

1. DENGUE: MARY ELIZABETH WILSON, MD***Clinical***

*Sabino EC, Loureiro P, Lopes ME, et al. Transfusion-transmitted dengue and associated clinical symptoms during the 2012 epidemic in Brazil. *J Infect Dis* 2016;213:694-702. Also editorial comment by Levi JID 2016;213:689-90.

During an epidemic in Brazil of DENV-4, >0.5% of blood donations were dengue-RNA positive. Approximately 1/3 of components led to transfusion transmission.

*Whitehorn J, Nguyen CVV, Khanh LP, et al. Lovastatin for the treatment of adult patients with dengue: a randomized, double-blind, placebo-controlled trial. *Clin Infect Dis* 2016;62(4):468-76.

Lovastatin was safe and well tolerated in adults with dengue. It showed no evidence of benefit in patients with acute dengue.

Co-Infections: Dengue, Chikungunya, Zika; Immune Enhancement

*Dejnirattisai W, et al. Dengue virus sero-cross-reactivity drives antibody-dependent enhancement of infection with Zika virus. *Nature Immunology*. Published online 23 June 2016.

Plasma immune to DENV cross reacted to ZIKV; able to drive antibody-dependent enhancement (ADE) of Zika infection.

*Priyamvada L, et al. Human antibody responses after dengue virus infection are highly cross-reactive to Zika virus. *PNAS* 2016;113(28):7852-7857.

Extensive cross reactivity. Preexisting immunity to DENV may affect immune response to Zika; may influence Zika virulence and disease activity in DENV-experienced populations.

*Waggoner JJ, et al. Viremia and clinical presentation in Nicaraguan patients infected with Zika virus, chikungunya virus, and dengue virus. *Clin Infect Dis* 2016;Published online Oct 20, 2016.

Epidemiology

*Duong V, Lambrechts L, Paul Rd, et al. Asymptomatic humans transmit dengue virus to mosquitoes. *PNAS* 2015;112:14688-14693.

Asymptomatic persons are infectious to mosquitoes. They may contribute significantly more to transmission than previously recognized.

*Waggoner JJ, Balmaseda A, Gresh L, et al. Homotypic dengue virus reinfections in Nicaraguan children. *J Infect Dis* 2016;214(7):986-993.

Virologically confirmed homotypic reinfections were documented as part of an ongoing pediatric cohort study in Nicaragua.

Vaccines and Their Use

*Durbin AP, Kirkpatrick BD, Pierce KK, et al. A 12-month-interval dosing study in adults indicates that a single dose of the National Institute of Allergy and Infectious Diseases tetravalent dengue vaccine induces a robust neutralizing antibody response. *J Infect Dis* 2016;214:832-835.

First vaccine dose elicited sterilizing immunity to all four serotypes for at least one year.

*Ferguson NM, Rodriguez-Barraquer I, Dorigatti I, et al. Benefits and risk of the Sanofi-Pasteur dengue vaccine: modeling optimal deployment. *Science* 2016;353:1033-36.

Authors hypothesize that live attenuated vaccine acts like silent natural infection. Vaccine effectiveness depends on age group and intensity of local transmission. In low transmission areas vaccination may increase incidence of more severe infections. Risk of hospitalization is increased in individuals vaccinated when seronegative. In high transmission settings, vaccination would benefit whole population.

*Hadinegoro SR, Arredondo-Garcia JL, Capeding MR, et al. Efficacy and long-term safety of a dengue vaccine in regions of endemic disease. *N Engl J Med* 2015;373(13):1195-206.

Long-term follow up interim analyses are provided for >35,000 children from Asia-Pacific and Latin American countries. Higher incidence of hospitalization in year 3 among children <9 years. Pooled efficacy for symptomatic dengue during 25 months were 65.6% for those 9 years and older; 44.6% among those <9 years.

*Kirkpatrick BD, Whitehead SS, Pierce KK, et al. The live attenuated dengue vaccine TV003 elicits complete protection against dengue in a human challenge model. *ScienceTranslationalMed* 2016;8(330-336).

In randomized double-blind, placebo-controlled trial, recipients of TV003 and placebo were challenged 6 months later with a DENV-2 strain. Vaccine gave complete protection against infection.

*Olivera-Botello G, Coudeville L, Fanouillere K, et al. Tetravalent dengue vaccine reduces symptomatic and asymptomatic dengue virus infections in healthy children and adolescents aged 2-16 years in Asia and Latin America. *J Infect Dis* 2016;214:994-1000.

Annual incidence of symptomatic dengue was 3.4%; annual incidence of asymptomatic dengue was 14.8%. Vaccine had efficacy of 33.5% against asymptomatic infection.

*WHO. Weekly Epidemiological Record. Dengue vaccine: WHO position paper – July 2016. 2016;91(30):349-364. Background material presented. Comparative modelling of dengue vaccine public health impact (CMDVI) March 2016

http://www.who.int/immunization/sage/meetings/2016/april/2_CMDVI_Report_FINAL.pdf

This paper and supporting models lay out the rational for recommending introducing the licensed vaccine, Dengvaxia (Sanofi Pasteur) only in regions with high endemicity (seroprevalence 70% or higher; not recommended when seroprevalence is <50% in age group targeted for vaccine). Recommended for use in those 9 years and older.

Vectors and Their Control

*Achee NL, Gould F, Perkins TA, et al. A critical assessment of vector control for dengue prevention. *PLoS NTD*. 2015;9(5). May 2015.

The Partnership for Dengue Control believes that no single intervention will be sufficient to control dengue disease and support the concept of integrated intervention. Vector control will continue to need vector control even with effective dengue vaccine.

*Bowman LR, Donegan S, McCall PJ. Is dengue vector control deficient in effectiveness or evidence? Systematic review and meta-analysis. *PLoS NTD*. 2015;10(3): e0004551

Remarkable paucity of reliable evidence for the effectiveness of any dengue vector control method.

Burden and Economic

*L’Azou, Moureau A, Sarti E, et al. Symptomatic dengue in children in 10 Asian and Latin American countries. *N Engl J Med* 2016;374:1155-1166.

Documents burdens from dengue in children in 10 Asian and Latin American countries. Approximately 10% of febrile episodes were virologically confirmed dengue. Rates were generally higher and disease more severe in Asian than in Latin American countries.

Stanaway JD, Shepard DS, Undurraga EA, et al. The global burden of dengue: an analysis from the Global Burden of Disease Study 2013. *Lancet Infect Dis* 2016. Published online Feb 10, 2016.

Authors provide best estimates of mortality and incidence. Number of cases has more than doubled every decade.

2. LEISHMANIASIS: ANDREA BOGGILD, MSC, MD, DTMH, FRCPC

Epidemiology

Schaut RG, Robles-Murguía M, Juelsgaard R, Esch KJ, Bartholomay LC, Ramalho-Ortigao M, Petersen CA. Vectorborne Transmission of Leishmania infantum from Hounds, United States. *Emerg Infect Dis*. 2015 Dec;21(12):2209-12. doi: 10.3201/eid2112.141167.

Elmahallawy EK, Cuadros-Moronta E, Liébana-Martos MC, Rodríguez-Granger JM, Sampedro-Martínez A, Agil A, Navarro-Mari JM, Bravo-Soto J, Gutierrez-Fernández J. Seroprevalence of Leishmania infection among asymptomatic renal transplant recipients from southern Spain. *Transpl Infect Dis*. 2015 Dec;17(6):795-9. doi: 10.1111/tid.12444.

World Health Organization. Leishmaniasis in high-burden countries: an epidemiological update based on data reported in 2014. *Wkly Epidemiol Rec*. 2016 Jun 3;91(22):287-96.

Okwor I, Uzonna J. Social and Economic Burden of Human Leishmaniasis. *Am J Trop Med Hyg*. 2016 Mar;94(3):489-93. doi: 10.4269/ajtmh.15-0408. [REVIEW]

Stamm LV. Human Migration and Leishmaniasis-On the Move. *JAMA Dermatol*. 2016 Apr;152(4):373-4. doi: 10.1001/jamadermatol.2015.4765. [REVIEW]

Ramdas S, van der Geest S, Schallig HD. Nuancing stigma through ethnography: the case of cutaneous leishmaniasis in Suriname. *Soc Sci Med*. 2016 Feb;151:139-46. doi: 10.1016/j.socscimed.2015.12.044.

Harkins KM, Schwartz RS, Cartwright RA, Stone AC. Phylogenomic reconstruction supports supercontinent origins for Leishmania. *Infect Genet Evol*. 2016 Mar;38:101-9. doi: 10.1016/j.meegid.2015.11.030.

Pathogenesis

França-Costa J, Andrade BB, Khouri R, Van Weyenbergh J, Malta-Santos H, da Silva Santos C, Brodyskn CI, Costa JM, Barral A, Bozza PT, Boaventura V, Borges VM. Differential Expression of the Eicosanoid Pathway in Patients With Localized or Mucosal Cutaneous Leishmaniasis. *J Infect Dis*. 2016 Apr 1;213(7):1143-7. doi: 10.1093/infdis/jiv548.

Carneiro PP, Conceição J, Macedo M, Magalhães V, Carvalho EM, Bacellar O. The Role of Nitric Oxide and Reactive Oxygen Species in the Killing of Leishmania braziliensis by Monocytes from Patients with Cutaneous Leishmaniasis. *PLoS One*. 2016 Feb 3;11(2):e0148084. doi: 10.1371/journal.pone.0148084.

Carlsen ED, Liang Y, Shelite TR, Walker DH, Melby PC, Soong L. Permissive and protective roles for neutrophils in leishmaniasis. *Clin Exp Immunol*. 2015 Nov;182(2):109-18. doi: 10.1111/cei.12674. [REVIEW]

Bifeld E, Clos J. The genetics of Leishmania virulence. *Med Microbiol Immunol*. 2015 Dec;204(6):619-34. doi: 10.1007/s00430-015-0422-1. [REVIEW]

Fernández-Figueroa EA, Imaz-Rosshandler I, Castillo-Fernández JE, Miranda-Ortiz H, Fernández-López JC, Becker I, Rangel-Escareño C. Down-Regulation of TLR and JAK/STAT Pathway Genes Is Associated with Diffuse Cutaneous Leishmaniasis: A Gene Expression Analysis in NK Cells from Patients Infected with Leishmania mexicana. *PLoS Negl*

Trop Dis. 2016 Mar 31;10(3):e0004570. doi: 10.1371/journal.pntd.0004570. Erratum in: PLoS Negl Trop Dis. 2016 Apr;10(4):e0004666.

Clinical Features and Course

Azeredo-Coutinho RB, Pimentel MI, Zanini GM, Madeira MF, Cataldo JI, Schubach AO, Quintella LP, de Mello CX, Mendonça SC. Intestinal helminth coinfection is associated with mucosal lesions and poor response to therapy in American tegumentary leishmaniasis. *Acta Trop.* 2016 Feb;154:42-9. doi: 10.1016/j.actatropica.2015.10.015.

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Jimenez-Marco T, Fisa R, Girona-Llobera E, Cancino-Faure B, Tomás-Pérez M, Berenguer D, Guillen C, Pujol A, Iniesta L, Serra T, Mascaró M, Gascó J, Riera C. Transfusion-transmitted leishmaniasis: a practical review. *Transfusion.* 2016 Mar;56 Suppl 1:S45-51. doi: 10.1111/trf.13344. [REVIEW]

Diagnosis

Medley GF, Hollingsworth TD, Olliaro PL, Adams ER. Health-seeking behaviour, diagnostics and transmission dynamics in the control of visceral leishmaniasis in the Indian subcontinent. *Nature.* 2015 Dec 3;528(7580):S102-8. doi: 10.1038/nature16042.

Handler MZ, Patel PA, Kapila R, Al-Qubati Y, Schwartz RA. Cutaneous and mucocutaneous leishmaniasis: Differential diagnosis, diagnosis, histopathology, and management. *J Am Acad Dermatol.* 2015 Dec;73(6):911-26; 927-8. doi: 10.1016/j.jaad.2014.09.014. [REVIEW]

Saldarriaga OA, Castellanos-Gonzalez A, Porrozzi R, Baldeviano GC, Lescano AG, de Los Santos MB, Fernandez OL, Saravia NG, Costa E, Melby PC, Travi BL. An Innovative Field-Applicable Molecular Test to Diagnose Cutaneous Leishmania Viannia spp. *Infections.* *PLoS Negl Trop Dis.* 2016 Apr 26;10(4):e0004638. doi: 10.1371/journal.pntd.0004638.

Siriyasatien P, Chusri S, Kraivichian K, Jariyapan N, Hortiwakul T, Silpapojakul K, Pym AM, Phumee A. Early detection of novel Leishmania species DNA in the saliva of two HIV-infected patients. *BMC Infect Dis.* 2016 Feb 24;16:89. doi: 10.1186/s12879-016-1433-2.

Zampieri RA, Laranjeira-Silva MF, Muxel SM, Stocco de Lima AC, Shaw JJ, Floeter-Winter LM. High Resolution Melting Analysis Targeting hsp70 as a Fast and Efficient Method for the Discrimination of Leishmania Species. *PLoS Negl Trop Dis.* 2016 Feb 29;10(2):e0004485. doi: 10.1371/journal.pntd.0004485.

Treatment and Management

de O Prates FV, Dourado MEF, Silva SC, Schrieffer A, Guimaraes LH, das Gracias O Brito M, Almeida J, Carvalho EM, Machado PRL. Fluconazole in the Treatment of Cutaneous Leishmaniasis Caused by Leishmania braziliensis: A Randomized Controlled Trial. *Clin Infect Dis.* (2016) doi: 10.1093/cid/ciw662.

Cota GF, de Sousa MR, Fereguetti TO, Saleme PS, Alvarisa TK, Rabello A. The Cure Rate after Placebo or No Therapy in American Cutaneous Leishmaniasis: A Systematic Review and Meta-Analysis. *PLoS One.* 2016 Feb 19;11(2):e0149697. doi: 10.1371/journal.pone.0149697.

van Griensven J, Gadisa E, Aseffa A, Hailu A, Beshah AM, Diro E. Treatment of Cutaneous Leishmaniasis Caused by *Leishmania aethiopica*: A Systematic Review. PLoS Negl Trop Dis. 2016 Mar 3;10(3):e0004495. doi: 10.1371/journal.pntd.0004495.

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Prevention / Vaccine Development

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Higa LH, Arnal L, Vermeulen M, Perez AP, Schilrreff P, Mundiña-Weilenmann C, Yantorno O, Vela ME, Morilla MJ, Romero EL. Ultradeformable Archaeosomes for Needle Free Nanovaccination with Leishmania braziliensis Antigens. PLoS One. 2016 Mar 2;11(3):e0150185. doi: 10.1371/journal.pone.0150185.

3. ZIKA: SUSAN HILLS, MBBS, MTH

General Reviews

Petersen LR, Jamieson DJ, Powers AM, et al. Zika virus. *N Engl J Med* 2016; 374:1552-1563.

Musso D, Gubler DJ. Zika virus. *Clin Microbiol Rev* 2016; 29:487-524.

Specific Clinical Presentations

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Furtado JM, Espósito DL, Klein TM, et al. Uveitis associated with Zika virus infection. *N Engl J Med* 2016; 375:394-396.

New Transmission Scenarios

Deckard DT, Chung WM, Brooks JT, et al. Male-to-male sexual transmission of Zika virus--Texas, January 2016. *MMWR Morb Mortal Wkly Rep* 2016; 65:372-374.

Brooks RB, Carlos MP, Myers RA, et al. Likely sexual transmission of Zika virus from a man with no symptoms of infection - Maryland, 2016. *MMWR Morb Mortal Wkly Rep* 2016; 65:915-916

Davidson A, Slavinski S, Komoto K, et al. Suspected female-to-male sexual transmission of Zika virus - New York City, 2016. *MMWR Morb Mortal Wkly Rep* 2016. 65:716-717.

Barjas-Castro ML, Angerami RN, Cunha MS, et al. Probable transfusion-transmitted Zika virus in Brazil. *Transfusion* 2016; 56:1684-1688.

Congenital Infection

Moore CA, Staples JE, Dobyns WB et al. Characterizing the pattern of anomalies in congenital Zika syndrome for pediatric clinicians. *JAMA Pediatr*. Published online November 3, 2016

Johansson MA, Mier-y-Teran-Romero L, Reefhuis J, et al. Zika and the risk of microcephaly. *N Engl J Med* 2016; 375:1-4.

Melo AS, Aguiar RS, Amorim MM, et al. Congenital Zika virus infection: Beyond neonatal microcephaly. *JAMA Neurol* 2016; Published online October 3, 2016

Management and guidelines

Oduyebo T, Igbinsola I, Petersen EE, et al. Update: Interim guidance for health care providers caring for pregnant women with possible Zika virus exposure - United States, July 2016. *MMWR Morb Mortal Wkly Rep* 2016; 65:739-744

Petersen EE, Meaney-Delman D, Neblett-Fanfair R, et al. Update: Interim guidance for preconception counseling and prevention of sexual transmission of Zika virus for persons with possible Zika virus exposure - United States, September 2016. *MMWR Morb Mortal Wkly Rep* 2016; 65:1077-1081.

Russell K, Oliver SE, Lewis L, et al. Update: Interim guidance for the evaluation and management of infants with possible congenital Zika virus infection - United States, August 2016. *MMWR Morb Mortal Wkly Rep* 2016; 65:870-878.

Rabe IB, Staples JE, Villanueva J, et al. Interim Guidance for interpretation of Zika virus antibody test results. *MMWR Morb Mortal Wkly Rep* 2016; 65:543-546.

Vaccine Development

Lipstich M, Cowling BJ. Zika vaccine trials. *Science* 2016; 353:1094-1095

Dowd KA, Ko SY, Morabito KM, et al. Rapid development of a DNA vaccine for Zika virus. *Science* 2016; 354:237-240.

Abbink P, Larocca RA, De La Barrera RA, et al. Protective efficacy of multiple vaccine platforms against Zika virus challenge in rhesus monkeys. *Science* 2016; 353:1129-1132.

4. MALARIA: JOHANNA P. DAILY, MD

Epidemiology

US Malaria Surveillance

Malaria Surveillance — United States, 2013. Cullen KA, Mace KE, Arguin PM. *MMWR Surveill Summ* 2016;65(No. SS-2):1–22. *Increasing prevalence of malaria in US. Clinical details of fatalities described.*

Worldwide Artemisinin Resistance

A Worldwide Map of Plasmodium falciparum K13-Propeller Polymorphisms. Menard D et al. *N Engl J Med*. 2016 Jun 23;374(25):2453-64. *Artemisinin resistance limited to South East Asia and China for now.*

***Plasmodium falciparum* Mortality in Africa**

Mapping *Plasmodium falciparum* Mortality in Africa between 1990 and 2015. Gething et al. *N Engl J Med*. 2016 Oct 10. *Decrease in mortality from malaria in sub-Saharan Africa of 57% over past 15 years. Countries with high mortality are associated with low coverage of antimalarial treatment and prevention programs.*

Malaria vaccine (RTS,S/AS01) efficacy at seven years.

Seven-Year Efficacy of RTS,S/AS01 Malaria Vaccine among Young African Children. Olotu et al. *N Engl J Med* 2016;374:2519-29. *Vaccine efficacy wanes over time, and a rebound effect occurs in high transmission regions.*

Antimalarial treatment during Ebola is associated with differences in mortality

Effect of Artesunate–Amodiaquine on Mortality Related to Ebola Virus Disease. Gignoux et al, *N Engl J Med* 2016;374:23-32. *Malaria treatment regimens were associated with differential Ebola mortality.*

Malaria: Ebola interaction

Plasmodium Parasitemia Associated With Increased Survival in Ebola Virus–Infected Patients **Clinical Infectious Diseases** 2016;63(8):1026–33. Rosenke K et al. *Patients PCR positive for malaria had increased survival during Ebola.*

Clinical Management

Effectiveness of twice a week prophylaxis with atovaquone–proguanil (MalaroneVR) in long-term travellers to West Africa **Journal of Travel Medicine**. 2016, 1-5. *Is atovaquone-proguanil 2x a week sufficient anti-malarial prophylaxis? This observational study presents insufficient evidence for this approach.*

Treatment of *Plasmodium knowlesi* Malaria

The Treatment of *Plasmodium knowlesi* Malaria. Barber BE, Grigg MJ, William T, Yeo TW, Anstey NM. **Trends Parasitol**. 2016 Oct 1. pii: S1471-4922(16)30158-1. *Review by experts in the field.*

Diagnosis and Treatment of *Plasmodium vivax*

Diagnosis and Treatment of *Plasmodium vivax* Malaria Baird JK, Valecha N, Duparc S, White NJ, Price RN. **Am J Trop Med Hyg**. 2016 Oct 5. pii: 16-0171. *Thorough review of the topic by experts in the field.*

Malaria and Pregnancy

Four Artemisinin-Based Treatments in African Pregnant Women with Malaria. PREGACT Study Group, et al. **N Engl J Med**. 2016 Mar 10;374(10):913-27. *Artemether–lumefantrine was associated with the fewest adverse effects and with acceptable cure rates but provided the shortest post-treatment prophylaxis, whereas dihydroartemisinin–piperaquine had the best efficacy and an acceptable safety profile. Drug-related adverse events such as asthenia, poor appetite, dizziness, nausea, and vomiting occurred significantly more frequently in the mefloquine–artesunate group (50.6%) and the amodiaquine– artesunate group (48.5%) than in the dihydroartemisinin–piperaquine group (20.6%) and the artemether–lumefantrine group (11.5%) ($P<0.001$ for comparison among the four groups).*

Lumbar puncture safety during cerebral malaria

Safety of lumbar puncture in comatose children with clinical features of cerebral malaria. Moxon CA, Zhao L, Li C, Seydel KB, MacCormick IJ, Diggle PJ, Mallewa M, Solomon T, Beare NA, Glover SJ, Harding SP, Lewallen S, Kampondeni S, Potchen MJ, Taylor TE, Postels DG. **Neurology**. 2016 Oct 28. *Lumbar punctures did not change the risk of mortality in children with severe brain swelling on MRI or in those with papilledema.*