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, wt 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. Preexiting 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, chikungunua 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. ScienceTransationalMed 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-Murguia 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.

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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.

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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]

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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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Diagnosis

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Treatment and Management

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3. ZIKA: SUSAN HILLS, MBBS, MTH

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Vaccine Development

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<u>4. MALARIA: JOHANNA P. DAILY, MD</u>

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.*

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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 regiments 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.*

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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*.