**Vohra LI, Aqib M, Jamal H, Mehmood Q, Yasin F.**
15-02-2023
*Disaster Med Public Health Prep*.
https://pubmed.ncbi.nlm.nih.gov/36789658/

### Targeting first trimester trophoblast cell metabolism modulates its susceptibility to Zika virus infection.

**Kafer D, Marquez A, Merech F, Hauk V, Paparini D, Ramhorst R, Leirós CP, Garcia C, Vota D.**
15-02-2023
*J Cell Physiol*.
https://pubmed.ncbi.nlm.nih.gov/36790938/

In the last 15 years Zika virus (ZIKV) caused several outbreaks of increasing scale in Micronesia, South Pacific islands, and more recently in the Caribbean and South America. The severity of the clinical presentation in neonates from pregnant women infected with ZIKV during the last outbreak supports the relevance of unraveling the mechanism of infection and viral persistence in the placenta with local viral isolates. Here, we investigated the relevance of trophoblast metabolic rewiring for viral multiplication and the role of the vasoactive intestinal peptide (VIP) as an endogenous factor associated with placental restriction to ZIKV infection at early pregnancy. Our in vitro model demonstrated that ZIKV triggers metabolic rewiring in first trimester cytotrophoblast-derived cells by increasing glucose utilization as fuel to sustain its replication, decreasing long-chain polyunsaturated fatty acid uptake, and promoting lipid droplets accumulation to favor its multiplication. Of note, variations in nutrient availability modulated viral spread in trophoblast cultures. The presence of VIP during trophoblast infection impaired ZIKV infective particle production and viral replication, restoring cell migration and metabolism. Moreover, the blockade of endogenous VIP signaling increased viral particle production and the viral entry receptor AXL expression. These results highlight the potential role of VIP as an endogenous antiviral factor related to trophoblast cell permissiveness to ZIKV infection at early pregnancy.

### Zika virus spreads through infection of lymph node-resident macrophages.

**Reynoso GV, Gordon DN, Kalia A, Aguilar CC, Malo CS, Aleshnick M, Dowd KA, Cherry CR, Shannon JP, Vrba SM, Holmes AC, Alippe Y, Maciejewski S, Asano K, Diamond MS, Pierson TC, Hickman HD.**
15-02-2023
*Cell Rep*.
https://pubmed.ncbi.nlm.nih.gov/36795561/

### Congenital Zika Virus Syndrome and Autoimmunity: Two Case Reports of Type 1 Diabetes Mellitus.

**Arrais NMR, Arrais RF, Coelho MC, Deghaide NHS, Donadi EA, Maia CRS, de Moraes-Pinto MI.**
14-02-2023
*Pediatr Infect Dis J*.
https://pubmed.ncbi.nlm.nih.gov/36795588/

### Arthropod-borne diseases among travellers arriving in Europe from Africa, 2015 to 2019.

**Gossner CM, Hallmaier-Wacker L, Briet O, Haussig JM, de Valk H, Wijermans A, Bakonyi T, Madubuko T, Frank C, Noel H, Abdulaziz M.**
Feb-2023
*Euro Surveill*.
https://pubmed.ncbi.nlm.nih.gov/36795503/

BackgroundTravellers are generally considered good sentinels for infectious disease surveillance.AimTo investigate whether health data from travellers arriving from Africa to Europe could provide evidence to support surveillance systems in Africa.MethodsWe examined disease occurrence and estimated risk of infection among travellers arriving from Africa to Europe from 2015 to 2019 using surveillance data of arthropod-borne disease cases collected through The European Surveillance System (TESSy) and flight passenger volumes from the International Air Transport Association.ResultsMalaria was the most common arthropod-borne disease reported

among travellers from Africa, with 34,235 cases. The malaria travellers' infection rate (TIR) was 28.8 cases per 100,000 travellers, which is 36 and 144 times higher than the TIR for dengue and chikungunya, respectively. The malaria TIR was highest among travellers arriving from Central and Western Africa. There were 956 and 161 diagnosed imported cases of dengue and chikungunya, respectively. The highest TIR was among travellers arriving from Central, Eastern and Western Africa for dengue and from Central Africa for chikungunya in this period. Limited numbers of cases of Zika virus disease, West Nile virus infection, Rift Valley fever and yellow fever were reported.ConclusionsDespite some limitations, travellers' health data can efficiently complement local surveillance data in Africa, particularly when the country or region has a sub-optimal surveillance system. The sharing of anonymised traveller health data between regions/continents should be encouraged.

## Bioinformatics analysis of mutations sheds light on the evolution of Dengue NS1 protein with implications in the identification of potential functional and druggable sites.

**Sharma A, Krishna S, Sowdhamini R.**
16-02-2023
*Mol Biol Evol.*
https://pubmed.ncbi.nlm.nih.gov/36795614/

## Octopamine and tyramine signalling in Aedes aegypti: Molecular characterization and insight into potential physiological roles.

**Finetti L, Paluzzi JP, Orchard I, Lange AB.**
16-02-2023
*PLoS One.*
https://pubmed.ncbi.nlm.nih.gov/36795713/

In insects, the biogenic amines octopamine (OA) and tyramine (TA) are involved in controlling several physiological and behavioural processes. OA and TA act as neurotransmitters, neuromodulators or neurohormones, performing their functions by binding to specific receptors belonging to the G protein-coupled receptor (GPCR) superfamily. OA and TA along with their receptors are involved in reproduction, smell perception, metabolism, and homeostasis. Moreover, OA and TA receptors are targets for insecticides and antiparasitic agents, such as the formamidine Amitraz. In the dengue and yellow fever vector, Aedes aegypti, limited research has been reported on their OA or TA receptors. Here, we identify and molecularly characterize the OA and TA receptors in A. aegypti. Bioinformatic tools were used to identify four OA and three TA receptors in the genome of A. aegypti. The seven receptors are expressed in all developmental stages of A. aegypti; however, their highest transcript abundance is observed in the adult. Among several adult A. aegypti tissues examined, including the central nervous system, antennae and rostrum, midgut, Malpighian tubules, ovaries, and testes, the type 2 TA receptor (TAR2) transcript is most abundant in the ovaries and the type 3 TA receptor (TAR3) is enriched in the Malpighian tubules,

leading us to propose putative roles for these receptors in reproduction and diuresis, respectively. Furthermore, a blood meal influenced OA and TA receptor transcript expression patterns in adult female tissues at several time points post blood meal, suggesting these receptors may play key physiological roles associated with feeding. To better understand OA and TA signalling in A. aegypti, the transcript expression profiles of key enzymes in their biosynthetic pathway, namely tyrosine decarboxylase (Tdc) and tyramine β-hydroxylase (Tβh), were examined in developmental stages, adult tissues, and brains from blood-fed females. These findings provide information for better understanding the physiological roles of OA, TA, and their receptors in A. aegypti, and additionally, may help in the development of novel strategies for the control of these human disease vectors.

## Epidemiological serosurvey of chikungunya fever post outbreak at Tanjung Sepat, Malaysia.

**Khor CS, Teoh BT, Sam SS, Khoo HY, Azizan NS, CheMatSeri A, Chin KL, Hamim ZR, Mohamed-Romai-Noor NA, Yaacob CN, Abd-Jamil J, Lee HY, Soh YH, AbuBakar S.**
31-01-2023
*J Infect Dev Ctries.*
https://pubmed.ncbi.nlm.nih.gov/36795935/

Introduction: Chikungunya fever is a mosquito-borne viral disease that usually presents with prominent arthralgia. An outbreak of chikungunya fever was reported in Tanjung Sepat, Malaysia in 2019. The outbreak was limited in size with a low number of cases being reported. The present study sought to determine the possible variables that could have affected the transmission of the infection.

Methodology: A cross-sectional study involving 149 healthy adult volunteers from Tanjung Sepat was performed soon after the outbreak had subsided. All the participants donated blood samples and completed the questionnaires. Laboratory detection of anti-CHIKV IgM and IgG antibodies was performed using enzyme-linked immunoassays (ELISA). Risk factors associated with chikungunya seropositivity were determined using logistic regression.Results: The majority (72.5%, n = 108) of the study participants tested positive for CHIKV antibodies. Only 8.3% (n = 9) of the participants out of all the seropositive volunteers had an asymptomatic infection. Participants who resided with a febrile (p < 0.05, Exp(B) = 2.2, confidence interval [CI] 1.3-3.6) or a CHIKV-diagnosed person (p < 0.05, Exp(B) = 2.1, CI 1.2-3.6) in the same household were found likely to be tested positive for CHIKV antibodies.Conclusions: Findings from the study support that asymptomatic CHIKV infections and indoor transmission occurred during the outbreak. Hence, widespread community testing and indoor use of mosquito repellent are among the possible measures that can be implemented to reduce CHIKV transmission during an outbreak.

## Natural variation in gene expression and viral susceptibility revealed by neural progenitor cell villages.

**Wells MF, Nemesh J, Ghosh S, Mitchell JM, Salick MR, Mello CJ, Meyer D, Pietilainen O, Piccioni F, Guss EJ, Raghunathan K, Tegtmeyer M, Hawes D, Neumann A, Worringer KA, Ho D, Kommineni S, Chan K, Peterson BK, Raymond JJ, Gold JT, Siekmann MT, Zuccaro E, Nehme R, Kaykas A, Eggan K, McCarroll SA.**
10-02-2023
*Cell Stem Cell*.
https://pubmed.ncbi.nlm.nih.gov/36796362/

## Early diagnostic indicators of dengue versus other febrile illnesses in Asia and Latin America (IDAMS study): a multicentre, prospective, observational study.

**Rosenberger KD, Phung Khanh L, Tobian F, Chanpheaktra N, Kumar V, Lum LCS, Sathar J, Pleiteés Sandoval E, Maroén GM, Laksono IS, Mahendradhata Y, Sarker M, Rahman R, Caprara A, Souza Benevides B, Marques ETA, Magalhaes T, Brasil P, Amaral Calvet G, Tami A, Bethencourt SE, Dong Thi Hoai T, Nguyen Tan Thanh K, Tran Van N, Nguyen Tran N, Do Chau V, Yacoub S, Nguyen Van K, Guzmán MG, Martinez PA, Nguyen Than Ha Q, Simmons CP, Wills BA, Geskus RB, Jaenisch T; International Research Consortium on Dengue Risk Assessment, Management, and Surveillance Investigators.**
Mar-2023
*Lancet Glob Health*.
https://pubmed.ncbi.nlm.nih.gov/36796983/

**Background:** Improvements in the early diagnosis of dengue are urgently needed, especially in resource-limited settings where the distinction between dengue and other febrile illnesses is crucial for patient management. **Methods:** In this prospective, observational study (IDAMS), we included patients aged 5 years and older with undifferentiated fever at presentation from 26 outpatient facilities in eight countries (Bangladesh, Brazil, Cambodia, El Salvador, Indonesia, Malaysia, Venezuela, and Viet Nam). We used multivariable logistic regression to investigate the association between clinical symptoms and laboratory tests with dengue versus other febrile illnesses between day 2 and day 5 after onset of fever (ie, illness days). We built a set of candidate regression models including clinical and laboratory variables to reflect the need of a comprehensive versus parsimonious approach. We assessed performance of these models via standard measures of diagnostic values. **Findings:** Between Oct 18, 2011, and Aug 4, 2016, we recruited 7428 patients, of whom 2694 (36%) were diagnosed with laboratory-confirmed dengue and 2495 (34%) with (non-dengue) other febrile illnesses and met inclusion criteria, and were included in the analysis. 2703 (52%) of 5189 included patients were younger than 15 years, 2486 (48%) were aged 15 years or older, 2179 (42%) were female and 3010 (58%) were male. Platelet count, white blood cell count, and the change in these variables from the previous day of illness had a strong association with dengue. Cough and rhinitis had strong associations with other febrile illnesses, whereas bleeding, anorexia, and skin flush were generally associated with dengue. Model performance increased between day 2 and 5 of illness. The comprehensive model (18 clinical and laboratory predictors) had sensitivities of 0·80 to 0·87 and specificities of 0·80 to 0·91, whereas the parsimonious model (eight clinical and laboratory predictors) had sensitivities of 0·80 to 0·88 and specificities of 0·81 to 0·89. A model that includes laboratory markers that are easy to measure (eg, platelet count or white blood cell count) outperformed the models based on clinical variables only. **Interpretation:** Our results confirm the important role of platelet and white blood cell counts in diagnosing dengue, and the importance of serial measurements over subsequent days. We successfully quantified the performance of clinical and laboratory markers covering the early period of dengue. Resulting algorithms performed better than published schemes for distinction of dengue from other febrile illnesses, and take into account the dynamic changes over time. Our results provide crucial information needed for the update of guidelines, including the Integrated Management of Childhood Illness handbook.

## The Incompetence of Mosquitoes-Can Zika Virus Be Adapted To Infect Culex tarsalis Cells?

**Gallichotte EN, Samaras D, Murrieta RA, Sexton NR, Robison A, Young MC, Byas AD, Ebel GD, Rückert C.**
16-02-2023
*mSphere*.
https://pubmed.ncbi.nlm.nih.gov/36794947/

## Differentiating dengue from other febrile illnesses: a dilemma faced by clinicians in dengue endemic countries.

**Malavige GN, Wijewickrama A, Ogg GS.**
Mar-2023
*Lancet Glob Health*.
https://pubmed.ncbi.nlm.nih.gov/36796966/

## In Vitro Dengue Virus Inhibition by Aqueous Extracts of Aegle marmelos, Munronia pinnata and Psidium guajava.

**Jayasekara KG, Soysa P, Suresh TS, Goonasekara CL, Gunasekera KM.**
15-02-2023
*Altern Lab Anim*.
https://pubmed.ncbi.nlm.nih.gov/36793154/

Dengue is an arboviral (insect-transmitted) infection of global concern. Currently, there are still no specific dengue antiviral agents to treat the disease. Plant extracts have been used in traditional medicine for treating various viral infections - thus, in the present study, aqueous extracts of dried flowers of *Aegle marmelos* (AM), whole plant of *Munronia pinnata* (MP) and leaves of *Psidium guajava* (PG) were investigated for their potential capacity to inhibit dengue virus infection of Vero cells. The maximum non-toxic dose (MNTD) and the 50% cytotoxic concentration ($CC_{50}$) were determined by using the MTT assay. A plaque reduction antiviral assay was carried out with dengue virus

types 1 (DV1), 2 (DV2), 3 (DV3) and 4 (DV4), in order to calculate the half-maximum inhibitory concentration (IC$_{50}$). AM extract inhibited all four virus serotypes tested; MP extract inhibited DV1, DV2 and DV4, but not DV3; PG extract inhibited DV1, DV2 and DV4, but not DV3. Thus, the results suggest that AM is a promising candidate for the pan-serotype inhibition of dengue viral activity.

## Insecticide Resistance Status of Aedes albopictus (Diptera: Culicidae) Populations from Cuba.

**Piedra LA, Rodriguez MM, Lopez I, Ruiz A, Martinez LC, Garcia I, Rey J, Bisset JA.**
15-02-2023
*J Med Entomol*.
https://pubmed.ncbi.nlm.nih.gov/36791252/

## Venous thromboembolism in viral diseases: A comprehensive literature review.

**Zerangian N, Erabi G, Poudineh M, Monajjem K, Diyanati M, Khanlari M, Khalaji A, Allafi D, Faridzadeh A, Amali A, Alizadeh N, Salimi Y, Ghane Ezabadi S, Abdi A, Hasanabadi Z, ShojaeiBaghini M, Deravi N.**
05-02-2023
*Health Sci Rep*.
https://pubmed.ncbi.nlm.nih.gov/36778773/

Venous thromboembolism (VTE) is known to be a common respiratory and/or cardiovascular complication in hospitalized patients with viral infections. Numerous studies have proven human immunodeficiency virus infection to be a prothrombotic condition. An elevated VTE risk has been observed in critically ill H1N1 influenza patients. VTE risk is remarkably higher in patients infected with the Hepatitis C virus in contrast to uninfected subjects. The elevation of D-dimer levels supported the association between Chikungunya and the Zika virus and the rise of clinical VTE risk. Varicella-zoster virus is a risk factor for both cellulitis and the consequent invasive bacterial disease which may take part in thrombotic initiation. Eventually, hospitalized patients infected with the coronavirus disease of 2019 (COVID-19), the cause of the ongoing worldwide pandemic, could mainly suffer from an anomalous risk of coagulation activation with enhanced venous thrombosis events and poor quality clinical course. Although the risk of VTE in nonhospitalized COVID-19 patients is not known yet, there are a large number of guidelines and studies on thromboprophylaxis administration for COVID-19 cases. This study aims to take a detailed look at the effect of viral diseases on VTE, the epidemiology of VTE in viral diseases, and the diagnosis and treatment of VTE.

## Effects of IL2/anti-IL2 antibody complex on chikungunya virus-induced arthritis in a mouse model.

**Tritsch SR, Porzucek AJ, Schwartz AM, Proctor AM, Amdur R, Latham PS, Simon GL, Mores CN, Chang AY.**
02-02-2023
*bioRxiv*.
https://pubmed.ncbi.nlm.nih.gov/36778306/

## Concurrent epidemics of dengue and COVID-19 in Peru: Which way forward?

**Hasan MM, Hernández-Yépez PJ, de Los Angeles Rivera-Cabrera M, Sarkar A, Dos Santos Costa AC, Essar MY.**
23-05-2022
*Lancet Reg Health Am*.
https://pubmed.ncbi.nlm.nih.gov/36776431/

## Fast expansion of dengue in Brazil.

**Codeco CT, Oliveira SS, Ferreira DAC, Riback TIS, Bastos LS, Lana RM, Almeida IF, Godinho VB, Cruz OG, Coelho FC.**
29-05-2022
*Lancet Reg Health Am*.
https://pubmed.ncbi.nlm.nih.gov/36776428/

## Dengue presenting as a case of acute pancreatitis-A rare case report.

**Acherjya GK, Tarafder K, Sayeed MA, Ghosh GK, Hossain MJ, Hossain S, Ali M, Kabir MA, Chakrabortty R.**
08-02-2023
*Clin Case Rep*.
https://pubmed.ncbi.nlm.nih.gov/36789296/

Atypical presentations may be presented with the common symptoms in Dengue. We, hereby, present a case of Dengue who was admitted in our hospital with the complaints of fever, upper abdominal pain, and vomiting, literally diagnosed as a case of acute pancreatitis.

## Stressors and Impact of the COVID-19 Pandemic on Vulnerable Hispanic Caregivers and Children.

**Rodríguez-Rabassa M, Torres-Marrero E, López P, Muniz-Rodriguez K, Borges-Rodríguez M, Appleton AA, Avilés-Santa L, Alvarado-Domenech LI.**
19-01-2023
*Int J Environ Res Public Health*.
https://pubmed.ncbi.nlm.nih.gov/36767218/

Psychological sequelae are important elements of the burden of disease among caregivers. Recognition of the impact of adversity and stress biomarkers is important to prevent mental health problems that affect rearing practices and child well-being. This cross-sectional study explored social determinants of health (SDoH)-mediated stressors during COVID-19 and risks for mental health problems among caregivers of children with prenatal Zika virus exposure. Twenty-five Hispanic caregivers completed surveys assessing SDoH vulnerabilities, COVID-exposures and impact, post-traumatic stress disorder (PTSD) symptomatology, and provided a hair sample for cortisol concentration (HCC). Most caregivers had low education, household income < $15,000/year, and were unemployed. Stressors included disrupted child education and specialized services, and food insecurity. While most reported PTSD symptomatology, multivariate linear regression models adjusted for the caregiver's age, education, and the child's sex, revealed that caregivers with high symptomatology had significantly lower HCC than those with low symptomatology and those with food insecurity had significantly higher HCC than participants

without food insecurity. The impact of COVID-19 on daily life was characterized on average between worse and better, suggesting variability in susceptibility and coping mechanisms, with the most resilient identifying community support and spirituality resources. SDoH-mediators provide opportunities to prevent adverse mental health outcomes for caregivers and their children.

# Rage

## [Safety and immunogenicity of freeze-dried rabies vaccine (Vero-cells) for human use in healthy people aged 9-65 years].

**Huang LL, Xie ZQ, Zhang W, Zhang K, Wang YX, Wang ZQ, Wu XJ, Liu DM.**
06-02-2023
*Zhonghua Yu Fang Yi Xue Za Zhi*.
https://pubmed.ncbi.nlm.nih.gov/36797580/

## AutoPLP: A Padlock Probe Design Pipeline for Zoonotic Pathogens.

**Krishnan SR, Soares RRG, Madaboosi N, Gromiha MM.**
15-02-2023
*ACS Infect Dis*.
https://pubmed.ncbi.nlm.nih.gov/36790094/

Emergence of novel zoonotic infections among the human population has increased the burden on global healthcare systems to curb their spread. To meet the evolutionary agility of pathogens, it is essential to revamp the existing diagnostic methods for early detection and characterization of the pathogens at the molecular level. Padlock probes (PLPs), which can leverage the power of isothermal nucleic acid amplification techniques (NAAT) such as rolling circle amplification (RCA), are known for their high sensitivity and specificity in detecting a diverse pathogen panel of interest. However, due to the complexity involved in deciding the target regions for PLP design and the need for optimization of multiple experimental parameters, the applicability of RCA has been limited in point-of-care testing for pathogen detection. To address this gap, we have developed a novel and integrated PLP design pipeline named AutoPLP, which can automate the probe design process for a diverse pathogen panel of interest. The pipeline is composed of three modules which can perform sequence data curation, multiple sequence alignment, conservation analysis, filtration based on experimental parameters ($T_m$, GC content, and secondary structure formation), and *in silico* probe validation via potential cross-hybridization check with host genome. The modules can also take into account the backbone and restriction site information, appropriate combinations of which are incorporated along with the probe arms to design a complete probe sequence. The potential applications of AutoPLP are showcased through the design of PLPs for the detection of rabies virus and drug-resistant strains of *Mycobacterium tuberculosis.*

## Fifty years of spring censuses in black grouse (Lyrurus tetrix) in the High Fens (Belgium): did the rabies vaccination has a negative impact on a fox prey population?

**Delcourt J, Hambuckers A, Vangeluwe D, Poncin P.**
2023
*Eur J Wildl Res*.
https://pubmed.ncbi.nlm.nih.gov/36789286/

## Regional variation in knowledge and practice regarding common zoonoses among livestock farmers of selective districts in Nepal.

**Bagale KB, Adhikari R, Acharya D.**
14-02-2023
*PLoS Negl Trop Dis*.
https://pubmed.ncbi.nlm.nih.gov/36787295/

Since 2017, a reinforcement programme was developed to save the last, endangered, Belgian population of black grouse (*Lyrurus tetrix*), in the High Fens Natural Park. To improve the success of this programme, an analysis of past data of this population was undertaken to understand the causes of its past decline. A time series analysis was applied, using annual spring male census data recorded between 1967 and 2016. In the period 1967-1993, there was a fluctuation around an equilibrium of a population of ca. 40-45 males. The peak of 85 males observed in 1971 was probably due to a succession of several favourable years in terms of environmental conditions, albeit without an exceptional annual growth rate. It seems that fox density, by using the occurrence of rabies as a proxy, has an impact on the black grouse population. After 1993, the population dynamic changed drastically, decreasing continuously until finally reaching quasi-extinction. On average, the population lost 15.4% of its size each year. Climate models, applied in previous studies to explain these population trends in the High Fens, failed to describe this major modification in this population's dynamic and its recent decline. We suggest that this negative effect was mainly induced by a significant increase in predation by red fox (*Vulpes vulpes*), whose abundance has increased considerably since the 1990s, in particular, as a consequence of the eradication of fox rabies. We also discuss alternative hypotheses, such as the impact of other predator species, modification of the natural environment and climatic modifications.

## Diagnostic sensitivity and specificity of immunohistochemistry for the detection of rabies virus in domestic and wild animals in South Africa.

**Claassen DD, Odendaal L, Sabeta CT, Fosgate GT, Mohale DK, Williams JH, Clift SJ.**
13-02-2023
*J Vet Diagn Invest*.
https://pubmed.ncbi.nlm.nih.gov/36782370/

## Revealing the complexity of vampire bat rabies "spillover transmission".

**Escobar LE, Velasco-Villa A, Satheshkumar PS, Nakazawa Y, Van de Vuurst P.**

**Background:** The term virus 'spillover' embodies a highly complex phenomenon and is often used to refer to viral transmission from a primary reservoir host to a new, naïve yet susceptible and permissive host species. Spillover transmission can result in a virus becoming pathogenic, causing disease and death to the new host if successful infection and transmission takes place. **Main text:** The scientific literature across diverse disciplines has used the terms virus spillover, spillover transmission, cross-species transmission, and host shift almost indistinctly to imply the complex process of establishment of a virus from an original host (source/donor) to a naïve host (recipient), which have close or distant taxonomic or evolutionary ties. Spillover transmission may result in unsuccessful onward transmission, if the virus dies off before propagation. Alternatively, successful viral establishment in the new host can occur if subsequent secondary transmission among individuals of the same novel species and among other sympatric susceptible species occurred. As such, virus spillover transmission is a common yet highly complex phenomenon that encompasses multiple subtle stages that can be deconstructed to be studied separately to better understand the drivers of disease emergence. Rabies virus (RABV) is a well-documented viral pathogen which still inflicts heavy impact on humans, companion animals, wildlife, and livestock throughout Latin America due substantial spatial temporal and ecological-natural and expansional-overlap with several virus reservoir hosts. Thereby, the rabies disease system represents a robust avenue through which the drivers and uncertainties surrounding spillover transmission can be unravel at its different subtle stages to better understand how they may be affected by coarse, medium, and fine scale variables. **Conclusions:** The continued study of viral spillover transmission necessitates the elucidation of its complexities to better assess the cross-scale impacts of ecological forces linked to the propensity of spillover success. Improving capacities to reconstruct and predict spillover transmission would prevent public health impacts on those most at risk populations across the globe.

### Transferrin Receptor Protein 1 Cooperates with mGluR2 To Mediate the Internalization of Rabies Virus and SARS-CoV-2.

**Wang X, Wen Z, Cao H, Luo J, Shuai L, Wang C, Ge J, Wang X, Bu Z, Wang J.**

### Transferrin Receptor Protein 1 Is an Entry Factor for Rabies Virus.

**Wang X, Wen Z, Cao H, Luo J, Shuai L, Wang C, Ge J, Wang X, Bu Z, Wang J.**

Rabies virus (RABV) is a prototypical neurotropic virus that causes rabies in human and animals with an almost 100% mortality rate. Once RABV enters the central nervous system, no treatment is proven to prevent death. RABV glycoprotein (G) interacts with cell surface receptors and then enters cells via clathrin-mediated endocytosis (CME); however, the key host factors involved remain largely unknown. Here, we identified transferrin receptor 1 (TfR1), a classic receptor that undergoes CME, as an entry factor for RABV. TfR1 interacts with RABV G and is involved in the endocytosis of RABV. An antibody against TfR1 or the TfR1 ectodomain soluble protein significantly blocked RABV infection in HEK293 cells, N2a cells, and mouse primary neuronal cells. We further found that the endocytosis of TfR1 is coupled with the endocytosis of RABV and that TfR1 and RABV are transported to early and late endosomes. Our results suggest that RABV hijacks the transport pathway of TfR1 for entry, thereby deepening our understanding of the entry mechanism of RABV. **IMPORTANCE** For most viruses, cell entry involves engagement with many distinct plasma membrane components, each of which is essential. After binding to its specific receptor(s), rabies virus (RABV) enters host cells through the process of clathrin-mediated endocytosis. However, whether the receptor-dependent clathrin-mediated endocytosis of RABV requires other plasma membrane components remain largely unknown. Here, we demonstrate that transferrin receptor 1 (TfR1) is a functional entry factor for RABV infection. The endocytosis of RABV is coupled with the endocytosis of TfR1. Our results indicate that RABV hijacks the transport pathway of TfR1 for entry, which deepens our understanding of the entry mechanism of RABV.

### Corrigendum: A single vaccination of nucleoside-modified Rabies mRNA vaccine induces prolonged highly protective immune responses in mice.

**Bai S, Yang T, Zhu C, Feng M, Zhang L, Zhang Z, Wang X, Yu R, Pan X, Zhao C, Xu J, Zhang X.**

### Regional and cell-type-specific afferent and efferent projections of the mouse claustrum.

**Wang Q, Wang Y, Kuo HC, Xie P, Kuang X, Hirokawa KE, Naeemi M, Yao S, Mallory M, Ouellette B, Lesnar P, Li Y, Ye M, Chen C, Xiong W, Ahmadinia L, El-Hifnawi L, Cetin A, Sorensen SA, Harris JA, Zeng H, Koch C.**

### A single vaccination of nucleoside-modified Rabies mRNA vaccine induces prolonged highly protective immune responses in mice.

**Bai S, Yang T, Zhu C, Feng M, Zhang L, Zhang Z, Wang X, Yu R, Pan X, Zhao C, Xu J, Zhang X.**

17-01-2023
*Front Immunol*.
https://pubmed.ncbi.nlm.nih.gov/36761167/

**Background:** Rabies is a lethal zoonotic disease that kills approximately 60,000 people each year. Although inactivated rabies vaccines are available, multiple-dose regimensare recommended for pre-exposure prophylaxis or post-exposure prophylaxis,which cuts down the cost- and time-effectiveness, especially in low- and middle incomecountries. **Methods:** We developed a nucleoside-modified Rabies mRNA-lipid nanoparticle vaccine (RABV-G mRNA-LNP) encoding codon-optimized viral glycoprotein and assessed the immunogenicity and protective efficacy of this vaccine in mice comparing to a commercially available inactivated vaccine. **Results:** We first showed that, when evaluated in mice, a single vaccination of RABV-G mRNA with a moderate or high dose induces more potent humoral and T-cell immune responses than that elicited by three inoculations of the inactivated vaccine. Importantly, mice receiving a single immunization of RABV-G mRNA, even at low doses, showed full protection against the lethal rabies challenge. We further demonstrated that the humoral immune response induced by single RABV-G mRNA vaccination in mice could last for at least 25 weeks, while a two-dose strategy could extend the duration of the highly protective response to one year or even longer. In contrast, the three-dose regimen of inactivated vaccine failed to do so. **Conclusion:** Our study confirmed that it is worth developing a single-dose nucleoside-modified Rabies mRNA-LNP vaccine, which could confer much prolonged and more effective protection.

### Identification and Evaluation of Cryptosporidium Species from New York City Cases of Cryptosporidiosis (2015 to 2018): a Watershed Perspective.

**Alderisio KA, Mergen K, Moessner H, Madison-Antenucci S.**
14-02-2023
*Microbiol Spectr*.
https://pubmed.ncbi.nlm.nih.gov/36688660/

# Trachome

### Exploring water, sanitation, and hygiene coverage targets for reaching and sustaining trachoma elimination: G-computation analysis.

**Sullivan KM, Harding-Esch EM, Keil AP, Freeman MC, Batcho WE, Bio Issifou AA, Bucumi V, Bella AL, Epee E, Bobo Barkesa S, Seife Gebretsadik F, Sanha S, Kalua KM, Masika MP, Minnih AO, Abdala M, Massangaie ME, Amza A, Kadri B, Nassirou B, Mpyet CD, Olobio N, Badiane MD, Elshafie BE, Baayenda G, Kabona GE, Kaitaba O, Simon A, Al-Khateeb TQ, Mwale C, Bakhtiari A, Westreich D, Solomon AW, Gower EW.**
13-02-2023
*PLoS Negl Trop Dis.*
https://pubmed.ncbi.nlm.nih.gov/36780437/

**Background:** Trachoma is the leading infectious cause of blindness. To reduce transmission, water, sanitation, and hygiene (WaSH) improvements are promoted through a comprehensive public health strategy. Evidence supporting the role of WaSH in trachoma elimination is mixed and it remains unknown what WaSH coverages are needed to effectively reduce transmission. **Methods/findings:** We used g-computation to estimate the impact on the prevalence of trachomatous inflammation-follicular among children aged 1-9 years (TF1-9) when hypothetical WaSH interventions raised the minimum coverages from 5% to 100% for "nearby" face-washing water (<30 minutes roundtrip collection time) and adult latrine use in an evaluation unit (EU). For each scenario, we estimated the generalized prevalence difference as the TF1-9 prevalence under the intervention scenarios minus the observed prevalence. Data from 574 cross-sectional surveys conducted in 16 African and Eastern Mediterranean countries were included. Surveys were conducted from 2015-2019 with support from the Global Trachoma Mapping Project and Tropical Data. When modeling interventions among EUs that had not yet met the TF1-9 elimination target, increasing nearby face-washing water and latrine use coverages above 30% was generally associated with consistent decreases in TF1-9. For nearby face-washing water, we estimated a ≥25% decrease in TF1-9 at 65% coverage, with a plateau upon reaching 85% coverage. For latrine use, the estimated decrease in TF1-9 accelerated from 80% coverage upward, with a ≥25% decrease in TF1-9 by 85% coverage. Among EUs that had previously met the elimination target, results were inconclusive. **Conclusions:** Our results support Sustainable Development Goal 6 and provide insight into potential WaSH-related coverage targets for trachoma elimination. Targets can be tested in future trials to improve evidence-based WaSH guidance for trachoma.

### Comparison of Five Camera Systems for Capturing and Grading Trachoma Images.

**Naufal F, Brady CJ, Muñoz B, Mkocha H, West SK.**
12-02-2023
*Ophthalmic Epidemiol*.
https://pubmed.ncbi.nlm.nih.gov/36775887/

# Ulcère de Buruli

### Identifying Hot Spots of Tuberculosis in Nigeria Using an Early Warning Outbreak Recognition System: Retrospective Analysis of Implications for Active Case Finding Interventions.

**Ogbudebe C, Jeong D, Odume B, Chukwuogo O, Dim C, Useni S, Okuzu O, Malolan C, Kim D, Nwariaku F, Nwokoye N, Gande S, Nongo D, Eneogu R, Odusote T, Oyelaran S, Chijioke-Akaniro O, Nihalani N, Anyaike C, Gidado M.**
08-02-2023
*JMIR Public Health Surveill*.
https://pubmed.ncbi.nlm.nih.gov/36753328/

**Background:** Undiagnosed tuberculosis (TB) cases are the major challenge to TB control in Nigeria. An early warning outbreak recognition system (EWORS) is a system that is primarily used to detect infectious disease outbreaks; this system can be used as a case-based geospatial tool for the real-time identification of hot spot areas with clusters of TB patients. TB screening targeted at such hot spots should yield more TB cases than screening targeted at non-hot spots. **Objective:** We aimed to demonstrate the effectiveness of an EWORS for TB hot spot mapping as a tool for detecting areas with increased TB case yields in high TB-burden states of Nigeria. **Methods:** KNCV Tuberculosis Foundation Nigeria deployed an EWORS to 14 high-burden states in Nigeria. The system used an advanced surveillance mechanism to identify TB patients' residences in clusters, enabling it to predict areas with elevated disease spread (ie, hot spots) at the ward level. TB screening outreach using the World Health Organization 4-symptom screening method was conducted in 121 hot spot wards and 213 non-hot spot wards selected from the same communities. Presumptive cases identified were evaluated for TB using the GeneXpert instrument or chest X-ray. Confirmed TB cases from both areas were linked to treatment. Data from the hot spot and non-hot spot wards were analyzed retrospectively for this study. **Results:** During the 16-month intervention, a total of 1,962,042 persons (n=734,384, 37.4% male, n=1,227,658, 62.6% female) and 2,025,286 persons (n=701,103, 34.6% male, n=1,324,183, 65.4% female) participated in the community TB screening outreaches in the hot spot and non-hot spot areas, respectively. Presumptive cases among all patients screened were 268,264 (N=3,987,328, 6.7%) and confirmed TB cases were 22,618 (N=222,270, 10.1%). The number needed to screen to diagnose a TB case in the hot spot and non-hot spot areas was 146 and 193 per 10,000 people, respectively. **Conclusions:** Active TB case finding in EWORS-mapped hot spot areas yielded higher TB cases than the non-hot spot areas in the 14 high-burden states of Nigeria. With the application of EWORS, the precision of diagnosing TB among presumptive cases increased from 0.077 to 0.103, and the number of presumptive cases needed to diagnose a TB case decreased from 14.047 to 10.255 per 10,000 people.

# Pian

### Conformity of yaws clinical features to combined rapid diagnostic test in children aged 2-15 years in an endemic area.

Menaldi SLS, Natasha J, Saputra J, Marissa M, Irawan Y, Friska D, Wahyudi DT.

**Introduction:** The diagnosis of yaws is established by clinical examination and confirmed through a laboratory test. Unrecognized lesions may lead to a missed opportunity for diagnosis and complete eradication of yaws. The use of Dual Path Platform (DPP® RDT) Syphilis Screen and Confirm RDT (Chembio, Medford, New York) has been recommended by the World Health Organization (WHO) for endemic areas with limited laboratory facilities. To date, there have not been any studies assessing the conformity of clinical features based on the WHO guidelines with DPP® RDT. **Methodology:** A cross-sectional study was conducted to evaluate the conformity of yaws clinical features based on the WHO guidelines to the DPP® RDT. We recruited children aged 2-15 years old in Alor, Indonesia. All subjects underwent clinical examination and were tested with DPP® RDT. Fisher's exact test was used to analyze the overall agreement between the clinical features and the DPP® RDT results. **Results:** A total of 197 study subjects (mean age 9 years) were enrolled. The most frequent skin lesion was a yaws scar (79.7%). Eight subjects (3%) were diagnosed with yaws based on the DPP® RDT examination. The overall agreement between clinical features and DPP® RDT was 26.9% (p = 0.202). **Conclusions:** The conformity of clinical features in suspected yaws to DPP® RDT is low; thus, clinical features should not be used as a sole initial reference in establishing yaws diagnosis, even in endemic areas.

# Lèpre

### Seventy years of evidence on the efficacy and safety of drugs for treating leprosy: a network meta-analysis.

Yang J, Kong J, Li B, Ji Z, Chen J, Liu M, Fan Y, Peng L, Song J, Wu X, Gao L, Ma W, Dong Y, Luo S, Liu A, Bao F.

**Objective:** The World Health Organization (WHO) recommends multidrug therapy (MDT) with rifampicin, dapsone, and clofazimine for treating leprosy, which based on very low-quality evidence. Here we performed a network meta-analysis (NMA) to produce quantitative evidence to strengthen current WHO recommendations. **Method:** All studies were obtained from Embase and PubMed from the date of establishment to October 9th, 2021. Data were synthesized with frequentist random-effects network meta-analyses. Outcomes were assessed using odds ratios (ORs), 95% confident intervals (95% CIs) and P score. **Results:** Sixty controlled clinical trials and 9256 patients were included. MDT was effective (range of OR: 1·06-1255584·25) for treating leprosy and multibacillary leprosy. Six treatments (Range of OR: 1.199-4.50) were more effective than MDT. Clofazimine (P score=0.9141) and dapsone+rifampicin (P score=0·8785) were effective for treating type 2 leprosy reaction. There were no significant differences in the safety of any of the tested drug regimens. **Conclusions:** The WHO MDT is effective for treating leprosy and multibacillary leprosy, but it may not be effective enough. Pefloxacin and ofloxacin may be good adjunct drugs for increasing MDT efficacy. Clofazimine and dapsone+rifampicin can be used in the treatment of a type 2 leprosy reaction. Single drug regimens are not efficient enough to treat leprosy, multibacillary leprosy, or a type 2 leprosy reaction. **Availability of data and materials:** All data generated or

analysed during this study are included in this published article [and its supplementary information files].

## Dapsone-induced photosensitivity: A case report and review of literature.

Shigehara Y, Kato M.
16-02-2023
*Photodermatol Photoimmunol Photomed*.

## Prospects for tuberculosis elimination in Ethiopia: feasibility, challenges, and opportunities.

Agizew TB, Dememew ZG, Leta T, Hiruy N, Tesema E, Abelti EA, Gebreyohannes A, Alemayehu YM, Omer AB, Suarez PG, Kassie Y, Kassa A, Gemechu D, Jerene D.
17-11-2022
*Pan Afr Med J*.

To end the global tuberculosis (TB) epidemic and eliminate TB, countries around the world committed to significantly expanding the scope of their efforts, including rapid uptake of new tools, interventions, and strategies, and envisioned a world free of TB. Between 2010 and 2020, Ethiopia experienced a 5% average annual decline in TB incidence. However, at that current rate, ending the TB epidemic (<10 TB cases/100,000 population) may not be possible soon. As a high TB and TB/HIV burden country, Ethiopia's TB epidemic is characterized by a high rate of transmission in the general population and hard-to-reach areas and progression of latent TB infection (LTBI) rather than cross-border migration. Studies suggest that a combination of interventions, such as intensive household screening with TB preventive therapy, has the potential to significantly decrease the incidence of TB. The feasibility of reducing the population-level TB incidence by a combination of interventions in Ethiopia is unknown. Based on the World Health Organization's TB elimination framework and the END TB strategic documents and previously published reviews in TB elimination we conducted a narrative review to summarize and estimated the effect of a combined intervention package (community-based TB screening for active case finding and TB and LTBI prevention and treatment among high-risk groups like household and close contacts). The projected annual decline of TB incidence was above 16%. With this level of impact and nationwide scale-up of the interventions, Ethiopia aligns well with ending the TB epidemic before 2035 and shifting toward TB elimination in the foreseeable future. In the Ethiopia setting, we recommend future studies generating evidence on the impact of the combination intervention package to reduce TB incidence in Ethiopia, which is aiming to shift from control to TB elimination.

## Genomic Epidemiological Analysis of Antimicrobial-Resistant Bacteria with Nanopore Sequencing.

Suzuki M, Hashimoto Y, Hirabayashi A, Yahara K, Yoshida M, Fukano H, Hoshino Y, Shibayama K, Tomita H.
2023
*Methods Mol Biol.*

Antimicrobial-resistant (AMR) bacterial infections caused by clinically important bacteria, including ESKAPE pathogens (Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter species) and mycobacteria (Mycobacterium tuberculosis and nontuberculous mycobacteria), have become a global public health threat. Their epidemic and pandemic clones often accumulate useful accessory genes in their genomes, such as AMR genes (ARGs) and virulence factor genes (VFGs). This process is facilitated by horizontal gene transfer among microbial communities via mobile genetic elements (MGEs), such as plasmids and phages. Nanopore long-read sequencing allows easy and inexpensive analysis of complex bacterial genome structures, although some aspects of sequencing data calculation and genome analysis methods are not systematically understood. Here we describe the latest and most recommended experimental and bioinformatics methods available for the construction of complete bacterial genomes from nanopore sequencing data and the detection and classification of genotypes of bacterial chromosomes, ARGs, VFGs, plasmids, and other MGEs based on their genomic sequences for genomic epidemiological analysis of AMR bacteria.

## A study about management of drugs for leprosy patients under medical monitoring: A solution based on AHP-Electre decision-making methods.

Falcão IWS, Souza DS, Cardoso DL, Costa FAR, Leite KTF, de M HD Junior, Salgado CG, da Silva MB, Barreto JG, da Costa PF, Santos AMD, Conde GAB, Seruffo MCDR.
13-02-2023
*PLoS One.*

## EphH, a unique epoxide hydrolase encoded by Rv3338 is involved in the survival of Mycobacterium tuberculosis under in vitro stress and vacuolar pH-induced changes.

Garg T, Das S, Singh S, Imran M, Mukhopadhyay A, Gupta UD, Chopra S, Dasgupta A.
26-01-2022
*Front Microbiol.*

Introduction: *Mycobacterium tuberculosis* (Mtb), one of the deadliest human pathogen, has evolved with different strategies of survival inside the host, leading to a chronic state of infection. Phagosomally residing Mtb encounters a variety of stresses, including increasing acidic pH. To better understand the host-pathogen interaction, it is imperative to identify the role of various genes involved in the survivability of Mtb during acidic pH environment. Methods: Bio-informatic and enzymatic analysis were used to identify Mtb gene, Rv3338, as epoxide hydrolase. Subsequently, CRISPRi knockdown strategy was used to

decipher its role for Mtb survival during acidic stress, nutrient starvation and inside macrophages. Confocal microscopy was used to analyse its role in subverting phagosomal acidification within macrophage. **Results:** The present work describes the characterization of Rv3338 which was previously known to be associated with the aprABC locus induced while encountering acidic stress within the macrophage. Bio-informatic analysis demonstrated its similarity to epoxide hydrolase, which was confirmed by enzymatic assays, thus, renamed EphH. Subsequently, we have deciphered its indispensable role for Mtb in protection from acidic stress by using the CRISPRi knockdown strategy. Our data demonstrated the pH dependent role of EphH for the survival of Mtb during nutrient starvation and in conferring resistance against elevated endogenous ROS levels during stress environment. **Conclusion:** To the best of our knowledge, this is the first report of an EH of Mtb as a crucial protein for bacterial fitness inside the host, a phenomenon central to its pathogenesis.

## Reimagining leprosy elimination with AI analysis of a combination of skin lesion images with demographic and clinical data.

**Barbieri RR, Xu Y, Setian L, Souza-Santos PT, Trivedi A, Cristofono J, Bhering R, White K, Sales AM, Miller G, Nery JAC, Sharman M, Bumann R, Zhang S, Goldust M, Sarno EN, Mirza F, Cavaliero A, Timmer S, Bonfiglioli E, Smith C, Scollard D, Navarini AA, Aerts A, Ferres JL, Moraes MO.**
03-02-2023
*Lancet Reg Health Am*.
https://pubmed.ncbi.nlm.nih.gov/36776278/

**Background:** Leprosy is an infectious disease that mostly affects underserved populations. Although it has been largely eliminated, still about 200'000 new patients are diagnosed annually. In the absence of a diagnostic test, clinical diagnosis is often delayed, potentially leading to irreversible neurological damage and its resulting stigma, as well as continued transmission. Accelerating diagnosis could significantly contribute to advancing global leprosy elimination. Digital and Artificial Intelligence (AI) driven technology has shown potential to augment health workers abilities in making faster and more accurate diagnosis, especially when using images such as in the fields of dermatology or ophthalmology. That made us start the quest for an AI-driven diagnosis assistant for leprosy, based on skin images. **Methods:** Here we describe the accuracy of an AI-enabled image-based diagnosis assistant for leprosy, called AI4Leprosy, based on a combination of skin images and clinical data, collected following a standardized process. In a Brazilian leprosy national referral center, 222 patients with leprosy or other dermatological conditions were included, and the 1229 collected skin images and 585 sets of metadata are stored in an open-source dataset for other researchers to exploit. **Findings:** We used this dataset to test whether a CNN-based AI algorithm could contribute to leprosy diagnosis and employed three AI models, testing images and metadata both independently and in combination. AI modeling indicated that the most important clinical signs are thermal sensitivity loss, nodules and papules, feet

paresthesia, number of lesions and gender, but also scaling surface and pruritus that were negatively associated with leprosy. Using elastic-net logistic regression provided a high classification accuracy (90%) and an area under curve (AUC) of 96.46% for leprosy diagnosis. **Interpretation:** Future validation of these models is underway, gathering larger datasets from populations of different skin types and collecting images with smartphone cameras to mimic real world settings. We hope that the results of our research will lead to clinical solutions that help accelerate global leprosy elimination.

## Acquired Cutaneous Lymphangiectasia of Vulva: A Novel Dermoscope Finding.

**Selvaarasan J, Palaniappan V, Karthikeyan K.**
28-07-2022
*Indian Dermatol Online J.*
https://pubmed.ncbi.nlm.nih.gov/36776196/

## Clinico-Trichoscopic and Histopathological Findings of Aseptic and Alopecic Nodules of Scalp: A Case Series.

**Bhat YJ, Trumboo T.**
21-09-2022
*Indian Dermatol Online J.*
https://pubmed.ncbi.nlm.nih.gov/36776184/

## Cutaneous Manifestations Associated with COVID-19 Infection in a COVID-Designated Hospital in North Chennai - A Descriptive Cross-Sectional Study.

**Kumar P, Radha G, Muthukrishnan M, Chandrasekaran B, Subbiah P, Raman J.**
29-12-2022
*Indian Dermatol Online J.*
https://pubmed.ncbi.nlm.nih.gov/36776182/

**Background:** Coronavirus disease 2019 (COVID-19) affects different organ systems, including the skin. There are reports on cutaneous manifestations of COVID-19 available in the literature. In this study, we have tried to describe the dermatological signs of COVID-19 in different categories of patients. **Materials and methods:** A descriptive cross sectional study was conducted to describe various cutaneous manifestations of COVID-19 in different categories of reverse transcriptase polymerase chain reaction (RT-PCR)-positive COVID-19 patients in a COVID-designated tertiary care hospital. Approval was obtained from the Institutional Ethical Committee, and 5460 RT-PCR-confirmed COVID-19-positive patients were included under five categories. Investigators following a strict COVID protocol examined and documented the findings. Investigations and treatment were carried out as per the protocol, and the study was conducted for a period of 6 months. **Results:** Out of the 5460 patients studied, 1.9% patients had cutaneous manifestations. Vasculitis (24%) and maculo papular rash (19%) were the common findings. The incidence of vasculitis was 44.4%, 61%, and 6.6% in categories A, B, and C, respectively. Maculopapular rash and urticaria were the common findings in categories

D and E, respectively. COVID digit was seen in only one case. Other manifestations such as acne, adverse drug reaction, erythroderma, and bullous disorders were also noted. **Conclusion:** Cutaneous manifestations because of vascular pathology were the most common association in severe COVID-19, which indicates that the presence of vasculitic skin signs correlated with disease severity and elevated d-dimer values. Urticaria and maculo-papular rash were transient and did not give any clue to the diagnosis or severity of the disease.

## A Cross-Sectional Study Comparing Application of Hanifin and Rajka Criteria in Indian Pediatric Atopic Dermatitis Patients to that of Other Countries.

**Shetty NS, Lunge S, Sardesai VR, Dalal AB.**
29-12-2022
*Indian Dermatol Online J.*
https://pubmed.ncbi.nlm.nih.gov/36776180/

## Occupational Dermatoses.

**Srinivas CR, Sethy M.**
14-12-2022
*Indian Dermatol Online J.*
https://pubmed.ncbi.nlm.nih.gov/36776171/

## Clinical and Demographic Patterns of Vulval Dermatoses and Their Impact on Quality of Life.

**Shaik H, Konala S, Kolalapudi SA, Alluri R, Godha V, Navya B.**
14-12-2022
*Indian Dermatol Online J.*
https://pubmed.ncbi.nlm.nih.gov/36776168/

**Background:** Vulval dermatoses may present with varied manifestations ranging from asymptomatic to chronic disabling conditions. The multifactorial nature of symptoms and physical expression of the disease on the vulva complicate the evaluation and management of genital dermatoses, thereby severely impairing the quality of life of patients. **Objectives:** To study the clinical patterns and socio-demographic features of vulval dermatoses and their impact on the quality of life using the dermatology life quality index (DLQI) questionnaire. **Materials and methods:** Female patients of all age groups who attended our outpatient department (OPD) from October 2019 to March 2021 with vulval lesions were included in the study after a detailed history and complete examination. Based on sites of involvement, the lesions were classified as genital lesions alone, genital and skin lesions, oro-genital lesions, and oro-genital and skin lesions. DLQI score was assessed using the DLQI questionnaire. **Results:** In total, 520 patients were recruited for the study after following the inclusion and exclusion criteria. The most common age group was 31-40 years (33.65%). The majority of the patients were married (91.92%), housewives (82.88%), and illiterate (49.61%) women. The most common presenting symptom was itching (43%). The most common vulval dermatoses were infections, seen in 401 (77.11%) patients, followed by inflammatory diseases in 78 (15%) patients, and immunobullous diseases (1.53%). Patients

with genital, skin, and oral involvement showed statistically significant higher DLQI scores (*P* value < 0.05). Patients with immunobullous disorders had the highest mean DLQI scores. **Limitations:** As this study was a hospital-based study, the observations may not represent and reflect the general population. **Conclusion:** Patients with genital, skin, and oral lesions had the highest DLQI scores, indicating higher impact on the quality of life. Assessment of the disease's impact on the quality of life is essential because it not only aids in early management but also helps in minimizing the duration of the ailment.

## Hijama Blister.

**Karthikeyan K, Sadhasivamohan A.**
21-10-2022
*Indian Dermatol Online J.*
https://pubmed.ncbi.nlm.nih.gov/36776165/

## Diffuse Hypopigmented Keratoses: An Under-Reported and Often Misdiagnosed Entity.

**Sane RR, Manoharan K, Sukanya G, Udhayini KV.**
14-12-2022
*Indian Dermatol Online J.*
https://pubmed.ncbi.nlm.nih.gov/36776162/

The appearance of widely diffuse hypopigmented keratotic lesions has been linked to a number of dermatological conditions like pityriasis versicolor, stucco keratoses, confetti leukoderma, and guttate leukoderma of Darier's disease. Specific clinical and histologic characteristics distinguish them from one another. One of the differentials for diffuse hypopigmented keratotic lesions has been a novel entity called disseminated hypopigmented keratoses (DHK). We are hereby highlighting the importance of bedside investigations like potassium hydroxide wet mount and dermatoscopy in ruling out such misleading dermatological conditions. It looks to be benign and slowly progressing, albeit not linked to any systemic symptoms. We hereby present a case of diffuse hypopigmented keratoses with no proven underlying cause.

## Bronchitis, COPD, and pneumonia after viral endemic of patients with leprosy on Sorok Island in South Korea.

**Lee JH, Kanwar B, Khattak A, Altschuler E, Sergi C, Lee SJ, Choi SH, Park J, Coleman M, Bourbeau J.**
11-02-2022
*Naunyn Schmiedebergs Arch Pharmacol.*
https://pubmed.ncbi.nlm.nih.gov/36773052/

## Linear focal elastosis.

**Palaniappan V, Selvaarasan J, Murthy AB, Karthikeyan K.**
11-11-2022
*Clin Exp Dermatol.*
https://pubmed.ncbi.nlm.nih.gov/36763712/

Linear focal elastosis (LFE) is an uncommon, benign, acquired elastotic condition with uncertain pathogenesis. It is characterized clinically by asymptomatic, multiple, yellowish, elevated, irregularly indurated, striae-like lines

or bands distributed horizontally across the lower and middle part of the posterior trunk. The histopathological hallmark of LFE is a focal increase of elastic fibres in the dermis. The differential diagnosis is varied, and striae distensae is the closest mimic of LFE. Response of LFE to treatment is often poor. The focus of this article is to provide insights into this condition for dermatologists.

## Nairobi eye - "Wake and see" disease.

**Sadhasivamohan A, Palaniappan V, Karthikeyan K.**
02-11-2022
*Oman J Ophthalmol.*
https://pubmed.ncbi.nlm.nih.gov/36760943/

## Identifying Hot Spots of Tuberculosis in Nigeria Using an Early Warning Outbreak Recognition System: Retrospective Analysis of Implications for Active Case Finding Interventions.

**Ogbudebe C, Jeong D, Odume B, Chukwuogo O, Dim C, Useni S, Okuzu O, Malolan C, Kim D, Nwariaku F, Nwokoye N, Gande S, Nongo D, Eneogu R, Odusote T, Oyelaran S, Chijioke-Akaniro O, Nihalani N, Anyaike C, Gidado M.**
08-02-2023
*JMIR Public Health Surveill.*
https://pubmed.ncbi.nlm.nih.gov/36753328/

Background: Undiagnosed tuberculosis (TB) cases are the major challenge to TB control in Nigeria. An early warning outbreak recognition system (EWORS) is a system that is primarily used to detect infectious disease outbreaks; this system can be used as a case-based geospatial tool for the real-time identification of hot spot areas with clusters of TB patients. TB screening targeted at such hot spots should yield more TB cases than screening targeted at non-hot spots. Objective: We aimed to demonstrate the effectiveness of an EWORS for TB hot spot mapping as a tool for detecting areas with increased TB case yields in high TB-burden states of Nigeria. Methods: KNCV Tuberculosis Foundation Nigeria deployed an EWORS to 14 high-burden states in Nigeria. The system used an advanced surveillance mechanism to identify TB patients' residences in clusters, enabling it to predict areas with elevated disease spread (ie, hot spots) at the ward level. TB screening outreach using the World Health Organization 4-symptom screening method was conducted in 121 hot spot wards and 213 non-hot spot wards selected from the same communities. Presumptive cases identified were evaluated for TB using the GeneXpert instrument or chest X-ray. Confirmed TB cases from both areas were linked to treatment. Data from the hot spot and non-hot spot wards were analyzed retrospectively for this study. Results: During the 16-month intervention, a total of 1,962,042 persons (n=734,384, 37.4% male, n=1,227,658, 62.6% female) and 2,025,286 persons (n=701,103, 34.6% male, n=1,324,183, 65.4% female) participated in the community TB screening outreaches in the hot spot and non-hot spot areas, respectively. Presumptive cases among all patients screened were 268,264 (N=3,987,328, 6.7%) and confirmed TB cases were 22,618 (N=222,270, 10.1%). The number needed to screen to diagnose a TB case in the hot spot and non-hot spot areas was 146 and 193 per 10,000 people, respectively. Conclusions: Active TB case finding in EWORS-mapped hot spot areas yielded higher TB cases than the non-hot spot areas in the 14 high-burden states of Nigeria. With the application of EWORS, the precision of diagnosing TB among presumptive cases increased from 0.077 to 0.103, and the number of presumptive cases needed to diagnose a TB case decreased from 14.047 to 10.255 per 10,000 people.

## Intra-cranial involvement of trigeminal nerve in a patient with borderline tuberculoid leprosy in type 1 lepra reaction.

**Sharma A, Narang T, Mehta H, Mahajan R, Takkar A, Prakash M, Dogra S.**
Feb-2023
*Australas J Dermatol.*
https://pubmed.ncbi.nlm.nih.gov/36683361/

## World Health Organization strategic framework for integrated control and management of skin-related neglected tropical diseases: what does this mean for dermatologists?

**Yotsu RR, Fuller LC, Murdoch ME, Revankar C, Barogui YT, Pemmaraju VRR, Ruiz-Postigo JA, Dagne DA, Asiedu K, Hay RJ.**
10-02-2023
*Br J Dermatol.*
https://pubmed.ncbi.nlm.nih.gov/36630642/

## Type 1 lepra reaction induced by a COVID-19 vaccine.

**Hsu CH, Yang CS, Yen CY.**
Mar-2023
*J Eur Acad Dermatol Venereol.*
https://pubmed.ncbi.nlm.nih.gov/36377290/

## Pentoxifylline in dermatology.

**Balazic E, Axler E, Konisky H, Khanna U, Kobets K.**
Feb-2023
*J Cosmet Dermatol.*
https://pubmed.ncbi.nlm.nih.gov/36208009/

Background: Pentoxifylline was initially marketed for use in patients with intermittent claudication due to chronic occlusive arterial disease of the extremities but has since been shown to have several off-label uses in dermatology. Aims: The aim of this review is to increase awareness of the several applications of pentoxifylline in the field of dermatology. Methods: A comprehensive PubMed search was conducted in May 2022 using the following phrases "dermatology" AND "pentoxifylline." Our search period spanned 34 years from 1988 to 2022. All available literature was reviewed. Reference lists of identified articles were included. Studies were excluded if they were not in English and if the study was out of scope. Eighty-one articles were included in this review. Results: Pentoxifylline has been used to treat various dermatological conditions

including peripheral vascular disease, vasculitis and vasculopathies, chilblains, pigmented purpuric dermatosis, granuloma annulare, necrobiosis, keloids, lichen sclerosis et atrophicus, scars, radiation-induced fibrosis, vitiligo, alopecia areata, leishmaniasis, and leprosy. Conclusions: Pentoxifylline's use in dermatology is growing. However, there are limited larger studies and randomized control trials on the use of pentoxifylline in dermatology and more investigation is needed to evaluate its use for many dermatologic conditions. Pentoxifylline's unique mechanism of action as well as its good tolerability, cost-effectiveness, and minimal drug interactions make it a convenient primary or adjunctive option in many dermatological conditions.

## Clinical update on cutaneous and subcutaneous sarcomas.

**Kumari J, Das K, Patil A, Babaei M, Cockerell CJ, Goldust M.**
Feb-2023
*J Cosmet Dermatol*.
https://pubmed.ncbi.nlm.nih.gov/36074118/

## Therapeutic application of machine learning in psoriasis: A Prisma systematic review.

**Lunge SB, Shetty NS, Sardesai VR, Karagaiah P, Yamauchi PS, Weinberg JM, Kircik L, Giulini M, Goldust M.**
Feb-2023
*J Cosmet Dermatol*.
https://pubmed.ncbi.nlm.nih.gov/35621249/

Dermatology, being a predominantly visual-based diagnostic field, has found itself to be at the epitome of artificial intelligence (AI)-based advances. Machine learning (ML), a subset of AI, goes a step further by recognizing patterns from data and teaches machines to automatically learn tasks. Although artificial intelligence in dermatology is mostly developed in melanoma and skin cancer diagnosis, advances in AI and ML have gone far ahead and found its application in ulcer assessment, psoriasis, atopic dermatitis, onychomycosis, etc. This article is focused on the application of ML in the therapeutic aspect of psoriasis.

# Trypanosomes (trypanosomiase et maladie de Chagas)

## Structural differences between hypoxanthine phosphoribosyltransferase family members highlight opportunities for antiparasitic drug design in neglected diseases.

**Santos J, Fernández Villamil SH, Delfino JM, Valsecchi WM.**
14-02-2023
*Arch Biochem Biophys*.

https://pubmed.ncbi.nlm.nih.gov/36796662/

## Genetic diversity of Trypanosoma cruzi infecting raccoons (Procyon lotor) in 2 metropolitan areas of southern Louisiana: implications for parasite transmission networks.

**Majeau A, Cloherty E, Anderson AN, Straif-Bourgeois SC, Dumonteil E, Herrera C.**
20-01-2023
*Parasitology*.
https://pubmed.ncbi.nlm.nih.gov/36788672/

*Trypanosoma cruzi*, the aetiological agent of Chagas disease, exists as an anthropozoonosis in Louisiana. Raccoons are an important reservoir, as they demonstrate high prevalence and maintain high parasitaemia longer than other mammals. Given the complex nature of parasite transmission networks and importance of raccoons as reservoirs that move between sylvatic and domestic environments, detailing the genetic diversity of *T. cruzi* in raccoons is crucial to assess risk to human health. Using a next-generation sequencing approach targeting the mini-exon, parasite diversity was assessed in 2 metropolitan areas of Louisiana. Sequences were analysed along with those previously identified in other mammals and vectors to determine if any association exists between ecoregion and parasite diversity. Parasites were identified from discrete typing units (DTUs) TcI, TcII, TcIV, TcV and TcVI. DTUs TcII, TcV and TcVI are previously unreported in raccoons in the United States (US). TcI was the most abundant DTU, comprising nearly 80% of all sequences. All but 1 raccoon harboured multiple haplotypes, some demonstrating mixed infections of different DTUs. Furthermore, there is significant association between DTU distribution and level III ecoregion in Louisiana. Finally, while certain sequences were distributed across multiple tissues, others appeared to have tissue-specific tropism. Taken together, these findings indicate that ongoing surveillance of *T. cruzi* in the US should be undertaken across ecoregions to fully assess risk to human health. Given potential connections between parasite diversity and clinical outcomes, deep sequencing technologies are crucial and interventions targeting raccoons may prove useful in mitigating human health risk.

## Phenology and environmental predictors of Triatoma sanguisuga dispersal in east-central Texas, United States.

**Fimbres-Macias JP, Harris TA, Hamer SA, Hamer GL.**
12-02-2023
*Acta Trop*.
https://pubmed.ncbi.nlm.nih.gov/36787862/

## Cytokinesis in Trypanosoma brucei relies on an orphan kinesin that dynamically crosslinks microtubules.

**Sladewski TE, Campbell PC, Billington N, D'Ordine A, Cole JL, de Graffenried CL.**

10-02-2023
*Curr Biol*.

## Trypanosoma cruzi Isolates Naturally Adapted to Congenital Transmission Display a Unique Strategy of Transplacental Passage.

Faral-Tello P, Greif G, Romero S, Cabrera A, Oviedo C, González T, Libisch G, Arévalo AP, Varela B, Verdes JM, Crispo M, Basmadjián Y, Robello C.
14-02-2023
*Microbiol Spectr*.

## Retrospective Review of Chromane Analogues as Anti-Protozoal Leads: A Decade's Worth of Evolution.

Rajkumar Jadhav S, Karan Kumar B, Parasuraman Joshi R, Suryakant Chougule K, Chandu A, -Ur-Rehman MM, Mahadu Khetmalis Y, Nandikolla A, Murugesan S, Venkata Gowri Chandra Sekhar K.
14-02-2023
*Curr Top Med Chem*.

Tropical, vector-borne, and neglected diseases with a limited number of medication therapies include Leishmaniasis, Malaria, Chagas and Human African Trypanosomiasis (HAT). Chromones are a large class of heterocyclic compounds with significant applications. This heterocycle has long aroused the interest of scientists and the general public from biosynthetic and synthetic points of view owing to its interesting pharmacological activities. Chromones and their hybrids and isomeric forms proved to be an exciting scaffold to investigate these diseases. The in vitro activities of Chromone, Chromane, and a panel of other related benzopyran class compounds against Trypanosoma brucei rhodesiense, Trypanosoma brucei gambiense, Trypanosoma cruzi, and numerous Leishmanial and Malarial species were investigated in our previous studies. The current article briefly describes the neglected diseases and the current treatment. This review aims to attempt to find better alternatives by scrutinizing natural and synthetic derivatives for which chromones and their analogues were discovered to be a new and highly effective scaffold for the treatment of neglected diseases, including compounds with dual activity or activity against multiple parasites. Additionally, the efficacy of other new scaffolds was also thoroughly examined. This article also discusses prospects for identifying more unique targets for the disease, focusing on flavonoids as drug molecules that are less cytotoxic and high antiprotozoal potential. It also emphasizes the changes that can be made while searching for potential therapies-comparing existing treatments against protozoal diseases and the advantages of the newer chromone analogues over them. Finally, the structure-activity relationship at each atom of the chromone has also been highlighted.

## Are patents important indicators of innovation for Chagas disease treatment?

Caroli AP, Mansoldo FRP, Cardoso VS, Lage CLS, Carmo FL, Supuran CT, Beatriz Vermelho A.
15-02-2023
*Expert Opin Ther Pat*.

## Chagas Disease.

Hochberg NS, Montgomery SP.
14-02-2023
*Ann Intern Med*.

Chagas disease, which is caused by infection with the parasite *Trypanosoma cruzi*, is a leading neglected tropical disease in the United States. An estimated 240 000 to 350 000 persons in the United States are infected, primarily immigrants from Mexico, Central America, and South America, where the disease is endemic. The parasite is transmitted by the triatomine bug but can also be passed through blood transfusion, via organ transplant, or congenitally. Approximately 30% of infected persons later develop cardiac and/or gastrointestinal complications. Health care providers should consider screening at-risk patients with serologic testing. Early diagnosis and treatment with benznidazole or nifurtimox can help prevent complications.

## Genetic Characterization of Trypanosoma cruzi I Populations from an Oral Chagas Disease Outbreak in Venezuela: Natural Resistance to Nitroheterocyclic Drugs.

Muñoz-Calderón A, Ramírez JL, Díaz-Bello Z, Alarcón de Noya B, Noya O, Schijman AG.
13-02-2023
*ACS Infect Dis*.

The oral transmission of Chagas disease (oCD) in Venezuela announced its appearance in 2007. Different from other populations affected by oCD and despite close supervision during treatment with nitroheterocyclic drugs, the result was treatment failure. We studied genetic features of natural bloodstream parasite populations and populations after treatment of nine patients of this outbreak. In total, we studied six hemoculture isolates, eight Pre-Tx blood samples, and 17 samples collected at two or three Post-Tx time-points between 2007 and 2015. Parasitic loads were determined by quantitative polymerase chain reaction (qPCR), and discrete typing units (DTU), minicircle signatures, and *Tcntr-1* gene sequences were searched from blood samples and hemocultures. Half-maximal inhibitory concentration ($IC_{50}$) values were measured from the hemocultures. All patients were infected by TcI. Significant decrease in parasitic loads was observed between Pre-Tx and Post-Tx samples, suggesting the evolution from acute to chronic phase of Chagas disease. 60% of intra-DTU-I variability was observed between Pre-Tx and Post-Tx minicircle

signatures in the general population, and 43 single-nucleotide polymorphisms (SNPs) were detected in a total of 12 *Tcntr-1* gene sequences, indicative of a polyclonal source of infection. SNPs in three post-Tx samples produced stop codons giving rise to putative truncated proteins or displaced open reading frames, which would render resistance genes. IC$_{50}$ values varied from 5.301 ± 1.973 to 104.731 ± 4.556 µM, demonstrating a wide range of susceptibility. The poor drug response in the Pre-Tx parasite populations may be associated with the presence of naturally resistant parasite clones. Therefore, any information that can be obtained on drug susceptibility from in vitro assays, in vivo assays, or molecular characterization of natural populations of *Trypanosoma cruzi* becomes essential when therapeutic guidelines are designed in a given geographical area.

## Frequency variation and dose modification of benznidazole administration for the treatment of Trypanosoma cruzi infection in mice, dogs and non-human primates.

**Bustamante JM, White BE, Wilkerson GK, Hodo CL, Auckland LD, Wang W, McCain S, Hamer SA, Saunders AB, Tarleton RL.**
02-02-2023
*bioRxiv*.
https://pubmed.ncbi.nlm.nih.gov/36778432/

## Drugging the Undruggable Trypanosoma brucei Monothiol Glutaredoxin 1.

**Favaro A, Bolcato G, Comini MA, Moro S, Bellanda M, Sturlese M.**
28-01-2023
*Molecules*.
https://pubmed.ncbi.nlm.nih.gov/36770941/

Trypanosoma brucei is a species of kinetoplastid causing sleeping sickness in humans and nagana in cows and horses. One of the peculiarities of this species of parasites is represented by their redox metabolism. One of the proteins involved in this redox machinery is the monothiol glutaredoxin 1 (1CGrx1) which is characterized by a unique disordered N-terminal extension exclusively conserved in trypanosomatids and other organisms. This region modulates the binding profile of the glutathione/trypanothione binding site, one of the functional regions of 1CGrx1. No endogenous ligands are known to bind this protein which does not present well-shaped binding sites, making it target particularly challenging to target. With the aim of targeting this peculiar system, we carried out two different screenings: (i) a fragment-based lead discovery campaign directed to the N-terminal as well as to the canonical binding site of 1CGrx1; (ii) a structure-based virtual screening directed to the 1CGrx1 canonical binding site. Here we report a small molecule that binds at the glutathione binding site in which the binding mode of the molecule was deeply investigated by Nuclear Magnetic Resonance (NMR). This compound represents an important step in the attempt to develop a novel strategy to interfere with the peculiar Trypanosoma Brucei redox system, making it possible to shed light on the perturbation of this biochemical machinery and eventually to novel therapeutic possibilities.

## Bioactive Clerodane Diterpenoids from the Leaves of Casearia coriacea Vent.

**Ledoux A, Hamann C, Bonnet O, Jullien K, Quetin-Leclercq J, Tchinda A, Smadja J, Gauvin-Bialecki A, Maquoi E, Frédérich M.**
25-01-2023
*Molecules*.
https://pubmed.ncbi.nlm.nih.gov/36770864/

## N-Containing α-Mangostin Analogs via Smiles Rearrangement as the Promising Cytotoxic, Antitrypanosomal, and SARS-CoV-2 Main Protease Inhibitory Agents.

**Pyae NYL, Maiuthed A, Phongsopitanun W, Ouengwanarat B, Sukma W, Srimongkolpithak N, Pengon J, Rattanajak R, Kamchonwongpaisan S, Ei ZZ, Chunhacha P, Wilasluck P, Deetanya P, Wangkanont K, Hengphasatporn K, Shigeta Y, Rungrotmongkol T, Chamni S.**
22-01-2023
*Molecules*.
https://pubmed.ncbi.nlm.nih.gov/36770770/

New *N*-containing xanthone analogs of α-mangostin were synthesized via one-pot Smiles rearrangement. Using cesium carbonate in the presence of 2-chloroacetamide and catalytic potassium iodide, α-mangostin (**1**) was subsequently transformed in three steps to provide ether **2**, amide **3**, and amine **4** in good yields at an optimum ratio of 1:3:3, respectively. The evaluation of the biological activities of α-mangostin and analogs **2**-**4** was described. Amine **4** showed promising cytotoxicity against the non-small-cell lung cancer H460 cell line fourfold more potent than that of cisplatin. Both compounds **3** and **4** possessed antitrypanosomal properties against *Trypanosoma brucei rhodesiense* at a potency threefold stronger than that of α-mangostin. Furthermore, ether **2** gave potent SARS-CoV-2 main protease inhibition by suppressing 3-chymotrypsinlike protease (3CL$^{pro}$) activity approximately threefold better than that of **1**. Fragment molecular orbital method (FMO-RIMP2/PCM) indicated the improved binding interaction of **2** in the 3CL$^{pro}$ active site regarding an additional ether moiety. Thus, the series of *N*-containing α-mangostin analogs prospectively enhance druglike properties based on isosteric replacement and would be further studied as potential biotically active chemical entries, particularly for anti-lung-cancer, antitrypanosomal, and anti-SARS-CoV-2 main protease applications.

## Generation of Aurachin Derivatives by Whole-Cell Biotransformation and Evaluation of Their Antiprotozoal Properties.

**Kruth S, Zimmermann CJ, Kuhr K, Hiller W, Lütz S, Pietruszka J, Kaiser M, Nett M.**
20-01-2023
*Molecules*.

The natural product aurachin D is a farnesylated quinolone alkaloid, which is known to possess activity against the causative agent of malaria, *Plasmodium* spp. In this study, we show that aurachin D inhibits other parasitic protozoa as well. While aurachin D had only a modest effect on *Trypanosoma brucei rhodesiense*, two other trypanosomatids, *T. cruzi* and *Leishmania donovani*, were killed at low micromolar and nanomolar concentrations, respectively, in an in vitro assay. The determined $IC_{50}$ values of aurachin D were even lower than those of the reference drugs benznidazole and miltefosine. Due to these promising results, we set out to explore the impact of structural modifications on the bioactivity of this natural product. In order to generate aurachin D derivatives with varying substituents at the C-2, C-6 and C-7 position of the quinolone ring system, we resorted to whole-cell biotransformation using a recombinant *Escherichia coli* strain capable of aurachin-type prenylations. Quinolone precursor molecules featuring methyl, methoxy and halogen groups were fed to this *E. coli* strain, which converted the substrates into the desired analogs. None of the generated derivatives exhibited improved antiprotozoal properties in comparison to aurachin D. Obviously, the naturally occurring aurachin D features already a privileged structure, especially for the inhibition of the causative agent of visceral leishmaniasis.

### Crystal Structure of Inhibitor-Bound Bacterial Oligopeptidase B in the Closed State: Similarity and Difference between Protozoan and Bacterial Enzymes.

Petrenko DE, Karlinsky DM, Gordeeva VD, Arapidi GP, Britikova EV, Britikov VV, Nikolaeva AY, Boyko KM, Timofeev VI, Kuranova IP, Mikhailova AG, Bocharov EV, Rakitina TV.

### Knowledge, attitudes, behaviors, and serological status related to Chagas disease among Latin American migrants in Germany: A cross-sectional study in six German cities.

Wirth M, Gálvez RI, Jochum J, Strauss R, Kristensen K, Stich A, Stegemann M, Stahl P, Puchner KP, Strasen J, Parisi S, Braasch T, Bender M, Hörning A, Hanke M, Störk S, Jacobs T, Pritsch M, Zoller T.

# Leishmaniose

### Variants of NOD2 in Leishmania guyanensis-infected patients with cutaneous leishmaniasis and correlations with plasma circulating pro-inflammatory cytokines.

Mesquita TGR, Junior JDES, Souza JL, Silva LSD, Nascimento TAD, Souza MLG, Guerra MVF, Ramasawmy R.

Leishmaniases, a group of vector-borne diseases, are caused by the protozoan intracellular parasite Leishmania (L.) and are transmitted by the phlebotomine sandflies. A wide range of clinical manifestations in L- infection is observed. The clinical outcome ranges from asymptomatic, cutaneous leishmaniasis (CL) to severe mucosal leishmaniasis (ML) or visceral leishmaniasis (VL), depending on the L. species. Interestingly, only a fraction of L.-infected individuals progress to disease development, suggesting a key role of host genetics in the clinical outcome. NOD2 plays a critical role in the control of host defense and inflammation. The NOD2-RIK2 pathway is involved in developing a Th1- type response in patients with VL and C57BL/6 mice infected with L. infantum. We investigated whether variants in the NOD2 gene (R702W rs2066844, G908R rs2066845, and L1007fsinsC rs2066847) are associated with susceptibility to CL caused by L. guyanensis (Lg) in 837 patients with Lg-Cl and 797 healthy controls (HC) with no history of leishmaniasis. Both patients and HC are from the same endemic area of the Amazonas state of Brazil. The variants R702W and G908R were genotyped by polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP), and L1007fsinsC was by direct nucleotide sequencing. The minor allele frequency (MAF) of L1007fsinsC was 0.5% among the patients with Lg-CL and 0.6% in the healthy controls group. R702W genotypes frequencies were similar in both groups. Only 1% and 1.6% were heterozygous for G908R among the patients with Lg-CL and HC, respectively. None of the variants revealed any association with susceptibility to the development of Lg-CL. Correlations of genotypes with the level of plasma cytokines revealed that individuals with the mutant alleles of R702W tend to have low levels of IFN-γ. G908R heterozygotes also tend to have low IFN-γ, TNF-α, IL-17, and IL-8. Variants of NOD2 are not involved in the pathogenesis of Lg-CL.

### Efficacy of intralesional meglumine antimoniate in the treatment of canine tegumentary leishmaniasis: A Randomized controlled trial.

Lago J, Fraga D, Guimarães LH, Lago T, Santos Y, Lago E, Werneck GL, Bacellar O, Carvalho EM.

### Development of quantitative PCR and digital PCR for the quantification of Leishmania infantum in dogs.

Pereira DCA, Teixeira-Neto RG, Lopes VV, Pena HP, Paz GF, Custodio CHX, Belo VS, da Fonseca Júnior AA, da Silva ES.

Mol Cell Biochem.
https://pubmed.ncbi.nlm.nih.gov/36790551/

## A patient with leishmaniasis presenting with longstanding pancytopenia and hepatosplenomegaly.

**Onsongo S, Mulwa E, Mutiso B.**
10-02-2023
*Clin Case Rep.*
https://pubmed.ncbi.nlm.nih.gov/36789304/

Leishmaniasis is a common cause of pancytopenia and hepatosplenomegaly in tropical and subtropical regions. A high index of suspicion is required to diagnose and manage patients with leishmaniasis. Travel history should always be elicited in a patient with suggestive clinical presentation.

## Para Kala-Azar Dermal Leishmaniasis: A Case Report.

**Moniruzzaman M, Been Sayeed SKJ, Rahim MA, Hassan R, Rahman MM.**
12-01-2023
*Cureus*.
https://pubmed.ncbi.nlm.nih.gov/36788910/

Rarely, post-kala-azar dermal leishmaniasis (PKDL) may coexist with visceral leishmaniasis (VL). The concomitant PKDL and VL are referred to as Para-kala-azar dermal Leishmaniasis. We report a case of Para kala-azar dermal leishmaniasis in a chronic Hepatitis-B virus-infected patient who presented with an abdominal lump and multiple maculopapular skin lesions and is resistant to sodium stibogluconate but successfully treated with liposomal Amphotericin-B.

## Development of a TaqMan qPCR assay for trypanosomatid multi-species detection and quantification in insects.

**Barranco-Gómez O, De Paula JC, Parada JS, Gómez-Moracho T, Marfil AV, Zafra M, Orantes Bermejo FJ, Osuna A, De Pablos LM.**
14-02-2023
*Parasit Vectors.*
https://pubmed.ncbi.nlm.nih.gov/36788540/

## Immunoproteomics approach for the discovery of antigens applied to the diagnosis of canine visceral leishmaniasis.

**Costa SS, Santos LMO, Freire LC, Tedeschi ALF, Ribeiro NR, Queiroz MHR, Neto EB, Pimenta DC, Galvani NC, Luiz GP, de Oliveira ME, de Ávila RAM, Carvalho AMRS, Brigido BVS, Reis AB, Fernandes APSM, Coelho EAF, Roatt BM, Menezes-Souza D, Duarte MC.**
12-02-2023
*Acta Trop*.
https://pubmed.ncbi.nlm.nih.gov/36787861/

In the present study, an immunoproteomic approach using Leishmania infantum parasites isolated from naturally infected dogs from an endemic region of the disease, was carried out to identify new antigens to be used in the diagnosis of canine visceral leishmaniasis (CVL). Protein extracts, obtained from parasites isolated from asymptomatic (CanLA) and symptomatic (CanLS) dogs, were used to perform the two-dimensional gels. Western Blotting assays were carried out by employing a pool of sera from dogs with visceral leishmaniasis (CanLA or CanLS), healthy dogs from an endemic area, or dogs with similar diseases associated with cross-reactions (babesiosis and ehrlichiosis). With these results, it was possible to exclude the spots that showed a cross-reactivity of the sera from groups of healthy dogs, and those with babesiosis or ehrlichiosis. Taken together, 20 proteins were identified, 15 of which have already been described in the literature and 5 of which are hypothetical. An immunogenomic screen strategy was applied to identify conserved linear B-cell epitopes in the identified hypothetical proteins. Two peptides were synthesized and tested in ELISA experiments as a proof of concept for the validation of our immunoproteomics findings. The results demonstrated that the antigens presented sensitivity and specificity values ranging from 81.93% to 97.59% and 78.14 to 85.12%, respectively. As a comparative antigen, a preparation of a Leishmania extract showed sensitivity and specificity values of 75.90% and 74.88%, respectively. The present study was able to identify proteins capable of being used for the serodiagnosis of canine visceral leishmaniasis.

## Synchrotron-Infrared Microspectroscopy of Live Leishmania major Infected Macrophages and Isolated Promastigotes and Amastigotes.

**Chakkumpulakkal Puthan Veettil T, Duffin RN, Roy S, Vongsvivut J, Tobin MJ, Martin M, Adegoke JA, Andrews PC, Wood BR.**
14-02-2023
*Anal Chem*.
https://pubmed.ncbi.nlm.nih.gov/36787387/

## The Therapeutic Effects of Curcumin-coated Gold Nanoparticle Against Leishmania Major Causative Agent of Zoonotic Cutaneous Leishmaniasis (ZCL): An In Vitro and In Vivo Study.

**Amini SM, Hadighi R, Najm M, Alipour M, Hasanpour H, Vosoogh M, Vosough A, Hajizadeh M, Badirzadeh A.**
13-02-2023
*Curr Microbiol*.
https://pubmed.ncbi.nlm.nih.gov/36781499/

We synthesized and characterized curcumin-coated gold nanoparticles (Cur@AuNPs) and investigated their stability, cytotoxicity, leishmanicidal activity in in vitro and in in vivo experiments. Cur@AuNPs synthesized through a simple one-pot green chemistry technique. The in vitro leishmanicidal activity of curcumin-coated gold nanoparticles against extracellular promastigotes and intracellular amastigotes of protozoan parasite Leishmania major (L. major) was determined by applying the tetrazolium reduction colorimetric quantitative MTT technique. For in vivo assessment, the footpad lesion size

and parasite burden in two infection site organs including lymph nodes and footpads of susceptible BALB/c mice infected with L. major were measured. Mice immune responses in all study groups were quantified by measuring the levels of gamma interferon (IFN-γ) and interleukin-4 (IL-4). Viability of Leishmania promastigotes significantly diminished with the inhibition in promastigotes growth ($IC_{50}$) of 64.79 µg/mL and 29.89 µg/mL for 24 h and 48 h, respectively. In vitro nanoparticles treatment efficiently cleared the L. major amastigotes explanted in macrophages but had no harmful toxicity on the mice cells. In the in vivo condition, in the treated infected BALB/c mice the CL lesion size, Leishmania parasite burden, and IL-4 were decreased, while IFN-γ was significantly increased. The results suggest that Cur@AuNP was an effective compound against Leishmania parasite in vitro and in vivo, efficiently induced T-helper 1 (Th1) responses and augmented host cellular immune responses, and ending in a reduced Leishmania parasite burden. Therefore, it may be identified as a novel potential therapeutic approach for the local therapy of zoonotic CL treatment with high cure rates.

## PCR for detection of Leishmania donovani from microscopically negative tissue smears of suspected patients in Gondar, Ethiopia.

**Melkamu R, Berhane N, Jacobs BKM, Mohammed R, Kassa M, Yeshanew A, Fikre H, Atnafu S, van Henten S, van Griensven J, Pareyn M.**
13-02-2023
*PLoS Negl Trop Dis*.
https://pubmed.ncbi.nlm.nih.gov/36780561/

## Co-infection of Phlebotomus papatasi (Diptera: Psychodidae) gut bacteria with Leishmania major exacerbates the pathological responses of BALB/c mice.

**Amni F, Maleki-Ravasan N, Nateghi-Rostami M, Hadighi R, Karimian F, Meamar AR, Badirzadeh A, Parvizi P.**
26-01-2023
*Front Cell Infect Microbiol*.
https://pubmed.ncbi.nlm.nih.gov/36779192/

## Life in plastic, it's fantastic! How Leishmania exploit genome instability to shape gene expression.

**Black JA, Reis-Cunha JL, Cruz AK, Tosi LRO.**
26-01-2023
*Front Cell Infect Microbiol*.
https://pubmed.ncbi.nlm.nih.gov/36779182/

## Exploring drug repositioning for leishmaniasis treatment: Ivermectin plus polymeric micelles induce immunological response and protection against tegumentary leishmaniasis.

**Freitas CS, Lage DP, Machado AS, Vale DL, Martins VT, Cardoso JMO, Oliveira-da-Silva JA, Reis TAR, Tavares GSV, Ramos FF, Ludolf F, Pereira IAG, Bandeira RS,**

**Fujiwara RT, Bueno LL, Roatt BM, Chávez-Fumagalli MA, Coelho EAF.**
10-02-2023
*Cytokine*.
https://pubmed.ncbi.nlm.nih.gov/36774730/

Leishmania amazonensis can cause a wide spectrum of the clinical manifestations of leishmaniasis in humans. The development of new therapeutics is a long and expensive task; in this context, drug repositioning could be considered a strategy to identify new biological actions of known products. In the present study, ivermectin (IVE) was tested against distinct Leishmania species able to cause disease in humans. In vitro experiments showed that IVE was effective to reduce the infection degree and parasite load in Leishmania donovani- and L. amazonensis-infected macrophages that were treated with it. In addition, using the culture supernatant of treated macrophages, higher production of IFN-γ and IL-12 and lower levels of IL-4 and IL-10 were found. Then, IVE was used in a pure form or incorporated into Poloxamer 407-based polymeric micelles (IVE/M) for the treatment of L. amazonensis-infected BALB/c mice. Animals (n = 16 per group) were infected and later received saline, empty micelles, amphotericin B (AmpB), IVE, or IVE/M. They were euthanized at one (n = 8 per group) and 30 (n = 8 per group) days after treatment and, in both endpoints, immunological, parasitological, and biochemical evaluations were performed. Results showed that both IVE and IVE/M induced higher levels of IFN-γ, IL-12, GM-CSF, nitrite, and IgG2a antibodies, as well as higher IFN-γ expression evaluated by RT-qPCR in spleen cell cultures. Such animals showed low organic toxicity, as well as significant reductions in the lesion's average diameter and parasite load in their infected tissue, spleen, liver, and draining lymph node. The efficacy was maintained 30 days post-therapy, while control mice developed a polarized Th2-type response and high parasite load. In this context, IVE could be considered as a new candidate to be applied in future studies for the treatment against distinct Leishmania species.

## Anti-Trypanosomatidae Activity of Essential Oils and Their Main Components from Selected Medicinal Plants.

**Bailén M, Illescas C, Quijada M, Martínez-Díaz RA, Ochoa E, Gómez-Muñoz MT, Navarro-Rocha J, González-Coloma A.**
02-02-2023
*Molecules*.
https://pubmed.ncbi.nlm.nih.gov/36771132/

Kinetoplastida is a group of flagellated protozoa characterized by the presence of a kinetoplast, a structure which is part of a large mitochondria and contains DNA. Parasites of this group include genera such as *Leishmania,* that cause disease in humans and animals, and *Phytomonas,* that are capable of infecting plants. Due to the lack of treatments, the low efficacy, or the high toxicity of the employed therapeutic agents there is a need to seek potential alternative treatments. In the present work, the antiparasitic activity on *Leishmania infantum* and *Phytomonas davidi* of 23 essential oils (EOs) from plants of

the Lamiaceae and Asteraceae families, extracted by hydrodistillation (HD) at laboratory scale and steam distillation (SD) in a pilot plant, were evaluated. The chemical compositions of the EOs were determined by gas chromatography-mass spectrometry. Additionally, the cytotoxic activity on mammalian cells of the major components from the most active EOs was evaluated, and their anti-*Phytomonas* and anti-*Leishmania* effects analyzed. *L. infantum* was more sensitive to the EOs than *P. davidi*. The EOs with the best anti-kinetoplastid activity were *S. montana*, *T. vulgaris*, *M. suaveolens*, and *L. luisieri*. Steam distillation increased the linalyl acetate, β-caryophyllene, and trans-α-necrodyl acetate contents of the EOs, and decreased the amount of borneol and 1,8 cineol. The major active components of the EOs were tested, with thymol being the strongest anti-*Phytomonas* compound followed by carvacrol. Our study identified potential treatments against kinetoplastids.

## Evaluation of Ruthenium(II) N-Heterocyclic Carbene Complexes as Enzymatic Inhibitory Agents with Antioxidant, Antimicrobial, Antiparasitical and Antiproliferative Activity.

**Al Nasr IS, Koko WS, Khan TA, Gürbüz N, Özdemir I, Hamdi N.**
31-01-2023
*Molecules*.
https://pubmed.ncbi.nlm.nih.gov/36771026/

## Bioactive Clerodane Diterpenoids from the Leaves of Casearia coriacea Vent.

**Ledoux A, Hamann C, Bonnet O, Jullien K, Quetin-Leclercq J, Tchinda A, Smadja J, Gauvin-Bialecki A, Maquoi E, Frédérich M.**
25-01-2023
*Molecules*.
https://pubmed.ncbi.nlm.nih.gov/36770864/

## Generation of Aurachin Derivatives by Whole-Cell Biotransformation and Evaluation of Their Antiprotozoal Properties.

**Kruth S, Zimmermann CJ, Kuhr K, Hiller W, Lütz S, Pietruszka J, Kaiser M, Nett M.**
20-01-2023
*Molecules*.
https://pubmed.ncbi.nlm.nih.gov/36770729/

The natural product aurachin D is a farnesylated quinolone alkaloid, which is known to possess activity against the causative agent of malaria, *Plasmodium* spp. In this study, we show that aurachin D inhibits other parasitic protozoa as well. While aurachin D had only a modest effect on *Trypanosoma brucei rhodesiense*, two other trypanosomatids, *T. cruzi* and *Leishmania donovani*, were killed at low micromolar and nanomolar concentrations, respectively, in an in vitro assay. The determined $IC_{50}$ values of aurachin D were even lower than those of the reference drugs benznidazole and miltefosine. Due to these promising results, we set out to explore the impact

of structural modifications on the bioactivity of this natural product. In order to generate aurachin D derivatives with varying substituents at the C-2, C-6 and C-7 position of the quinolone ring system, we resorted to whole-cell biotransformation using a recombinant *Escherichia coli* strain capable of aurachin-type prenylations. Quinolone precursor molecules featuring methyl, methoxy and halogen groups were fed to this *E. coli* strain, which converted the substrates into the desired analogs. None of the generated derivatives exhibited improved antiprotozoal properties in comparison to aurachin D. Obviously, the naturally occurring aurachin D features already a privileged structure, especially for the inhibition of the causative agent of visceral leishmaniasis.

## Potent Inhibitory Activity of Natural Product Anaephene B and Analogues against Leishmania tarentolae In Vitro.

**Zaman SM, Jones MA.**
18-01-2023
*Molecules*.
https://pubmed.ncbi.nlm.nih.gov/36770614/

## Retraction: Glucose deprivation induced upregulation of phosphoenolpyruvate carboxykinase modulates virulence in Leishmania donovani.

**[No authors listed]**
10-02-2023
*Mol Microbiol*.
https://pubmed.ncbi.nlm.nih.gov/36765454/

The above article, first published online on 24 September 2016 in Wiley Online Library (wileyonlinelibrary.com), has been retracted by agreement between the Editors, John D. Helmann and Thierry Soldati, and John Wiley & Sons Ltd. Following publication, concerns were raised by a third party regarding similar blots in Figure 5. Further investigation revealed that multiple figures in the article (2, 4, 5, 6, 7, 9) have been manipulated via splicing, duplication and/or mirror inversion. The retraction has been agreed because of concerns regarding the validity of the data and results presented.

## Natural products derived steroids as potential anti-leishmanial agents; disease prevalence, underlying mechanisms and future perspectives.

**Elawad MA, Elkhalifa MEM, Hamdoon AAE, Salim LHM, Ahmad Z, Ayaz M.**
09-02-2023
*Steroids*.
https://pubmed.ncbi.nlm.nih.gov/36764565/

## A Preliminary Study to Compare Recombinase Polymerase Amplification-Lateral Flow and Quantitative PCR in the Detection of Cutaneous Leishmania in Communities from the Volta Region of Ghana.

**Yeboah C, Mosore MT, Attram N, Shelite TR, Akuffo RA, Addo SO, Behene E, Agbodzi B, Bentil RE, Fox AT, Wilson M, Boakye D, Letizia AG, Melby PC, Travi BL.**

*Background:* Leishmaniasis is a parasitic disease that mostly affects populations in tropical and subtropical countries. In Ghana, cutaneous leishmaniasis (CL) is the most common form of the disease affecting communities of the Volta Region. Conventional parasitological method (microscopy) is the commonly used test for CL diagnosis in many endemic countries, but has low sensitivity in chronic cases. Therefore, there is a clear need for a sensitive and easy-to-use point-of-care diagnostic method like an isothermal recombinase polymerase amplification-lateral flow (RPA-LF) test, suitable for use in austere and low-resource settings for the identification of CL cases. This study compared the efficacy of RPA-LF test with quantitative PCR (qPCR) in detecting *Leishmania* in suspected CL cases from the Volta Region. **Methods:** Twenty-five participants between 5 and 14 years were enrolled in the study from whom a total of 26 samples were obtained. Lesion samples were collected using FTA® filter papers applied to ulcerated lesions for molecular diagnosis. DNA isolated from filter papers was used for both the RPA-LF test and qPCR. *Results:* Twenty-two participants (88%) presented with one or two ulcerated active lesions per individual, while the rest of them had plaques or dried lesions. Among the 26 samples, 19/26 (73%) had concordant results when comparing the two diagnostic methods. *Conclusion:* Data from this study suggest that the RPA-LF test can be used in addition to a conventional parasitological diagnostic test (microscopy) to detect CL cases in communities of the Volta Region.

## Label-Free Mass Spectrometry Proteomics Reveals Different Pathways Modulated in THP-1 Cells Infected with Therapeutic Failure and Drug Resistance Leishmania infantum Clinical Isolates.

**Tagliazucchi L, Perea-Martinez A, Fiorini G, Manzano JI, Genovese F, García-Hernández R, Pinetti D, Gamarro F, Costi MP.**

## Updating the knowledge of sand flies (Diptera, Psychodidae) in Rondônia State, Brazil.

**Pereira Júnior AM, Rodrigues MMS, Medeiros JF.**

## Phlebotomine sand flies (Diptera, Psychodidae) from Spain: an updated checklist and extended distributions.

**Bravo-Barriga D, Ruiz-Arrondo I, Peña RE, Lucientes J, Delacour-Estrella S.**

Phlebotomine sand flies (Diptera: Psychodidae) are the natural vectors of *Leishmania* spp. (Kinetoplastida: Trypanosomatidae) and phleboviruses (Bunyavirales: Phenuiviridae). In Spain, these vectors appear to be increasing their geographical distribution and have serious repercussions on public and veterinary health, encouraging studies of sand flies and their associated pathogens. An up-to-date and easily accessible compendium of current and historical data on their presence and detailed distribution is a crucial step towards the development and implementation of appropriate preventive strategies. A checklist on the presence and distribution of sand flies in Spain is compiled from data extracted from a comprehensive review of scientific literature published between 1909 and 2021 and our new records on the presence of sand flies specimens collected under the entomological surveillance of bluetongue vectors from the Spanish Ministry of Agriculture, Fishery and Food (MAPA) during the period 2004-2021. In total, 13 Spanish species of sand flies (two of them with controversial status) belonging to two genera and six subgenera are presented in this updated checklist, including new distribution data for seven species, among which several stand out as confirmed or suspected vectors of *Leishmaniainfantum*: *Phlebotomusariasi*, *Ph.langeroni*, *Ph.mascittii*, *and Ph.perniciosus*.

## Expanding the scope of novel 1,2,3-triazole derivatives as new antiparasitic drug candidates.

**Carlucci R, Di Gresia G, Mediavilla MG, Cricco JA, Tekwani BL, Khan SI, Labadie GR.**

We have previously shown that prenyl and aliphatic triazoles are interesting motifs to prepare new chemical entities for antiparasitic and antituberculosis drug development. In this opportunity a new series of prenyl-1,2,3-triazoles were prepared from isoprenyl azides and different alkynes looking for new antimalarial drug candidates. The compounds were prepared by copper(i) catalyzed dipolar cycloaddition of the isoprenyl azide equilibrium mixture providing exclusively 1,4-disubstituted 1,2,3-triazoles in a regiospecific fashion. The complete collection of 64 compounds was tested on chloroquine-sensitive (CQ sensitive), Sierra Leone (D6), and the chloroquine-resistant, Indochina (W2), strains of *Plasmodium falciparum* and those compounds which were not previously reported were also tested against *Leishmania donovani*, the causative agent for visceral leishmaniasis. Thirteen analogs displayed antimalarial activity with $IC_{50}$ below 10 μM, while the antileishmanial activity of the newly reported analogs could not improve upon those previously reported. Compounds 1o and 1r were identified as the most promising antimalarial drug leads with $IC_{50}$ below 3.0 μM for both CQ-sensitive and resistant *P. falciparum* strains with high selectivity index. Finally, a chemoinformatic *in silico* analysis was performed

to evaluate physicochemical parameters, cytotoxicity risk and drug score. The validation of a bifunctional farnesyl/geranylgeranyl diphosphate synthase *Pf*FPPS/GGPPS as the potential target of the antimalarial activity of selected analogs should be further investigated.

## Computational multi-target approach to target essential enzymes of Leishmania donovani using comparative molecular dynamic simulations and MMPBSA analysis.

**Saha D, Nath Jha A.**
09-02-2023
*Phytochem Anal.*
https://pubmed.ncbi.nlm.nih.gov/36760044/

## Exploration of ethylene glycol linked nitrofurantoin derivatives against Leishmania: Synthesis and in vitro activity.

**Ndlovu K, Kannigadu C, Aucamp J, van Rensburg HDJ, N'Da DD.**
09-02-2023
*Arch Pharm (Weinheim).*
https://pubmed.ncbi.nlm.nih.gov/36759973/

## Interleukin 6 and interferon gamma haplotypes are related to cytokine serum levels in dogs in an endemic Leishmania infantum region.

**Álvarez L, Marín-García PJ, Rentero-Garrido P, Martinez-Jimenez CP, Llobat L.**
10-02-2023
*Infect Dis Poverty.*
https://pubmed.ncbi.nlm.nih.gov/36759910/

**Background:** The Ibizan Hound is a canine breed native to the Mediterranean region, where leishmaniasis is an endemic zoonosis. Several studies indicate a low prevalence of this disease in Ibizan Hound dogs, whereas other canine breeds present a high prevalence. However, the underlying molecular mechanisms still remain unknown. The aim of this work is to analyse the relationship between serum levels of cytokines and the genomic profiles in two canine breeds, Ibizan Hound (resistant canine breed model) and Boxer (susceptible canine breed model). **Methods:** In this study, we analyse the haplotypes of genes encoding cytokines related to immune response of Leishmania infantum infection in twenty-four Boxers and twenty-eight Ibizan Hounds apparently healthy using CanineHD DNA Analysis BeadChip including 165,480 mapped positions. The haplo.glm extension of haplo.score was used to perform a General Linear Model (GLM) regression to estimate the magnitude of individual haplotype effects within each cytokine. **Results:** Mean levels of interferon gamma (IFN-γ), interleukin 2 (IL-2) and IL-18 in Boxer dogs were $0.19 \pm 0.05$ ng/ml, $46.70 \pm 4.54$ ng/ml, and $36.37 \pm 30.59$ pg/ml, whereas Ibizan Hound dogs present $0.49 \pm 0.05$ ng/ml, $64.55 \pm 4.54$ ng/ml, and $492.10 \pm 31.18$ pg/ml, respectively. The GLM regression shows fifteen haplotypes with statistically significant effect on the cytokine serum levels ($P < 0.05$). The more relevant are IL6-CGAAG and IFNG-GCA haplotypes, which increase and decrease the IL-2, IL-8 and IFN-γ serum levels, respectively. **Conclusions:** Haplotypes in the IFNG and IL6 genes have been correlated to serum levels of IFN-γ, IL-2 and IL-18, and a moderate effect has been found on IL8 haplotype correlated to IL-8 and IL-18 serum levels. The results indicate that the resistance to L. infantum infection could be a consequence of certain haplotypes with a high frequency in the Ibizan Hound dog breed, while susceptibility to the disease would be related to other specific haplotypes, with high frequency in Boxer. Future studies are needed to elucidate whether these differences and haplotypes are related to different phenotypes in immune response and expression gene regulation to L. infantum infections in dogs and their possible application in new treatments and vaccines.

## High levels of infectiousness of asymptomatic Leishmania (Viannia) braziliensis infections in wild rodents highlights their importance in the epidemiology of American Tegumentary Leishmaniasis in Brazil.

**Marinho-Júnior JF, Monteiro JFCLS, Sales de Carvalho AW, de Carvalho FG, de Paiva Cavalcanti M, Shaw J, Courtenay O, Brandão-Filho SP.**
30-01-2023
*PLoS Negl Trop Dis.*
https://pubmed.ncbi.nlm.nih.gov/36716345/

## Synthesis and Testing of Analogs of the Tuberculosis Drug Candidate SQ109 against Bacteria and Protozoa: Identification of Lead Compounds against Mycobacterium abscessus and Malaria Parasites.

**Stampolaki M, Malwal SR, Alvarez-Cabrera N, Gao Z, Moniruzzaman M, Babii SO, Naziris N, Rey-Cibati A, Valladares-Delgado M, Turcu AL, Baek KH, Phan TN, Lee H, Alcaraz M, Watson S, van der Watt M, Coertzen D, Efstathiou N, Chountoulesi M, Shoen CM, Papanastasiou IP, Brea J, Cynamon MH, Birkholtz LM, Kremer L, No JH, Vázquez S, Benaim G, Demetzos C, Zgurskaya HI, Dick T, Oldfield E, Kolocouris AD.**
10-02-2023
*ACS Infect Dis.*
https://pubmed.ncbi.nlm.nih.gov/36706233/

## Usefulness of Matrix-Assisted Laser Desorption/Ionization-Time of Flight Mass Spectrometry in the Characterization of Leishmania Strains Causing Tegumentary Leishmaniasis in Bolivia versus hsp70 Gene Sequencing.

**Torrico MC, Fernández-Arévalo A, Ballart C, Solano M, Rojas E, Abras A, Gonzales F, Arnau A, Tebar S, Llovet T, Lozano D, Ariza-Vioque E, Gascón J, Picado A, Torrico F, Muñoz C, Gállego M.**
14-02-2023
*Microbiol Spectr.*

Matrix-assisted laser desorption/ionization-time of flight mass spectrometry (MALDI-TOF MS) is a proteomic technique with proven efficiency in the identification of microorganisms, such as bacteria, fungi, and parasites. The present study aimed to evaluate the usefulness of MALDI-TOF MS for the characterization of *Leishmania* species circulating in Bolivia using *hsp70* gene sequencing as a reference technique. 55 *Leishmania* strains that were isolated from patients with tegumentary leishmaniasis were analyzed. MALDI-TOF MS identified two species of the *L. braziliensis* complex (*L. braziliensis*, n = 26; *L. braziliensis* outlier, n = 18), one species of the *L. guyanensis* complex (*L. guyanensis*, n = 1), one species of the *L. lainsoni* complex (*L. lainsoni*, n = 2), and two species of the L. mexicana complex (L. amazonensis, n = 5; and *L. garnhami*, n = 3). All of the strains were correctly identified at the subgenus, genus, and complex level, but 10 of them (18%) were misidentified as other species within the same complex by the *hsp70* gene sequencing, with 7 of these corresponding to possible hybrids. Thus, one *L. braziliensis* corresponded to *L. peruviana*, two *L. braziliensis* corresponded to *L. braziliensis/L. peruviana* possible hybrids, two L. amazonensis corresponded to L. mexicana, and three *L. garnhami* and two L. amazonensis corresponded to L. mexicana/L. amazonensis possible hybrids. Accordingly, MALDI-TOF MS could be used as an alternative to molecular techniques for the identification of *Leishmania* spp., as it is low cost, simple to apply, and able to quickly produce results. In Bolivia, its application would allow for the improvement of the management of patient follow-ups, the updating of the epidemiological data of the *Leishmania* species, and a contribution to the control of tegumentary leishmaniasis. **IMPORTANCE** The objective of the study was to evaluate the usefulness of MALDI-TOF MS for the characterization of *Leishmania* species circulating in Bolivia, in comparison with the sequencing of the *hsp70* gene. In our study, all of the isolates could be identified, and no misidentifications were observed at the complex level. Although the equipment implies a high initial investment in our context, MALDI-TOF MS can be used in different areas of microbiology and significantly reduces the cost of testing. Once the parasite culture is obtained, the technique quickly yields information by accessing a free database that is available online. This would allow for the improvement of the management of patients and follow-ups, the updating of the epidemiological data of the species, and a contribution to the control of tegumentary leishmaniasis in Bolivia. Likewise, it can be used to determine a specific treatment to be given, according to the causal species of *Leishmania*, when there are protocols in this regard in the area.

### Interaction of novel proteins, centrin4 and protein of centriole in Leishmania parasite and their effects on the parasite growth.

**Vats K, Tandon R, Roshanara, Beg MA, Corrales RM, Yagoubat A, Reyaz E, Wani TH, Baig MS, Chaudhury A, Krishnan A, Puri N, Salotra P, Sterkers Y, Selvapandiyan A.**

### Protease inhibitors as a potential agent against visceral Leishmaniasis: A review to inspire future study.

**Sreedharan V, Rao KVB.**

Leishmaniasis is transmitted by sandfly which carries the intracellular protozoa in their midgut. Among visceral, cutaneous and mucocutaneous leishmaniasis, visceral type that is caused by Leishmania donovani is the most lethal one. Findings of leishmanial structure and species took place in 19th century and was initiated by Donovan. Leishmaniasis is still a major concern of health issues in many endemic countries in Asia, Africa, the Americas, and the Mediterranean region. Worldwide1.5-2 million new cases of cutaneous leishmaniasis and 500,000 cases of visceral leishmaniasis are reported each year. Leishmaniasis is endemic in nearly 90 countries worldwide and close to 12 million new cases of leishmaniasis are reported worldwide annually. Studies on antileishmanial drug development is of major concern as leishmaniasis are the second largest parasitic killer in the world and the available drugs are either toxic or costly. The major surface GP63 protease, also known as Zinc- metalloproteases present on the surface of leishmanial promastigotes, can be targeted for drug development. Protease inhibitors targeting such surface proteases show promising results. Different protease inhibitors have been isolated from marine actinobacteria against many infectious diseases. Metabolites produced by these actinobacteria may have greater importance for the discovery and development of new antileishmanial drugs. Hence, this review discusses the background, current situation, treatment, and protease inhibitors from marine actinobacteria for drug development against GP63 molecules.

### Partial characterization of purified glycoprotein from nutshell of Arachis hypogea L. towards macrophage activation and leishmaniacidal activity.

**Srinivasan S, Charan Raja MR, Kar A, Ramasamy A, Jayaraman A, Vadivel V, Kar Mahapatra S.**

### In vitro and in vivo therapeutic antileishmanial potential of ellagic acid against Leishmania donovani in murine model.

**Keshav P, Goyal DK, Kaur S.**

Parasite of genus Leishmania viz. L. donovani and L. infantum cause visceral leishmaniasis (VL) or Kala-azar,

systemic disease with significant enlargement of the liver and spleen, weight loss, anemia, fever and immunosuppression. The silent expansion of vectors, reservoir hosts and resistant strains is also of great concern in VL control. Considering all these issues, the present study focused on in vitro and in vivo antileishmanial screening of ellagic acid (EA) against L. donovani. The in vitro study was performed against the protozoan parasite L. donovani and a 50% inhibitory concentration was calculated. The DNA arrest in the sub-G0/G1 phase of the cell cycle was studied. In vivo studies included the assessment of parasite burden and immunomodulation in response to treatment of ellagic acid in BALB/c mice. The levels of Th1 and Th2 cytokines and isotype antibodies were assessed in different groups of mice. EA showed in vitro parasiticidal activity with $IC_{50}$ 18.55 µg/mL and thwarted cell-cycle progression at the sub-G0/G1 phase. Administration of ellagic acid to the BALB/c mice reported diminution of splenic and hepatic parasite burden coupled with an expansion of $CD4^+$ and $CD8^+$ T lymphocytes. EA further potentiated a protective immune response with augmentation of Th1 type immune response evidenced by elevation of serum IgG2a levels and DTH response. EA was reported to be safe and non-toxic to the THP-1 cell line as well as to the liver and kidneys of mice. These findings endorse the therapeutic potential of EA with significant immunomodulation and can serve as a promising agent against this debilitating parasitic disease.

## Similarity but not equivalence: Ecological niche comparison between sandflies from the Pleistocene and future scenarios in Central and South America.

**Galvis-Martinez CA, Moo-Llanes DA, Altamiranda-Saavedra M.**
Mar-2023
*Med Vet Entomol*.
https://pubmed.ncbi.nlm.nih.gov/36315035/

Sandfly species (Diptera: Psychodidae) are suspected or proven vectors of Leishmania spp. in the American region. Understanding niche conservatism (NC) in insect vectors allows an understanding of constraints on adaptive responses, and thus implications for disease ecology. Therefore, in this study, the authors evaluated NC in three vector species of leishmaniasis (Lutzomyia gomezi, Psathyromyia shannoni and Pintomyia ovallesi) in Central and South America. For this, the authors performed niche identity and similarity testing through paired comparisons in ENMTools and niche overlap in Niche Analyst. The authors found that species niches were more similar to each other than if the points had been randomly extracted, and they also found extensive similarity between Pa. shannoni and Lu. gomezi niches and in Pa. shannoni niches over different timescales. The authors suggest Pa. shannoni as a priority species due to fundamental niche similarity with phylogenetically related species and also its extensive evolutionary history and ecological plasticity that could affect the emergence and resurgence of leishmaniasis in areas endemic by this vector.

## Large scale systemic control short-circuits pathogen transmission by interrupting the sand rat (Psammomys obesus)-to-sand fly (Phlebotomus papatasi) Leishmania major transmission cycle.

**Tsurim I, Wasserberg G, Warburg A, Abbasi I, Ben Natan G, Abramsky Z.**
Mar-2023
*Med Vet Entomol*.
https://pubmed.ncbi.nlm.nih.gov/36054150/

# Cysticercose

## Regional variation in knowledge and practice regarding common zoonoses among livestock farmers of selective districts in Nepal.

**Bagale KB, Adhikari R, Acharya D.**
14-02-2023
*PLoS Negl Trop Dis.*
https://pubmed.ncbi.nlm.nih.gov/36787295/

Background: The majority of Nepalese people are involved in farming. However, due to limited knowledge of zoonoses and poor preventive practices on the part of livestock farmers, vulnerabilities to zoonotic diseases are very high. The main objective of this study was to assess the regional variation in zoonoses-related knowledge and preventive practices of livestock farmers in different ecological regions of Nepal. Material and methods: Descriptive cross-sectional quantitative research design was followed in the study. The total sample size was 380 livestock farmers from randomly selected three ecological regions of Nepal. Systematic sampling techniques were applied for data collection. Data were entered into an excel sheet and then imported into Statistical Package for Social Sciences (SPSS) software. The data were calculated using descriptive statistics. Univariate, and bivariate analyses were performed, and the result of the study was presented in the form of text and tables based on their nature. Results: Of the studied six zoonotic diseases, most of the respondents (95.8%) knew about zoonotic bird flu; 90.7% of them, were about rabies; and 54.2% knew about swine flu. However, a few respondents knew about bovine tuberculosis, neurocysticercosis, and brucellosis. Ecologically, the highest number of respondents in Nawalpur had knowledge of rabies (95.3%), and swine flu (61.6%), whereas 98.3% of them had knowledge of avian influenza in Tanahun; and 12.5% of neurocysticercosis in Manang. Regarding zoonoses preventive practices such as regular hand washing with soap water, mask-wearing, gloves, boots, the respondents' representation of 60.8%, 6.6%, 1.8%, and 1.3% respectively in such practices show that although these are easy and cost-effective, personal protective equipment (PPE), such preventive practices were extremely underperformed. Not only that, only 12% of respondents maintain a standard distance (>15m.) between their house and shed. Similarly, 17% still consumed meat from sick animals, and vaccination of livestock was also found poor coverage (36%) in the study. Conclusions: Livestock farmers need to be more

knowledgeable about many common zoonotic diseases, and their preventive practices still need improvement, with significant regional variation in the study. This has invited various zoonosis threats for them. Therefore, it is recommended that the interventional programs related to common zoonoses be conducted for livestock farmers to solve the problem.

## A rare case of human taeniasis caused by Taenia saginata with species undetermined cysticercosis.

Hou J, Chen W, Chen R, He C, Ma Y, Qu J.

Taeniasis and cysticercosis, which are caused by *Taenia saginata*, *Taenia solium* and *Taenia asiatica*, are zoonotic parasitic infections with a significant disease burden worldwide. There is consensus amongst experts that *T. saginata* is a common tapeworm that causes taeniasis in humans as opposed to cysticercosis. This case study of a middle-aged Tibetan man conducted in 2021 challenges the prevailing notion that *T. saginata* exclusively causes taeniasis and not cysticercosis by documenting symptoms and laboratory studies related to both taeniasis and multiple cysticercosis. The patient's medical record with the symptoms of taeniasis and cysticercosis was reviewed, and the tapeworm's proglottids and cyst were identified from the patient by morphological evaluation, DNA amplification and sequencing. The patient frequently experienced severe headaches and vomiting. Both routine blood screenings and testing for antibodies against the most common parasites were normal. After anthelmintic treatment, an adult tapeworm was found in feces, and medical imaging examinations suggested multiple focal nodules in the brain and muscles of the patient. The morphological and molecular diagnosis of the proglottids revealed the Cestoda was *T. saginata.* Despite the challenges presented by the cyst's morphology, the molecular analysis suggested that it was most likely *T. saginata*. This case study suggests that *T. saginata* infection in humans has the potential to cause human cysticercosis. However, such a conclusion needs to be vetted by accurate genome-wide analysis in patients with *T. saginata* taeniasis associated with cysts. Such studies shall provide new insights into the pathogenicity of *T. saginata*.

# Dracunculose

## Zoonotic helminths - why the challenge remains.

Thompson RCA.

Helminth zoonoses remain a global problem to public health and the economy of many countries. Polymerase chain reaction-based techniques and sequencing have resolved many taxonomic issues and are now essential to understanding the epidemiology of helminth zoonotic infections and the ecology of the causative agents. This is clearly demonstrated from research on *Echinococcus* (echinococcosis) and *Trichinella* (trichinosis). Unfortunately, a variety of anthropogenic factors are worsening the problems caused by helminth zoonoses. These include cultural factors, urbanization and climate change. Wildlife plays an increasingly important role in the maintenance of many helminth zoonoses making surveillance and control increasingly difficult. The emergence or re-emergence of helminth zoonoses such as *Ancylostoma ceylanicum*, *Toxocara*, *Dracunculus* and *Thelazia* exacerbate an already discouraging scenario compounding the control of a group of long neglected diseases.

## Aerial roots elevate indoor plant health: physiological and morphological responses of three high-humidity adapted Araceae species to indoor humidity levels.

Sheeran L, Rasmussen A.

Heightened by the COVID-19 pandemic there has been a global increase in urban greenspace appreciation. Indoor plants are equally important for improving mental health and air quality but despite evolving in humid (sub)tropical environments with aerial root types, planting systems ignore aerial resource supply. This study directly compared nutrient uptake preferences of aerial and soil-formed roots of three common houseplant species under high and ambient relative humidities. Growth and physiology parameters were measured weekly for Anthurium andreanum, Epipremnum aureum and Philodendron scandens grown in custom made growth chambers. Both aerial and soil-formed roots were then fed mixtures of nitrate, ammonium and glycine, with one source labelled with $^{15}$ N to determine uptake rates and maximum capacities. Aerial roots were consistently better at nitrogen uptake than soil roots but no species, root type or humidity condition showed a preference for a particular nitrogen source. All three species grew more in high humidity, with aerial roots demonstrating the greatest biomass increase. Higher humidities for indoor niches, together with fertiliser applications to aerial roots will support indoor plant growth, creating lush calming indoor environments for people inhabitants.

## Efficient Accumulation of Amylopectin and Its Molecular Mechanism in the Submerged Duckweed Mutant.

Liu Y, Yan R, Li Z, Fan S, Li C, Yu R, Liu H, Kong Y, Li H, Tang X, Zhou G.

Large-scale use of fossil fuels has brought about increasingly serious problems of environmental pollution, development and utilization of renewable energy is one of

the effective solutions. Duckweed has the advantages of fast growth, high starch content and no occupation of arable land, so it is a promising starchy energy plant. A new submerged duckweed mutant (*sub-1*) with abundant starch accumulation was obtained, whose content of amylopectin accounts for 84.04% of the starch granules. Compared with the wild type (*Lemna aequinoctialis*), the branching degree of starch in *sub-1* mutant was significantly increased by 19.6%. Chain length DP 6-12, DP 25-36 and DP > 36 of amylopectin significantly decreased, while chain length DP 13-24 significantly increased. Average chain length of wild-type and *sub-1* mutant starches were greater than DP 22. Moreover, the crystal structure and physical properties of starch have changed markedly in *sub-1* mutant. For example, the starch crystallinity of *sub-1* mutant was only 8.94%, while that of wild-type was 22.3%. Compared with wild type, water solubility of starch was significantly reduced by 29.42%, whereas swelling power significantly increased by 97.07% in *sub-1* mutant. In order to further analyze the molecular mechanism of efficient accumulation of amylopectin in *sub-1* mutant, metabolome and transcriptome were performed. The results showed that glucose accumulated in *sub-1* mutant, then degradation of starch to glucose mainly depends on α-amylase. At night, the down-regulated β-amylase gene resulted in the inhibition of starch degradation. The starch and sucrose metabolism pathways were significantly enriched. Up-regulated expression of *SUS*, *AGPase2*, *AGPase3*, *PYG*, *GPI* and *GYS* provide sufficient substrate for starch synthesis in *sub-1* mutant. From the 0H to 16H light treatment, granule-bound starch synthase (*GBSS1*) gene was inhibited, on the contrary, the starch branching enzyme (*SBE*) gene was induced. Differential expression of *GBSS1* and *SBE* may be an important reason for the decrease ratio of amylose/amylopectin in *sub-1* mutant. Taken together, our results indicated that the *sub-1* mutant can accumulate the amylopectin efficiently, potentially through altering the differential expression of *AGPase*, *GBSS1, SBE,* and *BAM*. This study also provides theoretical guidance for creating crop germplasm with high amylopectin by means of synthetic biology in the future.

## High-throughput sequencing application in the detection and discovery of viruses associated with the regulated citrus leprosis disease complex.

**Padmanabhan C, Nunziata S, Leon M G, Rivera Y, Mavrodieva VA, Nakhla MK, Roy A.**
24-01-2023
*Front Plant Sci.*
https://pubmed.ncbi.nlm.nih.gov/36762187/

Citrus leprosis (CiL) is one of the destructive emerging viral diseases of citrus in the Americas. Leprosis syndrome is associated with two taxonomically distinct groups of *Brevipalpus*-transmitted viruses (BTVs), that consist of positive-sense *Cilevirus*, *Higrevirus*, and negative-sense *Dichorhavirus*. The localized CiL symptoms observed in multiple citrus species and other alternate hosts indicates that these viruses might have originated from the mites and eventually adopted citrus as a secondary host. Genetic diversity in the genomes of viruses associated with the CiL disease complex have complicated current detection and diagnostic measures that prompted the application of High-Throughput Sequencing (HTS) protocols for improved detection and diagnosis. Two cileviruses are known to infect citrus, and among them only citrus leprosis virus C2 (CiLV-C2) hibiscus strain (CiLV-C2H) has been reported in hibiscus and passion fruit in the US. Based on our current CiL disease complex hypothesis, there is a high probability that CiL disease is associated with more viruses/strains that have not yet been identified but exist in nature. To protect the citrus industry, a Ribo-Zero HTS protocol was utilized for detection of cileviruses infecting three different hosts: *Citrus* spp., *Swinglea glutinosa*, and *Hibiscus rosa-sinensis*. Real-time RT-PCR assays were used to identify plants infected with CiLV-C2 or CiLV-C2H or both in mixed infection in all the above-mentioned plant genera. These results were further confirmed by bioinformatic analysis using HTS generated data. In this study, we utilized HTS assay in confirmatory diagnostics to screen BTVs infecting *Dieffenbachia* sp. (family: Araceae), *Passiflora edulis* (Passifloraceae), and *Smilax auriculata* (Smilacaceae). Through the implementation of HTS and downstream data analysis, we detected not only the known cileviruses in the studied hosts but also discovered a new strain of CiLV-C2 in hibiscus from Colombia. Phylogenetically, the new hibiscus strain is more closely related to CiLV-C2 than the known hibiscus strain, CiLV-C2H. We propose this strain to be named as CiLV-C2 hibiscus strain 2 (CiLV-C2H2). The findings from the study are critical for citrus growers, industry, regulators, and researchers. The possible movement of CiLV-C2H2 from hibiscus to citrus by the *Brevipalpus* spp. warrants further investigation.

# Echinococcose

## Prevalence of Gastrointestinal Helminths of Dogs and Associated Factors in Hawassa City of Sidama Region, Ethiopia.

**Dubie T, Sire S, Fentahun G, Bizuayehu F.**
06-02-2023
*J Parasitol Res.*
https://pubmed.ncbi.nlm.nih.gov/36793767/

A cross-sectional study was carried out in the Sidama region's Hawassa town from March 2021 to July 2021 with the aim of estimating the prevalence and associated factors of dog gastrointestinal helminths. A total of 384 dogs were randomly selected, and their feces were examined using a flotation technique. For data analysis, descriptive statistics and chi-square analyses were employed, and a $P$-value of less than 0.05 was considered as significant. Accordingly, 56% ($n$ = 215; 95% CI, 49.26-62.66) of dogs had gastrointestinal helminth parasite infection, of which 42.2% ($n$ = 162) had a single infection and 13.8% ($n$ = 53) had a mixed infection. In this study, *Strongyloides* sp. was the most detected helminth (24.2%), followed by *Ancylostoma* sp. (15.37%), *Trichuris vulpis* (14.6%), *Toxocara canis* (5.73%), *Echinococcus* sp. (5.47%), and *Dipylidium caninum* (4.43%). Out of the total sampled dogs tested positive for one or more gastrointestinal

helminths, 37.5% (*n* = 144) were males and 18.5% (*n* = 71) were females. The total prevalence of helminth infections did not change significantly (*P* > 0.05) by the gender, age, and breed of dogs. The present study's high prevalence of dog helminthiasis reflects a high occurrence of infection and a concern to the public's health. In light of this conclusion, it is advised that dog owners improve their standards of hygiene. In addition, they should regularly take their animals to veterinary care and frequently administer the appropriate anthelmintics available to their dogs.

## Zoonotic helminths - why the challenge remains.

Thompson RCA.
15-02-2023
*J Helminthol.*

## Hydatid disease (Echinococcosis granulosis) diagnosis from skeletal osteolytic lesions in an early seventh-millennium BP forager community from preagricultural northern Vietnam.

Vlok M, Buckley HR, Domett K, Willis A, Tromp M, Trinh HH, Minh TT, Mai Huong NT, Nguyen LC, Matsumura H, Huu NT, Oxenham MF.
Jan-2022
*Am J Biol Anthropol.*

**Objectives:** Con Co Ngua is a complex, sedentary forager site from northern Vietnam dating to the early seventh millennium BP. Prior research identified a calcified Echinococcus granulosis cyst, which causes hydatid disease. Osteolytic lesions consistent with hydatid disease were also present in this individual and others. Hydatid disease is observed in high frequencies in pastoralists, and its presence in a hunter-gatherer community raises questions regarding human-animal interaction prior to farming. The objective of this article is to identify and describe the epidemiology of hydatid disease in the human skeletal assemblage at Con Co Ngua. **Materials and methods:** One hundred and fifty-five individuals were macroscopically assessed for lesions. Of these, eight individuals were radiographed. Hydatid disease was diagnosed using a new threshold criteria protocol derived from clinical literature, which prioritizes lesions specific to the parasite. **Results:** Twenty-two individuals (14.2%) presented with osteolytic lesions consistent with hydatid disease, affecting the distal humerus, proximal femur and forearm, and pelvis. Seven individuals radiographed (4.5%) had multilocular cystic lesions strongly diagnostic for hydatid disease. All probable cases had lesions of the distal humerus. The remaining lesions were macroscopically identical to those radiographed and were considered possible cases. **Discussion:** While hydatid disease has previously been found in pre-agricultural communities, the high prevalence at Con Co Ngua is non-incidental. We propose that the presence of wild canids and management of wild buffalo and deer increased the risk of disease transmission. These findings further reveal subsistence complexity among hunter-gatherers living millennia prior to the adoption of farming in Southeast Asia.

## Endogenous IL-33 Accelerates Metacestode Growth during Late-Stage Alveolar Echinococcosis.

Autier B, Manuel C, Lundstroem-Stadelmann B, Girard JP, Gottstein B, Gangneux JP, Samson M, Robert-Gangneux F, Dion S.
14-02-2023
*Microbiol Spectr.*

During the course of the infectious disease alveolar echinococcosis (AE), the larval stage of Echinococcus multilocularis develops in the liver, where an initial Th1/Th17 immune response may allow its elimination in resistant individuals. In patients susceptible to infection and disease, the Th2 response initiates later, inducing tolerance to the parasite. The role of interleukin 33 (IL-33), an alarmin released during necrosis and known to drive a Th2 immune response, has not yet been described during AE. Wild-type (WT) and IL-33$^{-/-}$ C57BL/6J mice were infected by peritoneal inoculation with E. multilocularis metacestodes and euthanized 4 months later, and their immune response were analyzed. Immunofluorescence staining and IL-33 enzyme-linked immunosorbent assay (ELISA) were also performed on liver samples from human patients with AE. Overall, metacestode lesions were smaller in IL-33$^{-/-}$ mice than in WT mice. IL-33 was detected in periparasitic tissues, but not in mouse or human serum. In infected mice, endogenous IL-33 modified peritoneal macrophage polarization and cytokine profiles. Th2 cytokine concentrations were positively correlated with parasite mass in WT mice, but not in IL-33$^{-/-}$ mice. In human AE patients, IL-33 concentrations were higher in parasitic tissues than in distant liver parenchyma. The main sources of IL-33 were CD31$^+$ endothelial cells of the neovasculature, present within lymphoid periparasitic infiltrates together with FOXP3$^+$ T$_{reg}$s. In the murine model, periparasitic IL-33 correlated with accelerated parasite growth putatively through the polarization of M2-like macrophages and release of immunosuppressive cytokines IL-10 and transforming growth factor β1 (TGF-β1). We concluded that IL-33 is a key alarmin in AE that contributes to the tolerogenic effect of systemic Th2 cytokines. **IMPORTANCE** Infection with the metacestode stage of Echinococcus multilocularis, known as alveolar echinococcosis, is the most severe cestodosis worldwide. However, less than 1% of exposed individuals, in which the immune system is unable to control the parasite, develop the disease. The factors responsible for this interindividual variability are not fully understood. In this *in vivo* study comparing wild-type and IL-33$^{-/-}$ infected mice, together with data from human clinical samples, we determined that IL-33, an alarmin released following tissue injury and involved in the pathogenesis of cancer and asthma, accelerates the progression of the disease by modulating the periparasitic microenvironment. This suggests that targeting IL-33 could be of interest for the management of patients with AE, and that IL-33 polymorphisms could be responsible for increased susceptibility to AE.

## Gastrointestinal Parasites of Dogs in Egypt: An Update on the Prevalence in Dakahlia Governorate and a Meta-Analysis for the Published Data from the Country.

**Abbas I, Baghdadi HB, Rizk MA, El-Alfy ES, Elmishmishy B, Gwida M.**
31-01-2023
*Animals (Basel).*
https://pubmed.ncbi.nlm.nih.gov/36766385/

## Comparison of multiplex copro PCR with coproscopy followed by PCR on recovered eggs for the detection of Echinococcus granulosus and Taenia spp. infection in dogs.

**Yasur-Landau D, Genad O, Salant H, Dvir E, Mazuz ML, Baneth G.**
Mar-2023
*Vet Parasitol.*
https://pubmed.ncbi.nlm.nih.gov/36696840/

## Cerebral echinococcosis: Case report and literature review.

**Trueba-Argamasilla AA, Iborra-Bendicho MA, Simón-Páez M, Ros-de San Pedro J, Segovia-Hernández M.**
Feb-2023
*Enferm Infecc Microbiol Clin (Engl Ed).*
https://pubmed.ncbi.nlm.nih.gov/35907775/

Echinococcosis is a zoonosis caused by the larval form of the cestode Echinococcus granulosus. The cerebral affectation in the human is uncommon; only in 1-2% cases is observed encephalic involvement. This condition occurs mainly in the pediatric population and it is characterized by the presence of single and unilocular cysts. We report a case of a 29-year-old patient who came to the emergency department with a disabling headache of several weeks of evolution. In the brain imaging study a mass of unknown origin was visualized, finally it turned out to be a bilobed hydatid cyst. Regarding this case, the clinic-epidemiological, diagnostics and treatments aspects of cerebral hydatid disease will be reviewed.

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

## Clonorchis sinensis legumain promotes migration and invasion of cholangiocarcinoma cells via regulating tumor-related molecules.

**Chu Y, Shi D, Wang N, Ren L, Liu N, Hu F, Meng W, Hong SJ, Bai X.**

16-02-2023
*Parasit Vectors.*
https://pubmed.ncbi.nlm.nih.gov/36797792/

## Opisthorchis viverrini, Clonorchis sinensis and Opisthorchis felineus liver flukes affect mammalian host microbiome in a species-specific manner.

**Pakharukova MY, Lishai EA, Zaparina O, Baginskaya NV, Hong SJ, Sripa B, Mordvinov VA.**
13-02-2023
*PLoS Negl Trop Dis.*
https://pubmed.ncbi.nlm.nih.gov/36780567/

Background: Opisthorchis felineus, Opisthorchis viverrini and Clonorchis sinensis are epidemiologically significant food-borne trematodes endemic to diverse climatic areas. O. viverrini and C. sinensis are both recognized to be 1A group of biological carcinogens to human, whereas O. felineus is not. The mechanisms of carcinogenesis by the liver flukes are studied fragmentarily, the role of host and parasite microbiome is an unexplored aspect. Methodology/principal findings: Specific pathogen free Mesocricetus auratus hamsters were infected with C. sinensis, O. viverrini and O. felineus. The microbiota of the adult worms, colon feces and bile from the hamsters was investigated using Illumina-based sequencing targeting the prokaryotic 16S rRNA gene. The analysis of 43 libraries revealed 18,830,015 sequences, the bacterial super-kingdom, 16 different phyla, 39 classes, 63 orders, 107 families, 187 genera-level phylotypes. O. viverrini, a fluke with the most pronounced carcinogenic potential, has the strongest impact on the host bile microbiome, changing the abundance of 92 features, including Bifidobacteriaceae, Erysipelotrichaceae, [Paraprevotellaceae], Acetobacteraceae, Coriobacteraceae and Corynebacteriaceae bacterial species. All three infections significantly increased Enterobacteriaceae abundance in host bile, reduced the level of commensal bacteria in the gut microbiome (Parabacteroides, Roseburia, and AF12). Conclusions/significance: O. felineus, O. viverrini, and C. sinensis infections cause both general and species-specific qualitative and quantitative changes in the composition of microbiota of bile and colon feces of experimental animals infected with these trematodes. The alterations primarily concern the abundance of individual features and the phylogenetic diversity of microbiomes of infected hamsters.

## Preparation of polyclonal anti-Schistosoma mansoni cysteine protease antibodies for early diagnosis.

**Farid A.**
11-02-2023
*Appl Microbiol Biotechnol.*
https://pubmed.ncbi.nlm.nih.gov/36773062/

In many parts of the tropics, schistosomiasis is a major parasitic disease second only to malaria as a cause of morbidity and mortality. Diagnostic approaches include microscopic sampling of excreta such as the Kato-Katz

method, radiography, and serology. Due to their vital role in many stages of the parasitic life cycle, proteases have been under investigation as targets of immunological or chemotherapeutic anti-Schistosoma agents. Five major classes of protease have been identified on the basis of the peptide hydrolysis mechanism: serine, cysteine, aspartic, threonine, and metalloproteases. Proteases of all five catalytic classes have been identified from S. mansoni through proteomic or genetic analysis. The study aimed to produce polyclonal antibodies (pAbs) against schistosomal cysteine proteases (CP) to be used in the diagnosis of schistosomiasis. This study was conducted on S. mansoni-infected patients from highly endemic areas and from outpatients' clinic and hospitals and other patients infected with other parasites (Fasciola, hookworm, hydatid, and trichostrongyloids). In this study, the produced polyclonal antibodies against S. mansoni cysteine protease antigens were labeled with horseradish peroxidase (HRP) conjugate and used to detect CP antigens in stool and serum samples of S. mansoni-infected patients by sandwich ELISA. The study involved 200 S. mansoni-infected patients (diagnosed by finding characteristic eggs in the collected stool samples), 100 patients infected with other parasites (Fasciola, hookworm, hydatid, and trichostrongyloids), and 100 individuals who served as parasite-free healthy negative control. The prepared pAb succeeded in detecting CP antigens in stool and serum samples of S. mansoni-infected patients by sandwich ELISA with a sensitivity of 98.5% and 98.0% respectively. A positive correlation was observed between S. mansoni egg counts and both stool and serum antigen concentrations. Purified 27.5 kDa CP could be introduced as a suitable candidate antigen for early immunodiagnosis using sandwich ELISA for antigen detection. KEY POINTS: • Detection of cysteine protease antigens can replace parasitological examination. • Sandwich ELISA has a higher sensitivity than microscopic examination of eggs. • Identification of antigens is important for the goal of obtaining diagnostic tools.

### Proteomic analysis of exosome-like vesicles from Fasciola gigantica adult worm provides support for new vaccine targets against fascioliasis.

**Sheng ZA, Wu CL, Wang DY, Zhong SH, Yang X, Rao GS, Peng H, Feng SW, Li J, Huang WY, Luo HL.**
23-02-2023
*Parasit Vectors*. 2023
https://pubmed.ncbi.nlm.nih.gov/36765398/

### The helminth derived peptide FhHDM-1 redirects macrophage metabolism towards glutaminolysis to regulate the pro-inflammatory response.

**Quinteros SL, von Krusenstiern E, Snyder NW, Tanaka A, O'Brien B, Donnelly S.**
25-01-2023
*Front Immunol*.
https://pubmed.ncbi.nlm.nih.gov/36761766/

We have previously identified an immune modulating peptide, termed FhHDM-1, within the secretions of the liver fluke, *Fasciola hepatica*, which is sufficiently potent to prevent the progression of type 1 diabetes and multiple sclerosis in murine models of disease. Here, we have determined that the FhHDM-1 peptide regulates inflammation by reprogramming macrophage metabolism. Specifically, FhHDM-1 switched macrophage metabolism to a dependence on oxidative phosphorylation fuelled by fatty acids and supported by the induction of glutaminolysis. The catabolism of glutamine also resulted in an accumulation of alpha ketoglutarate (α-KG). These changes in metabolic activity were associated with a concomitant reduction in glycolytic flux, and the subsequent decrease in TNF and IL-6 production at the protein level. Interestingly, FhHDM-1 treated macrophages did not express the characteristic genes of an M2 phenotype, thereby indicating the specific regulation of inflammation, as opposed to the induction of an anti-inflammatory phenotype *per se*. Use of an inactive derivative of FhHDM-1, which did not modulate macrophage responses, revealed that the regulation of immune responses was dependent on the ability of FhHDM-1 to modulate lysosomal pH. These results identify a novel functional association between the lysosome and mitochondrial metabolism in macrophages, and further highlight the significant therapeutic potential of FhHDM-1 to prevent inflammation.

### Uncovering local endemism from southeastern Myanmar: description of the new karst-associated terrestrial snail genus Burmochlamys (Eupulmonata, Helicarionidae).

**Pholyotha A, Sutcharit C, Lin A, Panha S.**
04-06-2022
*Zookeys*.
https://pubmed.ncbi.nlm.nih.gov/36761453/

### Practical guide to the diagnostics of ruminant gastrointestinal nematodes, liver fluke and lungworm infection: interpretation and usability of results.

**Sabatini GA, de Almeida Borges F, Claerebout E, Gianechini LS, Höglund J, Kaplan RM, Lopes WDZ, Mitchell S, Rinaldi L, von Samson-Himmelstjerna G, Steffan P, Woodgate R.**
08-02-2023
*Parasit Vectors*.
https://pubmed.ncbi.nlm.nih.gov/36755300/

The diagnostics of ruminant parasites remains one of the cornerstones for parasite control best practices. Field veterinarians have several techniques at their disposal (fecal egg count, coproculture, FAMACHA®, plasma pepsinogen, ELISA-Ostertagia, ELISA-Fasciola, Baermann and ELISA-Lungworm) for the identification and/or quantification of gastrointestinal nematodes, lungworms and liver fluke infecting small ruminants and cattle. Each of these diagnostic tools has its own strengths and weaknesses and is more appropriate for a specific production operation and/or age of the animal (young and adults). This review focuses on the usability and interpretation of the results of these diagnostic tools. The

most advanced technical information on sampling, storage, advantages and limitations of each tool for different types of production operations and animal categories is provided.

## Opisthorchis Felineus Infection is a Risk Factor for Cholangiocarcinoma in Western Siberia: A Hospital-based Case-control Study.

Fedorova OS, Kovshirina AE, Kovshirina YV, Hattendorf J, Onishchenko SV, Katanakhova LL, Taslicki SS, Chizhikov AV, Tataurov IA, Vtorushin SV, Sripa B, Ogorodova LM, Odermatt P.

# Filariose lymphatique

## Discovery of potent inhibitors targeting Glutathione S-transferase of Wuchereria bancrofti: a step toward the development of effective anti-filariasis drugs.

Sureshan M, Prabhu D, Rajamanikandan S, Saraboji K.

Lymphatic filariasis (LF) is one of the major health problems for the human kind in developing countries including India. LF is caused by three major nematodes namely Wuchereria bancrofti, Brugia malayi, and Brugia timori. The recent statistics of World Health Organization (WHO) showed that 51 million people were affected and 863 million people from 47 countries around worldwide remain threatened by LF. Among them, 90% of the filarial infection was caused by the nematode W. bancrofti. Approved drugs were available for the treatment of LF but many of them developed drug resistance and no longer effective in all stages of the infection. In the current research work, we explored the Glutathione S-transferase (GST) of W. bancrofti, the key enzyme responsible for detoxification that catalyzes the conjugation of reduced GSH (glutathione) to xenobiotic compounds. Initially, we analyzed the stability of the WbGST through 200 ns MD simulation and further structure-based virtual screening approach was applied by targeting the substrate binding site to identify the potential leads from small molecule collection. The in silico ADMET profiles for the top-ranked hits were predicted and the predicted non-toxic lead molecules showed the highest docking score in the range of - 12.72 kcal/mol to - 11.97 kcal/mol. The cross docking of the identified hits with human GST revealed the potential binding specificity of the hits toward WbGST. Through WbGST-lead complex simulation, the lead molecules were observed to be stable and also intactly bound within the binding site of WbGST. Based on the computational results, the five predicted non-toxic molecules were selected for the in vitro assay. The molecules showed significant percentage of inhibition against the filarial worm Setaria digitata which is the commonly used model organism to evaluate the filarial

activity. In addition, the molecules also showed better $IC_{50}$ than the standard drug ivermectin. The identified lead molecules will lay a significant insight for the development of new drugs with higher specificity and lesser toxicity to control and treat filarial infections.

## Detection of Wuchereria bancrofti in the city of São Luís, state of Maranhão, Brazil: New incursion or persisting problem?

Araújo TA, Lima de Albuquerque A, Melo DCTV, Santos EMM, Oliveira ALS, Ayres CFJ, Oliveira CMF.

Background: The elimination of lymphatic filariasis (LF) from Brazil by 2020 was not accomplished; however, this goal can be achieved in the upcoming years with the assistance of specific strategies. The surveillance of LF can be performed using molecular xenomonitoring (MX), a noninvasive method used to infer the presence of the parasite in the human population. Herein, São Luís (state of Maranhão) was the first city to be investigated to identify whether LF transmission in Brazil has been interrupted and if there were any new incursions. Methodology/principal findings: Mosquitoes were collected by aspiration at 901 points distributed among 11 neighborhoods in São Luís with records of patients with microfilaremia. Pools of engorged or gravid Culex quinquefasciatus females were evaluated by WbCx duplex PCR with endogenous control for mosquitoes and target for W. bancrofti for determining the vector infection rate. Among the 10,428 collected mosquitoes, the most abundant species were C. quinquefasciatus (85%) and Aedes aegypti (12%). Significantly larger numbers of mosquitoes were collected from the neighborhoods of Areinha and Coreia (p<0.05). MX performed using PCR validated 705 pools of engorged or gravid females, fifteen of which were positive for Wuchereria bancrofti in two neighborhoods. Conclusions: The high density of engorged C. quinquefasciatus females per home, inadequate sanitation, and detection of W. bancrofti-infected mosquitoes in the city of São Luís represent a warning of the possible upsurge of LF, a disease that is still neglected; this underscores the need for the ostensive monitoring of LF in Brazil.

# Mycetome

## Expansile Sphenoid Mycetoma Presenting With Headache and Galactorrhea.

Rogers GA.

This case report describes an immunocompetent woman in her 30s with daily vertex headaches over 13 months duration who developed spontaneous galactorrhea and was diagnosed with noninvasive fungal sinusitis.

### A rare subungual eumycetoma in a cancer survivor: A case report.

Maximov I, Kochergin N, Ditmarova Z, Borzova E.

# Schistosomiase

## In Vitro and In Vivo Antischistosomal Activity Profiling and Pharmacokinetics of Ozonide Carboxylic Acids.

Biendl S, Häberli C, Chen G, Wang W, Zhong L, Saunders J, Pham T, Wang X, Wu J, Charman SA, Vennerstrom JL, Keiser J.

Praziquantel, the only drug in clinical use for the treatment and control of schistosomiasis, is inactive against developing infections. Ozonides are synthetic peroxide derivatives inspired by the naturally occurring artemisinin and show particularly promising activity against juvenile schistosomes. We conducted an in-depth characterization of the *in vitro* and *in vivo* antischistosomal activity and pharmacokinetics of lead ozonide carboxylic acid OZ418 and four of its active analogs. *In vitro,* the ozonides featured rapid and consistent activity against schistosomula and adult schistosomes at double-digit micromolar $EC_{50}$ values. Potency did not vary considerably between *Schistosoma spp.* The zwitterionic OZ740 and OZ772 were more active *in vivo* compared to their non-amphoteric carboxylic acids OZ418 and OZ748, despite their much lower systemic plasma exposure (AUC). The most active compound *in vivo* was ethyl ester OZ780, which was rapidly transformed to its parent zwitterion OZ740 and achieved $ED_{50}$ values of 35 ± 2.4 and 29 ± 2.4 mg/kg against adult and juvenile *Schistosoma mansoni*, respectively. Ozonide carboxylic acids represent promising candidates for further optimization and development due to their good efficacy against both life stages together with their broad activity range against all relevant parasite species.

## Zoonotic helminths - why the challenge remains.

Thompson RCA.

## Urogenital schistosomiasis (UGS) and female genital schistosomiasis (FGS) in Cameroon: an observational assessment of key reproductive health determinants of girls and women in the Matta Health Area.

Makia CM, Fesuh NB, Amabo EN, Gamba VA, Oluwole AS, Stothard R.

**Objectives and setting:** Across sub-Saharan Africa, urogenital schistosomiasis (UGS), in particular female genital schistosomiasis (FGS), is a significant waterborne parasitic disease, with its direct burden on the sexual and reproductive health (SRH) of sufferers infrequently measured. UGS has an established control plan, which in most endemic regions as in Cameroon, still excludes FGS considerations. Highlighting existent associations between UGS and FGS could increase the management of FGS within UGS interventions. This study seeks to identify current associations among FGS and UGS with some reproductive health indicators, to provide formative information for better integrated control. **Participants:** 304 females aged 5-69 years were all examined for UGS by urine filtration and microscopy. Among these, 193 women and girls were eligible for clinical FGS assessment based on age (>13). After selective questioning for FGS symptoms, a subgroup of 67 women and girls consented for clinical examination for FGS using portable colposcopy, with observed sequelae classified according to the WHO FGS pocket atlas. **Outcome:** Overall UGS and FGS prevalence was measured, with FGS-related/UGS-related reproductive health symptoms recorded. Associations between FGS and UGS were investigated by univariate and multivariate logistic regression analyses. **Results:** Overall UGS prevalence was 63.8% (194/304), where FGS prevalence (subgroup) was 50.7% (34/67). FGS manifestation increased significantly with increasing age, while a significant decrease with ascending age was observed for UGS. Lower abdominal pain (LAP) vaginal itches (VI) and coital pain (CP) were identified as the main significant shared symptoms of both FGS and UGS, while LAP with menstrual irregularity (MI) appeared a strong symptomatic indicator for FGS. **Conclusion:** LAP, MI, CP and VI are the potential SRH indicators that could be exploited in future for targeting of praziquantel provision to FGS sufferers within primary care, complementary with existing praziquantel distribution for UGS sufferers in *Schistosoma haematobium* endemic areas.

## Impact of the COVID-19 pandemic on the actions of the Schistosomiasis Control Program in an endemic area in Northeastern Brazil.

Dantas NM, Andrade LA, da Paz WS, Borges WN, Barbosa VGB, da Hora DPG, da Silva CE, Feliciano do Carmo R, de Souza CDF, Dantas Dos Santos A, Wanderley FS, Negrão-Corrêa DA, Fujiwara RT, Bezerra-Santos M, Porto WJN.

## Helminth egg derivatives as proregenerative immunotherapies.

Maestas DR Jr, Chung L, Han J, Wang X, Sommerfeld SD, Kelly SH, Moore E, Nguyen HH, Mejías JC, Peña AN, Zhang H, Hooks JST, Chin AF, Andorko JI, Berlinicke CA, Krishnan K, Choi Y, Anderson AE, Mahatme R, Mejia C,

**Eric M, Woo J, Ganguly S, Zack DJ, Zhao L, Pearce EJ, Housseau F, Pardoll DM, Elisseeff JH.**
21-02-2023
https://pubmed.ncbi.nlm.nih.gov/36780522/

The immune system is increasingly recognized as an important regulator of tissue repair. We developed a regenerative immunotherapy from the helminth *Schistosoma mansoni* soluble egg antigen (SEA) to stimulate production of interleukin (IL)-4 and other type 2-associated cytokines without negative infection-related sequelae. The regenerative SEA (rSEA) applied to a murine muscle injury induced accumulation of IL-4-expressing T helper cells, eosinophils, and regulatory T cells and decreased expression of IL-17A in gamma delta (γδ) T cells, resulting in improved repair and decreased fibrosis. Encapsulation and controlled release of rSEA in a hydrogel further enhanced type 2 immunity and larger volumes of tissue repair. The broad regenerative capacity of rSEA was validated in articular joint and corneal injury models. These results introduce a regenerative immunotherapy approach using natural helminth derivatives.

## Musculoskeletal pain and quality of life in mothers of children with microcephaly, due to congenital Zika virus syndrome.

**Araújo LMC, Guimarães-do-Carmo VJ, Andrade TGVS, Claudino SC, Soares DM, Melo RS.**
Mar-2023
https://pubmed.ncbi.nlm.nih.gov/35959527/

## Preparation of polyclonal anti-Schistosoma mansoni cysteine protease antibodies for early diagnosis.

**Farid A.**
11-02-2023
https://pubmed.ncbi.nlm.nih.gov/36773062/

## Accuracy Study of Kato-Katz and Helmintex Methods for Diagnosis of Schistosomiasis Mansoni in a Moderate Endemicity Area in Sergipe, Northeastern Brazil.

**Menezes DL, Santos CTJ, Oliveira YLDC, Campos VTC, Negrão-Corrêa DA, Geiger SM, Silva JRS, Jain S, Oliveira LM, Fujiwara RT, Graeff-Teixeira C, Dolabella SS.**
31-01-2023
https://pubmed.ncbi.nlm.nih.gov/36766631/

Schistosomiasis is a neglected tropical disease (NTD) caused by blood flukes from the genus *Schistosoma.* Brazil hosts the main endemic area in the Americas, where *Schistosoma mansoni* is the only species causing the disease. Kato-Katz (KK) thick smear is the WHO recommended screening test for populational studies, but there is growing evidence for the sensitivity limitations associated with KK, especially in areas with low parasite loads. Helmintex (HTX) is another highly sensitive egg-detection method, based on the magnetic properties of *S. mansoni* eggs and their isolation in a magnetic field. The objective of this study is to evaluate both KK and HTX in a moderate endemic locality, Areia Branca, located in the municipality of Pacatuba, in the state of Sergipe in northeastern Brazil. From 234 individual fecal samples, two KK thick smears were prepared and evaluated for each sample. Similarly, 30 g of each fecal sample was processed by HTX protocol. Eggs were detected in 80 (34.18%) residents. Twenty-three (9.83%) samples were positive for eggs (only by KK), and 77 (32.91%) samples showed positive for eggs (only by HTX). Sensitivity, specificity, and accuracy estimates gave values of 28.75%, 100% and 75.64%, respectively, for KK, and 96.25%, 100% and 98.72% respectively, for HTX. The positive predictive value was 100% for both methods, while the negative predictive value was 72.99% for KK and 98.09% for HTX. Overall, HTX presented a superior performance compared to the one sample, two slides KK examination. The study confirms the role of HTX as a reference method for the definition of true-positive samples in comparative accuracy studies and its potential role in the late stages when the certification of schistosomiasis transmission interruption is required. Diagnostic tests are important tools for the elimination of this NTD, besides the effective implementation of safe water, basic sanitation, snail control, and the treatment of infected populations.

## Bulinus snails in the Lake Victoria Basin in Kenya: Systematics and their role as hosts for schistosomes.

**Babbitt CR, Laidemitt MR, Mutuku MW, Oraro PO, Brant SV, Mkoji GM, Loker ES.**
10-02-2023
https://pubmed.ncbi.nlm.nih.gov/36763676/

## Mycoplasma pneumoniae and Schistosoma mansoni co-infection in a young patient with extensive longitudinal acute transverse myelitis.

**Alayafi HA, Alruwaili M, Aljumah TK, Alshehri A, Alrasheed D, Alanazi MF, AlRuwaili R, Ali NH, Albarrak AM, AlRashdi BM, Taha AE.**
31-12-2022
https://pubmed.ncbi.nlm.nih.gov/36753653/

## IL-4 and helminth infection downregulate MINCLE-dependent macrophage response to mycobacteria and Th17 adjuvanticity.

**Schick J, Altunay M, Lacorcia M, Marschner N, Westermann S, Schluckebier J, Schubart C, Bodendorfer B, Christensen D, Alexander C, Wirtz S, Voehringer D, da Costa CP, Lang R.**
08-02-2023
https://pubmed.ncbi.nlm.nih.gov/36753434/

The myeloid C-type lectin receptor (CLR) MINCLE senses the mycobacterial cell wall component trehalose-6,6'-dimycolate (TDM). Recently, we found that IL-4 downregulates MINCLE expression in macrophages. IL-4 is a hallmark cytokine in helminth infections, which appear to increase the risk for mycobacterial infection and active tuberculosis. Here, we investigated functional consequences of IL-4 and helminth infection on MINCLE-driven macrophage activation and Th1/Th17 adjuvanticity. IL-4 inhibited MINCLE and cytokine induction after macrophage infection with *Mycobacterium bovis* bacille Calmette-Guerin (BCG). Infection of mice with BCG upregulated MINCLE on myeloid cells, which was inhibited by IL-4 plasmid injection and by infection with the nematode *Nippostrongylus brasiliensis* in monocytes. To determine the impact of helminth infection on MINCLE-dependent immune responses, we vaccinated mice with a recombinant protein together with the MINCLE ligand trehalose-6,6-dibehenate (TDB) as adjuvant. Concurrent infection with *N. brasiliensis* or with *Schistosoma mansoni* promoted T cell-derived IL-4 production and suppressed Th1/Th17 differentiation in the spleen. In contrast, helminth infection did not reduce Th1/Th17 induction by TDB in draining peripheral lymph nodes, where IL-4 levels were unaltered. Upon use of the TLR4-dependent adjuvant G3D6A, *N. brasiliensis* infection impaired selectively the induction of splenic antigen-specific Th1 but not of Th17 cells. Inhibition of MINCLE-dependent Th1/Th17 responses in mice infected with *N. brasiliensis* was dependent on IL-4/IL-13. Thus, helminth infection attenuated the Th17 response to MINCLE-dependent immunization in an organ- and adjuvant-specific manner via the Th2 cytokines IL-4/IL-13. Taken together, our results demonstrate downregulation of MINCLE expression on monocytes and macrophages by IL-4 as a possible mechanism of thwarted Th17 vaccination responses by underlying helminth infection.

## Activity of N-phenylbenzamide analogs against the neglected disease pathogen, Schistosoma mansoni.

**Kanyanta M, Lengwe C, Mambwe D, Francisco KR, Liu LJ, Uli Sun Y, Amarasinghe DK, Caffrey CR, Mubanga Cheuka P.**

For the Schistosoma mansoni flatworm pathogen, we report a structure-activity relationship of 25 derivatives of the N-phenylbenzamide compound, 1 (MMV687807), a Medicines for Malaria Venture compound for which bioactivity was originally identified in 2018. Synthesized compounds were cross-screened against the HEK 293 mammalian cells. Compounds 9 and 11 were identified as fast-acting schistosomicidal compounds whereby adult worm integrity was severely compromised within 1 h. Against HEK 293 mammalian cells, both compounds exhibited high $CC_{50}$ values (9.8 ± 1.6 and 11.1 ± 0.2 μM respectively) which could translate to comfortable selectivity. When evaluated in a concentration-response format, compound 9 was active in the nanomolar range ($EC_{50}$ = 80 nM), translating to a selectivity index of 123 over

HEK 293 cells. The data encourage the further investigation of N-phenylbenzamides as antischistosomals.

## A cercarial invadolysin interferes with the host immune response and facilitates infection establishment of Schistosoma mansoni.

**Hambrook JR, Hanington PC.**

## Parasitological and histopathological studies to the effect of aqueous extract of Moringa oleifera Lam. leaves combined with praziquantel therapy in modulating the liver and spleen damage induced by Schistosoma mansoni to male mice.

**Saad El-Din MI, Gad El-Hak HN, Ghobashy MA, Elrayess RA.**

This study assessed the effectiveness of an aqueous extract of Moringa Oleifera Lam. leaves (MOL) alone or in combination with praziquantel (PZQ) drug targeting-infected mice with Schistosoma mansoni-induced liver and spleen damage. Mice were divided into eight groups control mice group treated orally with saline. PZQ group: non-infected mice treated orally with 300 mg/kg bwt PZQ three consecutive days. MOL group: non-infected mice treated orally with 150 mg/kg bwt MOL extract for 15 days. PZQ/ MOL group: non-infected mice treated orally with 300 mg/kg bwt PZQ for three consecutive days and 150 mg/kg bwt MOL extract for 15 days. IF group: infected mice with 100 cercariae/mouse of the Egyptian strain of S. mansoni. IF/PZQ group infected mice with S. mansoni cercariae and treated orally with 300 mg/kg bwt PZQ for three consecutive days. IF/MOL group: infected mice with S. mansoni cercariae treated orally with 150 mg/kg bwt MOL extract for 15 days. IF/PZQ +MOL group: infected mice with S. mansoni cercariae treated orally with 300 mg/kg bwt PZQ for three consecutive days and 150 mg/kg bwt MOL extract for 15 days. Blood, liver, spleen, worm, and eggs were collected at the end of the experimental period. Treatment of infected mice with MOL and PZQ together significantly reduced the number of ova/g tissue and eliminated the parasites. In addition, the liver and spleen of infected mice showed less histopathological alteration and immunohistochemical expression of nuclear factor kappa β (NF-Kβ). We can conclude that MOL extract combined with PZ has a curative effect on S. mansoni infection and helped to lessen its pathological effects.

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

## Acute intestinal obstruction due to ascariasis in a child: A case report.

**Sulmiati, Nurmantu F, Ahmadwirawan, Mariana N, Habar TR, Faruk M.**
11-02-2023
*Int J Surg Case Rep*.
https://pubmed.ncbi.nlm.nih.gov/36791528/

Introduction and importance: Ascariasis is one of the most common parasitic infections worldwide, especially in tropical and subtropical developing countries with poor personal hygiene and sanitation. This condition is a staggering worldwide public health problem with high morbidity and mortality. Intestinal obstruction is an acute presentation that occurs in cases where clumps of worms form, causing partial or complete obstruction of the intestinal lumen. Case presentation: We report a case of a 5-year-old boy with total intestinal obstruction due to Ascaris lumbricoides, who underwent exploratory laparotomy and enterotomy to remove the worm masses. Clinical discussion: Infestation with roundworms is widespread in developing countries. While the majority of the intestinal obstruction they cause may be treated conservatively, in some circumstances, surgery may be required. Conclusion: Infestation with roundworms is widespread in developing countries, and although the majority of the intestinal obstruction they cause may be treated conservatively, in some circumstances, surgery may be required.

## Prevalence of Gastrointestinal Helminths of Dogs and Associated Factors in Hawassa City of Sidama Region, Ethiopia.

**Dubie T, Sire S, Fentahun G, Bizuayehu F.**
06-02-2023
*J Parasitol Res.*
https://pubmed.ncbi.nlm.nih.gov/36793767/

A cross-sectional study was carried out in the Sidama region's Hawassa town from March 2021 to July 2021 with the aim of estimating the prevalence and associated factors of dog gastrointestinal helminths. A total of 384 dogs were randomly selected, and their feces were examined using a flotation technique. For data analysis, descriptive statistics and chi-square analyses were employed, and a $P$-value of less than 0.05 was considered as significant. Accordingly, 56% ($n$ = 215; 95% CI, 49.26-62.66) of dogs had gastrointestinal helminth parasite infection, of which 42.2% ($n$ = 162) had a single infection and 13.8% ($n$ = 53) had a mixed infection. In this study, *Strongyloides* sp. was the most detected helminth (24.2%), followed by *Ancylostoma* sp. (15.37%), *Trichuris vulpis* (14.6%), *Toxocara canis* (5.73%), *Echinococcus* sp. (5.47%), and *Dipylidium caninum* (4.43%). Out of the total sampled dogs tested positive for one or more gastrointestinal helminths, 37.5% ($n$ = 144) were males and 18.5% ($n$ = 71) were females. The total prevalence of helminth infections did not change significantly ($P$ > 0.05) by the gender, age, and breed of dogs. The present study's high prevalence of dog helminthiasis reflects a high occurrence of infection and a concern to the public's health. In light of this conclusion, it is advised that dog owners improve their standards of hygiene. In addition, they should regularly take their animals to veterinary care and frequently administer the appropriate anthelmintics available to their dogs.

## An efficient method for viable cryopreservation of hookworms and other gastrointestinal nematodes in the laboratory.

**Li H, Gazzola D, Hu Y, Aroian RV.**
01-02-2023
*bioRxiv*.
https://pubmed.ncbi.nlm.nih.gov/36778351/

Hookworms (genera *Ancylostoma* and *Necator* ) are amongst of the most prevalent and important parasites of humans globally. These intestinal parasites ingest blood, resulting in anemia, growth stunting, malnutrition, and adverse pregnancy outcomes. They are also critical parasites of dogs and other animals. In addition, hookworms and hookworm products are being explored for their use in treatment of autoimmune and inflammatory diseases. There is thus a significant and growing interest in these mammalian host-obligate parasites. Laboratory research is hampered by the lack of good means of cryopreservation. Here, we describe a robust method for long-term (â‰¥3 year) cryoprotection and recovery of both *Ancylostoma* and *Necator* hookworms that is also applicable to two other intestinal parasites that passages through the infective third larval stage, *Strongyloides ratti* and H *eligmosomoides polygyrus bakeri* . The key is the use cryo-preserved first-staged larvae raised to the infective third larval stage using activated charcoal mixed with uninfected feces from a permissive host. This technique will greatly facilitate research on and availability of gastrointestinal parasitic nematodes with great importance to global health, companion animal health, and autoimmune/inflammatory disease therapies.

## Zoonotic helminths - why the challenge remains.

**Thompson RCA.**
15-02-2023
*J Helminthol.*
https://pubmed.ncbi.nlm.nih.gov/36790130/

Helminth zoonoses remain a global problem to public health and the economy of many countries. Polymerase chain reaction-based techniques and sequencing have resolved many taxonomic issues and are now essential to understanding the epidemiology of helminth zoonotic infections and the ecology of the causative agents. This is clearly demonstrated from research on *Echinococcus* (echinococcosis) and *Trichinella* (trichinosis).

Unfortunately, a variety of anthropogenic factors are worsening the problems caused by helminth zoonoses. These include cultural factors, urbanization and climate change. Wildlife plays an increasingly important role in the maintenance of many helminth zoonoses making surveillance and control increasingly difficult. The emergence or re-emergence of helminth zoonoses such as *Ancylostoma ceylanicum*, *Toxocara*, *Dracunculus* and *Thelazia* exacerbate an already discouraging scenario compounding the control of a group of long neglected diseases.

## Red palm olein-enriched biscuit supplementation lowers Ascaris lumbricoides reinfection at 6-month after anthelmintic treatment among schoolchildren with vitamin A deficiency (VAD).

**Tan PY, Loganathan R, Teng KT, Lee SC, Johari SNM, Selvaduray KR, Ngui R, Lim YA.**

Notwithstanding the global efforts made to control intestinal parasitic infections, soil-transmitted helminth (STH) infections are still one of the most prevalent infections globally, especially in developing countries. A double-blinded, randomized controlled trial was conducted on 343 primary schoolchildren (8-12 years old) with vitamin A deficiency (VAD) in rural areas of Malaysia to investigate the effects of red palm olein (RPO)-enriched biscuits on STH reinfection rates and infection intensities. The effects of the RPO-enriched biscuits (experimental group, n = 153) and palm olein (PO)-enriched biscuits (control group, n = 190), were assessed at 3- and 6-month after the administration of complete triple-dose albendazole (one dose of 400 mg for three consecutive days). The overall STH infection rate at baseline was recorded at 65.6%. At 6-month, a significantly lower reinfection rate of A. lumbricoides was observed in the experimental group (35.3%) compared to the control group (60.0%) (P< 0.05), and a significant reduction in fecal egg count (epg) of A. lumbricoides was observed in the experimental group from baseline (P< 0.001), but no significant reduction was observed in the control group. No significant differences in the reduction of infection intensities of T. trichiura and hookworm were observed between experimental and control groups at 3- and 6-month (P>0.05). These findings suggest the potential beneficial effects of RPO-enriched biscuit supplementation on the reinfection of A. lumbricoides, which could be attributed to its high carotenoids content by enhancing host immune response and mucosal epithelium integrity. However, further studies are warranted to confirm whether RPO supplementation could result in similar parasite-specific beneficial effects in other community settings, as well as to explore the underlying mechanisms.

# Gale

## Scabies Mite is Bright Green Under UV Dermatoscopy.

**Pietkiewicz P, Navarrete-Dechent C.**

## Reply to "oral ivermectin to treat scabies: a comparison of two different regimens".

**Potestio L, Ruggiero A, Fabbrocini G, Martora F, Costanzo L, Gallo L.**

## Artificial Infestation of Sarcoptes scabiei (Acari: Sarcoptidae) in Rabbits Exhibits Progressive Pathological Changes, Apoptosis, and Keratinization in the Skin.

**Guan K, Xu J, Gu X, He R, Xie Y, Jing B, Peng X, Yang G.**

*Sarcoptes scabiei* (*S. scabiei*) is an ectoparasite that can infest humans and 150 mammalian host species, primarily causing pruritus, crust, and alopecia. However, neither the pathological process of host skin under *S. scabiei* infection nor the mechanism of *S. scabiei* infection in regulating apoptosis and keratinization of host skin has been studied yet. In this study, a total of 56 rabbits were artificially infested with *S. scabiei*, and the skin samples were collected at seven different time points, including 6 h, 12 h, day 1, day 3, 1 week, 4 weeks, and 8 weeks, whereas a group of eight rabbits served as controls. We measured epidermal thickness by H&E staining, observed the skin ultrastructure by electron microscopy, and detected the degree of skin apoptosis by TUNEL staining. The level of transcription of genes related to apoptosis and keratinization was detected by quantitative real-time PCR (qRT-PCR), and the level of Bcl-2 protein expression was further detected using immunohistochemistry. Our results showed that, with increased infestation time, the epidermal layer of the rabbit skin exhibited significant thickening and keratinization, swollen mitochondria in the epidermal cells, and increased skin apoptosis. The level of caspase-1, 3, 8, 10, 14, and Bcl-2 mRNA expression was increased, whereas the level of keratin 1 and 5 was decreased after *S. scabiei* infestation. In conclusion, *S. scabiei* infestation causes thickening of the epidermis, which may be related to apoptosis-induced proliferation and skin keratinization.

## Prescriptions for scabies are rapidly increasing in Spain: An ecological study with national prescription data, 2008-2021.

**Martínez-García E, Grau-Pérez M, Buendía-Eisman A, García-Doval I.**
Mat-2023
*J Eur Acad Dermatol Venereol.*
https://pubmed.ncbi.nlm.nih.gov/36151936/

# Morsures de serpent

## Cat-eyed snake (Genus: Boiga) bites in Sri Lanka: First authentic case series.

**Rathnayaka RMMKN, Ranathunga PEAN, Silva MLI, Abeyrathna YNMP, Kularatne SAM.**
13-02-2023
*Toxicon.*
https://pubmed.ncbi.nlm.nih.gov/36791994/

Cat snakes (Genus: Boiga) are considered to be of lesser medical important in Sri Lanka, as their bites are known to cause only mild local effects such as local pain and swelling at the site of the bite. Five species of cat snakes are found in Sri Lanka, of which three are endemic. They are widely distributed all over the country. Out of seven cases of cat snake bites, including six adults and one child, five developed only mild local effects and two did not have any symptoms. Any of them did not develop systemic manifestations. The snakes responsible were the Sri Lanka cat snake (Boiga ceylonensis), Forsten's cat snake (Boiga forsteni), and also Ranawana's cat snake (Boiga ranawanei) which is the first report in Sri Lanka.

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

**Prusty S, Sharma A.**
14-02-2023
*J Agromedicine.*
https://pubmed.ncbi.nlm.nih.gov/36786390/

## Venom-Induced Reversible Leukoencephalopathy: A Novel Cause of Toxic Acute Leukoencephalopathy With Restricted Diffusion.

**Kamate M, Basavanagowda T, Hattiholi V.**
14-01-2023
*Pediatr Neurol.*
https://pubmed.ncbi.nlm.nih.gov/36774684/

## What Are the Neurotoxins in Hemotoxic Snake Venoms?

**Osipov A, Utkin Y.**
02-02-2023
*Int J Mol Sci.*
https://pubmed.ncbi.nlm.nih.gov/36769242/

Snake venoms as tools for hunting are primarily aimed at the most vital systems of the prey, especially the nervous and circulatory systems. In general, snakes of the Elapidae family produce neurotoxic venoms comprising of toxins targeting the nervous system, while snakes of the Viperidae family and most rear-fanged snakes produce hemotoxic venoms directed mainly on blood coagulation. However, it is not all so clear. Some bites by viperids results in neurotoxic signs and it is now known that hemotoxic venoms do contain neurotoxic components. For example, viperid phospholipases $A_2$ may manifest pre- or/and postsynaptic activity and be involved in pain and analgesia. There are other neurotoxins belonging to diverse families ranging from large multi-subunit proteins (e.g., C-type lectin-like proteins) to short peptide neurotoxins (e.g., waglerins and azemiopsin), which are found in hemotoxic venoms. Other neurotoxins from hemotoxic venoms include baptides, crotamine, cysteine-rich secretory proteins, Kunitz-type protease inhibitors, sarafotoxins and three-finger toxins. Some of these toxins exhibit postsynaptic activity, while others affect the functioning of voltage-dependent ion channels. This review represents the first attempt to systematize data on the neurotoxins from "non-neurotoxic" snake venom. The structural and functional characteristic of these neurotoxins affecting diverse targets in the nervous system are considered.

## Risks of snakebite and challenges to seeking and providing treatment for agro-pastoral communities in Tanzania.

**Francis MF, Vianney SJ, Heitz-Tokpa K, Kreppel K.**
10-02-2023
*PLoS One.*
https://pubmed.ncbi.nlm.nih.gov/36763599/

**Background:** Continuous occurrence of snakebite incidences and the vulnerability of some communities remain a critical problem in sub-Saharan Africa. Despite causing permanent disability to almost half a million people annually and numerous deaths, snakebite and associated complications are still largely neglected. This study aimed at elucidating risk factors associated with snakebite cases, treatment availability and case management practices for vulnerable agro-pastoralist communities in Northern Tanzania. **Methods:** Data was collected in the Monduli (Arusha region) and the Simanjiro (Manyara region) districts in Tanzania. Interviews with 101 snakebite victims or their guardians and 13 health professionals from 3 health centers in the districts were conducted. Additionally, case records of patients admitted between 2007 and 2019 to the Meserani Snakebite Clinic were obtained. **Results:** This study showed that appropriate treatment for snakebite including anti-venom, is difficult to access and that snakebite incidences were significantly linked to factors such as gender, age, socio-economic activity, season of the year, and whether being at home or out in the fields. Anti-venom and trained health professionals were only available at the Meserani Snake Park Clinic. Men were bitten most often ($\chi2$ = 62.08, df = 4, p-value < 0.0001). Overall, adults between the ages of 18 and 60 years ($\chi2$ = 62.08, df = 4, p-value < 0.0001) received most bites, usually while outdoors herding cattle in the dry season. A significant majority of victims looked for traditional treatment first (52.7%, $\chi2$ = 29.541, df = 2, p-value = 0.0001). The results of this study present crucial information on what is needed to improve the accessibility to appropriate treatment after a snakebite among agro-pastoral communities. **Conclusion:** The situation regarding morbidity and mortality due to the inaccessibility of common treatment for snakebite in northern Tanzania is

challenging. Reliance on traditional medicine exacerbates the situation. There is dire need to involve affected communities, researchers, the government, clinicians and the public in general, to work together and take part in the global snakebite initiative. Communities and health professionals recognise the underlying challenges and have valuable suggestions on how to improve the situation.

## Taxonomic delimitation and molecular identification of clusters within the species Zanthoxylumnitidum (Rutaceae) in China.

**Qin Y, Hu R, Zhao H, Wei G, Lu Z, Huang Y.**
12-05-2022
*PhytoKeys.*
https://pubmed.ncbi.nlm.nih.gov/36762030/

## Assessing knowledge and awareness regarding snakebite and management of snakebite envenoming in healthcare workers and the general population: A systematic review and meta-analysis.

**Afroz A, Siddiquea BN, Shetty AN, Jackson TNW, Watt AD.**
09-02-2023
*PLoS Negl Trop Dis.*
https://pubmed.ncbi.nlm.nih.gov/36757933/

**Background:** Snakebite envenoming is a serious and life-threatening medical condition that predominantly affects people living in rural communities across Africa, Asia, and Latin America. As our climate changes, there is a growing concern that negative human-snake interactions will increase. Our ability to prevent and manage snakebite requires effective antivenoms as well as knowledge regarding the prevention and management of snakebite among healthcare workers and affected communities across the globe. This systematic review aims to assess existing levels of knowledge regarding snakebite prevention and management in both healthcare workers and affected communities. **Methods:** This review was conducted on studies reporting quantitative measurements to evaluate knowledge and practice regarding snakebite prevention and management published in major databases between 1 January 2000 and 31 December 2021. Random effects modelling was used to obtain the pooled proportion. Heterogeneity (I2) was tested, and sensitivity analyses performed. **Results:** Out of 3,697 records, 16 studies from 12 countries assessing 7,640 participants were included. Four of the studies were ranked as good quality studies, 9 as fair, and 3 as poor. This study results demonstrated that 56% of the study population answered the knowledge question correctly (95% CI 48% to 63%, p < 0.001). High heterogeneity was observed (I2 = 97.29%), with marginal publication bias (Egger's regression test, p = 0.0814). Participants had relatively higher knowledge concerning use of antivenom as preferred treatment, followed by snakebite prevention, knowledge of signs and symptoms of snakebite, knowledge of first-aid, and knowledge of treatment. Participants had lower knowledge relating to types of snakes and the identification of snakes. **Conclusion:** Adequate knowledge about snakebites and its management among the general population and healthcare workers was 56%. Healthcare workers and communities across Asia showed higher relative knowledge compared to those in Africa and the Middle East. These data suggest that further education is needed in both the general population and among healthcare workers to ensure that appropriate preventative and patient management techniques are being utilised in snakebite endemic regions. Greater local awareness of the risks and appropriate management of snakebite is required to reduce the burden of snakebite mortality and morbidity.

## Epidemiology of snakebites in Colombia (2008-2016).

**León-Núñez LJ, Camero-Ramos G, Gutiérrez JM.**
Feb-2023
*Rev Salud Publica (Bogota).*
https://pubmed.ncbi.nlm.nih.gov/36753152/