the whitewater facility during the site visit. All 11 water-related samples taken from the facility were positive for N. fowleri. Of 5 samples taken from the natural river, 1 sediment sample was positive for N. fowleri.

Conclusion. This investigation documents a novel exposure to an artificial white-water river as the likely exposure causing PAM in this case. Conditions in the whitewater facility (warm, turbid water with little chlorine and heavy algal growth) rendered the water treatment ineffective and provided an ideal environment for N. fowleri to thrive. The combination of natural and engineered elements at the whitewater facility create a challenging environment to control the growth of N. fowleri.

Disclosures. All authors: No reported disclosures.

1018. Lyme Disease in Hispanics in Long Island, New York: A New Health Disparity in the U.S.
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Background. Lyme disease (LD) is the most commonly reported vector-borne illness in the U.S. A risk factor for acquiring LD is the exposure to outdoors. In Long Island, Hispanics comprise a large share of the outdoor occupational workforce.

Methods. A retrospective chart review was performed in all patients with ICD-9 or ICD-10 diagnostic codes for LD between 2011–2016 in SHH and 2010–2015 in SBHU. Cases were defined as a confirmed or presumed case of LD. Laboratory testing comprised serology, mononuclear cell cytotoxicity (lymphocytotoxicity) test and IFNα. CSF levels of anti-INFα may impair natural killer, T-cell and neuronal antiviral activity. Disruption of T-cell mediated immunity due to anti-IFNα could cause an adult-onset immunocompromised state with severe VZV reactivation. The association of high-titer neutralizing antibodies to IFNα in an adult with CNS VZV is novel and may be clinically relevant.

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1020. Development of a Novel Anthrax Vaccine Comprising LP-PA Chimera
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Background. Bacillus anthracis (BA), the etiological agent of anthrax, secretes protective antigen (PA), lethal factor (LF), and edema factor (EF) as major virulence factors. Among them, PA based vaccines are most indispensable for providing immunity against BA, but the low shelf life limits its reliability. Previous studies revealed that PA domain IV includes B-cell epitopes designated as ID 1, ID II, and ID III; among them, ID I and ID II have been found to possess more toxin neutralization activity and produce high antibody titre. Moreover, N-terminal region of both LF and EF acts as binding site of PA which are homologous to each other. Here, in this study we have developed and evaluated the vaccine efficacy of chimeric vaccine containing ID II-ID III region of PA and N-terminal region of LF and EF (ID-LFn).

Materials and Methods. ID-LFn was generated by overlapping PCR followed by cloning in pET28a. The recombinant protein was then expressed and purified by Ni-NTA chromatography. Reactivity of ID-LFn with anti-PA/LF/EF antibodies was checked by ELISA. Stability was assessed using Circular Dichroism Spectroscopy. The vaccine potential of ID-LFn was evaluated by toxin neutralization assay, lymphocyte proliferation assay, and cytokine analysis. The protection efficacy was analyzed by challenge studies in mice.

Results. ID-LFn was found to be significantly stable as compared with protective antigen. Anti-ID-LFn antibodies recognized PA, LF and EF. Though, the total antibody titre, toxin neutralization activity was found to be less than PA but surprisingly, the protection efficacy of ID-LFn was found similar as PA.

Conclusion. The ID-LFn vaccine might be second next generation vaccine showing equal protection but higher shelf life as PA with the capability of neutralizing PA, LF as well as EF at the same time. Thus, it may prove an efficient and reliable treatment strategy against anthrax.

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1019. Varicella-zoster virus Neurovasculitis (VZV-NV) in the Setting of Autotubodies to Interferon alpha (anti-IFNα)
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Background. VZV-NV resulting in CNS damage is rare in immunocompetent hosts, however, it is a major challenge in patients acquiring VZV and T-cell mediated immunity shields against reactivation of the latent virus. Individuals who are immunocompromised due to T-cell mediated defects can present with systemic VZV.

Methods. Case report of a previously healthy man who developed VZV-NV associated with autotubodies to IFNα.

Results. A previously healthy 64 year-old man developed an acute T3 Brown-Sequard syndrome. Symptoms progressed to include bilateral lower extremity weakness, piosis, ophthalmoalgia, and encephalopathy. Magnetic resonance imaging (MRI) showed diffuse T2 hyperintensities with enhancement throughout the spine and brain, including enhancement of his meninges, roots, and cranial nerves. Successive cerebrospinal fluid (CSF) studies revealed increasing B-cell lymphocytosis, (maximum 661 cells/ml), and CSF protein (maximum 242 mg/dL). CSF PCR was positive for VZV and IgM antibodies. Further testing showed anti-IFNα autoantibodies in the plasma and CSF. Serum anti-IFNα fluorescence intensity was 30 times normal, and his plasma blocked IFNα-induced STAT-1 phosphorylation in normal monocytes. Treatment with acyclovir and methylprednisolone resulted in improve- ment. Repeat LP following treatment revealed 32 WBC/mcl with normal protein. Follow-up MRI did not show any new lesions. Three years after initial presentation, he continues to be stable without clinical relapses, or subclinical changes on MRI. Serum studies were positive for VZV IgG and negative for IgM. CSF PCR was positive for VZV. Lastly, serum anti-IFNα fluorescence intensity remained 25 times normal, and his plasma continued to block IFNα-induced STAT-1 phosphorylation in normal monocytes.

Conclusion. This is the first identified case of CNS VZV-NV in the setting of binding and blocking autotubodies to IFNα in the serum and CSF. Elevated serum and CSF levels of anti-IFNα may impair natural killer, T-cell and neuronal antiviral activity. Disruption of T-cell mediated immunity due to anti-IFNα could cause an adult-onset immunocompromised state with severe VZV reactivation. The association of high-titer neutralizing antibodies to IFNα in a patient with CNS VZV is novel and may be clinically relevant.

Disclosures. All authors: No reported disclosures.

1021. Phase 1 Clinical Trial of a Replication-Defective Human Cytomegalovirus (CMV) Vaccine
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Background. Congenital CMV remains an unmet medical need worldwide. Naturally acquired CMV immunity in women prior to pregnancy has been shown to offer protection against vertical CMV transmission. V160 is a replication-defective CMV, and its replication in culture is controlled by a synthetic chemical. V160 can't replicate in humans but it maintains all virological properties for presenta tion-defective CMV, and its replication in culture is controlled by a synthetic chemical.

Methods. Approximately 190 CMV seronegative and seropositive adults at study entry received 3 doses of V160 or placebo administered via intramuscular (IM) or intradermal (ID) route on Day 1, Month 1, and Month 6. Four antigen levels (10, 30, 100, and 250 units per dose) formulated with or without aluminum adjuvant were evaluated. In each vaccination group, approximately 10 and 4 subjects received study vaccine and placebo, respectively. Injection site and systemic adverse events (AEs) were collected for 14 days after each vaccination. For potential neutralizing antibodies (NABs).

Results. At study entry received 3 doses of V160 or placebo administered via intramuscular (IM) or intradermal (ID) route on Day 1, Month 1, and Month 6. Four antigen levels (10, 30, 100, and 250 units per dose) formulated with or without aluminum phosphate adjuvant were evaluated. In each vaccination group, approximately 10 and 4 subjects received study vaccine and placebo, respectively. Injection site and systemic adverse events (AEs) were collected for 14 days after each vaccination. For potential neutralizing antibodies (NABs).

Conclusion. During the study, no serious AEs were reported and only one CMV seropositive subject had non-sero-type virus shedding. In both seronegative and
1022. Establishing Models of Herpes Simplex Virus Type 2 Superinfection of Herpes Simplex Virus Type 1 Seropositive Mice to Test The Efficacy of a Novel Vaccine

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Background. Multiple subunit vaccines that elicit neutralizing antibodies (nAbs) against the immunodominant HSV-2 glycoproteins D and/or B (gD and gB) were advanced into the clinic after demonstrating protection against disease in animal models. However, although the vaccines elicited nAbs in seronegative and boosted nAbs titers against gD-1 seropositive (HSV-1 +1) participants, prevented HSV-2 infection, suggesting that nAbs alone are not sufficient. The results also indicate that current animal models are not predictive of clinical trial outcomes. We recently engineered a candidate single cycle vaccine strain deleted in gD (AgD-2) and showed that it elicited high titer non-neutralizing Abs that provide complete protection against HSV-1 or HSV-2. The Abs passively protect naïve mice and activate the Fc receptor to induce antibody-dependent cell mediated cytotoxicity (ADCC). We hypothesize that AgD-2 will protect HSV-1 +1 individuals from HSV-2 because it elicits a different type of immune response. To test this hypothesis, we established a model of HSV-2 superinfection in HSV-1 +1 mice.

Methods. We infected mice by corneal scarification with serial dilutions of a clinical strain of HSV-1 (Bx 1.1) to identify a sublethal dose associated with serumconversion. We then superinfected mice on the skin with HSV-2 and monitored for disease. The presence of virus in doral root ganglia (DRG), the site of HSV latency, was determined by quantitative PCR.

Results. Corneal infection with 10-4 PFU of HSV-1 resulted in disease in 18/29 (62%) mice and 13/18 survived. Serumconversion was documented in 9/13 survivors. Survivors were superinfected 2 weeks post-recovery with HSV-2. All of the mice developed signs of disease, but only 2/9 who were HSV-1 +1 died compared with 4/4 seronegative mice (P = 0.02, Fisher exact test). HSV-2 DNA was detected in the DRG of 12/13 mice.

Conclusion. Sublethal HSV-1 corneal disease provides partial protection against HSV-2 superinfection and provides a model to test vaccine efficacy. We speculate that superinfection boosts preexisting nAb titters, a response consistent with immune repertoire freeze, but that AgD-2, because it elicits ADCC Abs, will overcome repertoire freeze and provide greater protection against HSV-2 superinfection.

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1023. Sustained Lesion and Shedding Rate Reductions in Genital Herpes Patients 24 Months after Immunization with GEN-003, a Genital Herpes Immunotherapeutic

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Background. Herpes simplex viruses (HSV) are the main cause of genital ulcers worldwide. GEN-003 is an investigational genital herpes immunotherapy composed of HSV-2 antigens gD2DM and tCP4.2, and the saponin-based adjuvant MatriX-M (MM2). In a Phase 2 dose-ranging study (GEN-003-002), 3 doses of GEN-003 reduced HSV-2 lesion rate (percent of days with genital lesions) and anogenital HSV-2 shedding rate (percent of days with detectable virus). The antiviral effect of GEN-003 persisted to 12 months after the 3-dose vaccination regimen. We report here the results of an expansion study to evaluate efficacy and immunogenicity of GEN-003 post 24 months post-vaccination.

Methods. GEN-003-002 subjects who received at least 1 dose of GEN-003 (dose groups: 30 or 60 µg of antigens combined with 25, 50 or 75 µg of MM2) were eligible to enroll in the extension study. At 24 months post-vaccination, anogenital swabs were collected twice daily for 28 days for HSV-2 DNA detection by quantitative PCR. During this period, subjects also reported genital herpes lesion data via a daily reporting tool. Blood samples were collected at the end of the swab collection period to evaluate humoral and cellular immune responses. HSV-2 immunoglobulin G (IgG) was measured by ELISA, and HSV-2 neutralizing antibodies were measured by a colormetric assay. Cellular responses were evaluated in peripheral blood mononuclear cells using an interferon-γ/gramyze B Fluorospot assay.

Results. 140 subjects were enrolled. At 24 months, those in the two best-performing groups (N = 100-102) had anogenital lesions combined with either 50 or 75 µg MM2 (60/50 and 60/75, respectively), recorded decreased mean viral shedding rates of 58% and 69% below baseline, similar to the 12-month shedding rate reductions, and mean anogenital lesion rates of 77% and 59% below baseline, respectively (Fig 1). In all dose groups, mean IgG titters to ICP4.2 and gD2TMR were sustained from 12 to 24 months. Similarly, mean neutralizing antibody titters did not change significantly from month 12 to 24.

Conclusion. GEN-003 induces reductions in HSV-2 shedding and genital herpes lesion rates that persist to 24 months following treatment. Humoral immune responses to GEN-003 are maintained at 24 months after immunization.

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1024. Estimating the Health and Economic Impact of Universal Varicella Vaccination in Jordan

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Background. To evaluate the impact of adding universal varicella vaccination (UVV) to the existing childhood vaccination programme in Jordan, and identify the most cost-effective strategy.

Methods. A dynamic transmission model of varicella infection was calibrated to available varicella seroprevalence data within the region and validated against local epidemiological data. Local direct and indirect costs and healthcare utilisation data were used. We considered the health and economic impact of one dose UVV administered concurrently with MMR at 12 months of age with 95% coverage, and two dose strategies with short (6 months) and long (4 years) intervals between First and Second dose. We took the societal perspective (direct and indirect costs) and discounted costs and QALYs by 3%/year to assess cost-effectiveness.

Results. The model estimated the current burden of varicella at 172,000 cases/year, an incidence rate of 2.200/100,000 persons. In the 5th-25th year after vaccination, all strategies substantially reduced total varicella incidence by 89.5%/96.6% (1 dose), 92.3%/98.0% (2 dose short), and 90.5%/98.3% (2 dose long), compared with no vaccination (Figure 1). In the absence of vaccination, an estimated $47.89 M ($28.81 M direct, $19.08 indirect) was spent annually on varicella treatment. The average annual total treatment costs over 25 years from the societal perspective were $4.01M (1 dose), $3.14M (2 dose short), and $3.13M (2 dose long). Considering a willingness to pay (WTP) threshold of $3,600 USD / QALY and the societal perspective, the 1 dose program was the most cost-effective with cost savings of $83.40 USD and health gain of 4.127 x 10^-3 QALYs per person. 2 dose programs are similarly cost-saving and highly effective compared with a scenario of no vaccination however, moving incrementally from a 1 dose strategy, incremental cost-effectiveness ratios (ICERS) were $6.9M/QALY (short vs. 1 dose) and $13.5M/QALY (long vs. short), both well as above the WTP threshold. All strategies reached.

Conclusion. One or two dose UVV in Jordan will significantly reduce varicella disease burden and is cost saving relative to no vaccine over 25 years.