

98a. Poster Session
Late Breaker Posters
Saturday, 12:30 p.m. – 2:00 p.m.
Hall E

LB-9 MDRD is Inferior to Adjusted Creatinine Clearance for Vancomycin Dosing in Elderly Patients

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Background: The Modification of Diet in Renal Disease equation (MDRD) is useful for monitoring renal disease progression, and GFR calculated by abbreviated MDRD (AMDRD) is reported with serum creatinine (Cr) in New Jersey. MDRD has not been validated or compared to Cr clearance from Cockcroft-Gault formula (CG CrCl) for medication dosing in elderly patients. We compared vancomycin (V) regimens derived from four methods of estimating renal function including MDRD, AMDRD, CG CrCl, and adjusted CG CrCl (ADJ CrCl) to optimized regimens determined from steady state V levels in patients over age 65. **Methods:** Hospitalized patients over 65 receiving V were monitored for appropriate dosing. We included only those with complete baseline data (age, sex, race, serum Cr, BUN, albumin, height, weight), stable renal function and V dose, and at least one steady state trough V level. Initial V regimens were optimized from steady state levels to achieve target troughs of 10–15 mcg/ml. This optimized level-based (LB) V dose was used to extrapolate each patient's LB CrCl range from the Moellering V dosing nomogram. Renal function was calculated by four different methods including MDRD, AMDRD, CG CrCl and ADJ CrCl and was then compared to LB CrCl range to see how well calculated CrCl matched LB CrCl. **Results:** From 5/05 to 6/06, 122 patients age ≥ 65 met criteria for inclusion in the analysis. The calculated ADJ CrCl matched the LB CrCl range for 84(69%) of patients. ADJ CrCl matched LB CrCl significantly more than other calculation methods: CG CrCl (34%), MDRD (26%), AMDRD (20%), $p < 0.05$. Renal function estimated by methods other than ADJ CrCl usually gave falsely elevated CrCl values. **Conclusion:** Estimates of renal function by AMDRD are readily available to clinicians, but only 20% of elderly patients would have had appropriate V dosing from AMDRD. MDRD, AMDRD, and CG CrCl were all significantly inferior to ADJ CrCl for predicting appropriate V dosing: most patients would have been overdosed using methods other than ADJ CrCl. MDRD and AMDRD should be used with caution for medication dosing adjustments in elderly patients.

LB-10 A Novel Compound (SXF-1) With Potent Antibacterial Activity And Low Propensity To Develop Resistance Against MRSA

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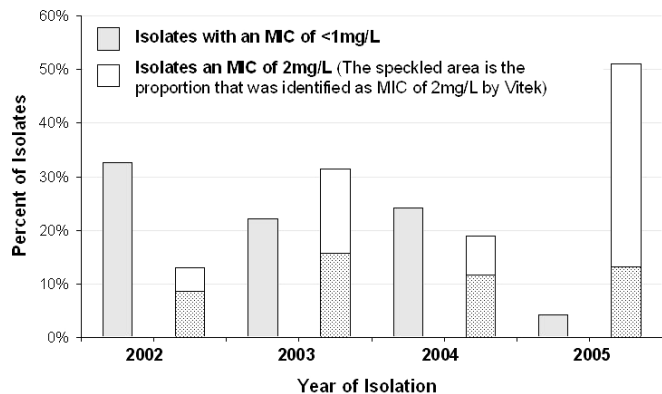
Background: New and novel compounds are needed to combat the continuous threat from MRSA. SXF-1 is a novel, porphyrin-based antibacterial compound with potent *in vitro* activity against *Staphylococcus aureus*, including the major MRSA clones circulating in hospitals (HA-MRSA) and community (CA-MRSA). Toxicological studies to support clinical evaluation of SXF-1 have been completed. In this study, we investigate the propensity of SXF-1 to cause mutational resistance, and determine the bactericidal activity and post antibiotic effect (PAE) of this compound. **Methods:** Minimum inhibitory and bactericidal concentrations (MIC and MBC respectively) were determined using a microdilution broth method (Clinical and Laboratory Standards Institute method). Five "Network on Antimicrobial Resistance in *Staphylococcus aureus*" (NARSA) strains were tested: NRS382, NRS383, NRS271, NRS123, NRS387. All 5 strains were passaged 50 \times at 0.5 \times MIC determined from the previous passage. Killing time (at 2, 4 & 8 \times MIC) and post antibiotic effect (PAE) (30 minutes exposure at 0.5, 1 & 2 \times MIC) were determined for NRS382 (HA-MRSA predominant US clone) and NRS123 (CA-MRSA with PVL). **Results:** Against all 5 strains, comparing the initial MIC value to that on completion of 50 passages showed no significant change in MIC. Killing time was 0.25 to 0.5 hours for both strains at 2–8 \times MIC. PAE ranged from 3.5 to 6 hours at 0.5–2 \times MIC. **Conclusion:** SXF-1 is a novel compound with strong *in vitro* and rapid bactericidal activity, a long PAE, and a low propensity for resistance development against major HA-MRSA and CA-MRSA clones. SXF-1 shows great potential for the treatment of MRSA infections and is an ideal candidate for clinical development.

LB-11 Trends in Vancomycin (vanco) Susceptibility (S) among Consecutive MRSA Bacteremia Isolates

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Background: Poor treatment outcomes to vanco were recently reported in patients with bacteremia due to MRSA with vanco MIC of 1–2 μ g/mL. Trends in vanco S among MRSA blood isolates have not been studied and the reliability of automated S testing in identifying isolates with an MIC of 2 μ g/mL

is uncertain. We examined trends in vanco S among consecutive MRSA blood isolates in a tertiary care hospital over 4 years. **Methods:** All 2002 through 2005 MRSA blood isolates were saved. Susceptibility was tested in duplicate using broth microdilution according to CLSI methodology. MICs were determined blinded as to isolation year. Comparison was made to automated systems (Vitek: to 2/2005, Vitek2: 3–12/2005). **Results:** All 223 initial and 40 subsequent isolates were tested. The MIC range was 0.125–2 μ g/mL. From 2002 to 2005, the geometric mean MIC, and the percentage of isolates with an MIC of >0.5 or 2 μ g/mL, increased from 0.9 to 1.4 μ g/mL, 67 to 96%, and 13 to 51%, respectively. Of those with an MIC of 2mg/L by broth, 44, 59, and 18% were identified as having such MIC by any Vitek systems, or Vitek, or Vitek2, respectively. MICs of initial and subsequent isolates were similar. In linear regression, higher vanco MICs were associated with a later year of isolation ($p = 0.02$). **Conclusion:** The overall S as well as the proportion



of MRSA blood isolates with a vanco MIC of <1 mg/L is decreasing. MIC 2 isolates were frequently missed by the automated systems, particularly by Vitek 2.

LB-12 In-Vitro 24 Hour Time Kill Studies of Vancomycin and Linezolid in Combination vs Methicillin Resistant *Staphylococcus aureus* (MRSA)

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Background: Antimicrobial management of MRSA infections, particularly bacteremia, have become increasingly problematic. Persistent MRSA bacteremia despite appropriate therapy and deep seated disease states have led some practitioners to alter therapies or even combine agents with limited data to support these approaches. The kinetics of vancomycin in some populations also will create overlap of drugs even when it is stopped as other agents are added or started. We studied 5 MRSA isolates in macrotube dilution 24 hour time kill studies with the combination of linezolid and vancomycin to evaluate these interactions. **Methods:** 24 hour time kill studies were performed on 5 genetically different MRSA isolates. Each organism was run at 1/4, 1/2, and 2 \times the MIC for each antimicrobial. 4 concurrent tubes of the isolate beginning with a 10^5 cfu/ml concentration were run with a control, linezolid alone, vancomycin alone and the combination vancomycin plus linezolid. samples at 0, 4, 8 and 24 hours were serially diluted and counted. **Results:** Studies performed at 2 \times MIC appeared optimal for delineating interactions. None of the isolates exhibited synergistic or additive effects of the two agents in combination. In 3 of 5 isolates the addition of linezolid appeared antagonistic to vancomycin activity alone. **Conclusion:** Clinicians should avoid the combination of linezolid and vancomycin when treating serious MRSA infections. This data must be kept in perspective with consideration for variations in tissue penetration and activity of these agents. Particular care may be needed in patients with delayed clearance of vancomycin when switching to linezolid.

LB-13 Carbapenem Resistances among *P. aeruginosa* (PSA) Isolated in an USA Medical Center: Report of Osteomyelitis Caused by an IMP-15 Producing Strain

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Background: Acquired carbapenem (CARB) resistance (R) due to metallo- β -lactamase (M β L) production is increasing rapidly in Asia, Europe and Latin America (LA), but is rarely reported in North America (NA) and particularly in the USA. We evaluated the CARB-R mechanisms among 50 multidrug-R PSA clinical strains (2001–2005) and report one case due to a M β L-producing strain. **Methods:** CARB-R (MIC ≥ 8 μ g/ml for imipenem or meropenem) isolates were evaluated. The isolates were tested for susceptibility (S) by Etest and screened for M β Ls by Etest M β L strips. M β L screen positive (inhibited by EDTA) strains were evaluated by PCR for *bla*_{IMP}, *bla*_{VIM} and *bla*_{SPM}, followed by gene sequencing. The role of hyper production of AmpC β -lactamase, efflux

pump and OMP alterations on the R was evaluated on all strains by testing CARBs±the AmpC (BRL 42715) and efflux pump (MC-207,110) inhibitors. **Results:** 46 strains showed hyper AmpC production, of which 3 showed significant decrease (≥8-fold) in CARB MICs with MC-207,110. One strain was MβL screen positive, and PCR-positive for *bla_{IMP}* and gene sequencing demonstrated *bla_{IMP-15}* (not previously described in NA). The patient was from Mexico where he was hospitalized in March 2005, for an open femur fracture, stabilized with nail fixation. The patient immigrated to the USA and was admitted to UK Health Care in August 2005, with wound drainage. Culture yielded MRSA, *E. faecalis* and the IMP-15 producing PSA. Despite treatment with polymyxin B and other agents, CARB-R PSA persisted. **Conclusions:** CARB-R due to MβL production remains rare in USA hospitals. However, CARB-R strains should be screened for MβL production, especially among patients from endemic geographic regions (LA) to facilitate the implementation of appropriate infection control measures to avoid the dissemination of these important, mobile R mechanisms.

LB-14 Severe *Clostridium difficile* associated disease (CDAD) in previously healthy women admitted to obstetrical and gynecological (OB/Gyn) services at a tertiary care center

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Recent outbreaks of severe CDAD associated with a hypervirulent strain of *C. difficile* have occurred, including populations previously at low risk, such as young, peripartum women. In 2006, six healthy women, ages 18–47, were admitted for OB/GYN-related care and CDAD. Hospital data identified no CDAD on OB/GYN floors in 2005. Among the 6, 2 underwent elective hysterectomy and received 2 doses of perioperative antibiotics. Two were in their second trimester of pregnancy when admitted with diarrhea after outpatient treatment for bacterial vaginosis. Another was admitted 3 weeks after cesarean section. The final patient was 12 weeks pregnant, admitted 8 days after laparoscopic cholecystectomy, for which she received one antibiotic dose. No common source for infection was identified. 5/6 women had severe diffuse colitis on abdominal CT. 4/6 were treated with both intravenous metronidazole and oral vancomycin; two of these were sent to the intensive care unit (ICU) for sepsis syndrome; receiving additional rectal vancomycin. One required total colectomy, continued to have sepsis syndrome, and underwent resection of a large portion of ileum. Despite 14 days of therapy, ileostomy fluid was (+) for *C. difficile* toxin; pathology of ileal tissue showed pseudomembranous enteritis. The patient died of complications from CDAD. The other ICU patient had continuous colonic vancomycin infusion, and sepsis resolved. 2/4 women not requiring ICU care responded to dual antibiotic therapy and were discharged on oral vancomycin. Both were diagnosed with recurrence of CDAD; one requiring a second hospitalization. **Conclusion:** Our 2006 experience confirms the changing epidemiology of severe CDAD to include healthy women of reproductive age. Clinicians should have heightened awareness for CDAD in this population.

LB-15 Intracolonic Vancomycin (ICV) as Adjunctive Therapy in Patients with Severe *Clostridium difficile*-associated disease (CDAD)

MAYA GUPTA, MD, SHU-WEN LIN, PharmD, MS, JUDITH A. O'DONNELL, MD; Drexel University College of Medicine, Philadelphia, PA. **Background:** Recent outbreaks of CDAD in N. America and Europe caused by a hypervirulent strain of *C. difficile* have been associated with increased morbidity and mortality. This strain has been identified in our institution and since early 2005 there has been an increase in the CDAD caseload, frequency of severe or recurrent disease, and need for colectomy. Anecdotal reports suggest adjunctive treatment of CDAD with ICV may be beneficial. **Methods:** This retrospective study evaluated CDAD patients treated with ICV for at least 24-hours and described ICV dosing, method of delivery, patient outcomes, and adverse effects. The institutional pharmacy database was queried to identify patients with an order for rectal vancomycin from January 2005 to June 2006 and data was extracted from their medical record. **Results:** 13 patients were identified as receiving ICV but 6 were excluded as they received ICV for less than 24 hours. In the 7 evaluable patients, the average duration of ICV was 16-days (range 3–29 days), with an average dose of 1 gram/24 hours (range 500 mg-2 g/24 hours). ICV was delivered via rectal tube, intracolonic catheter, or rectal enema. 3/7 patients received continuous infusion of ICV (1g/24 hours) in addition to the intermittent ICV every 6 hours. All received concomitant intravenous metronidazole and oral vancomycin. Two patients required colectomy; 1 died of complications of CDAD and the other had partial resolution of disease. The remaining 5 patients all had complete resolution of CDAD. No rectal, colonic injury or perforation was reported. One patient with chronic renal failure (CRF) on hemodialysis (HD) significantly absorbed vancomycin, with an elevated serum level of 31.5 mcg/mL. **Conclusion:** ICV may be an effective adjunctive therapy in patients with severe CDAD. Monitoring of serum levels are warranted in those with CRF on HD.

LB-16 The Novel Human Pathogen *Granulibacter bethesdensis* Causes Necrotizing Lymphadenitis in Chronic Granulomatous Disease

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Background: *Granulibacter bethesdensis*, a new genus and species in the family Acetobacteraceae, and the first member of this family to cause invasive human disease, caused necrotizing lymphadenitis in a patient with Chronic Granulomatous Disease (CGD) (PloS Pathogen 2006;2:e28). We now report the isolation of *G. bethesdensis* from 3 more patients from North and Central America. **Methods:** Clinical isolates grew on buffered charcoal yeast extract and mycobacterial media in small quantities. 16S rRNA was used for definitive identification. Pulsed Field Gel Electrophoresis (PFGE) was done with XbaI. A *G. bethesdensis* microarray chip was created and genomic DNA from all isolates was hybridized to the chip. Whole bacterial protein extracts were SDS-PAGE separated and immunoblotted with patient plasma. **Results:** X-linked CGD Patients from Georgia, Florida, and Panama had necrotizing lymphadenopathy that developed over >4 weeks in the cervical, thoracic and abdominal areas. One patient also had splenic lesions and ascites. A gram negative rod was isolated from each case. 16S sequence showed identity with the *G. bethesdensis* type strain, NIHCGD1, but PFGE showed each patient's isolate was distinct. Whole genome hybridization showed areas of genome plasticity, indicating that all the patients have unique strains. All 3 patients had antibody to *G. bethesdensis*. **Conclusion:** *G. bethesdensis* appears to cause a distinct entity of chronic necrotizing lymphadenitis in CGD. There is significant genetic variation within the species. The identification of 4 cases from North and Central America over 2 years suggests this is an emerging pathogen.

LB-17 Telavancin for the Treatment of Complicated Skin and Skin Structure Infections (cSSSI): Results of the ATLAS I Study

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Background: Telavancin (TLV) is a rapidly bactericidal lipoglycopeptide with a multifunctional mechanism of action that is active against Gram-positive bacteria including methicillin-resistant *Staphylococcus aureus* (MRSA). **Methods:** We conducted two identical multinational, parallel, randomized, double blind, active control, Phase 3 studies (ATLAS I&II) with a pre-specified pooled analysis design. Patients ≥ 18 years of age with cSSSI caused by suspected or confirmed Gram-positive pathogens were randomized to receive either vancomycin (VAN) 1 g IV q 12h or TLV 10 mg/kg IV q 24h for 7–14 days. **Results:** In the ATLAS I study, a total of 855 patients (VAN 429, TLV 426) were randomized at 40 sites in 8 countries, and received at least one dose of study medication. Overall 25% of the patients were diabetic, 19% were ≥65 years old, 44% had abscesses, 37% had cellulitis, and 36% had MRSA as a baseline pathogen. Baseline demographic, clinical characteristics and length of therapy were similar between the two groups. The primary efficacy objective of non-inferiority was met. In the clinically evaluable (CE) population, a successful clinical response was achieved in 86.5% and 87.9% of patients receiving VAN and TLV, respectively. In microbiologically evaluable (ME) patients with documented MRSA infection, successful clinical response was achieved in 85.5% for VAN and 87% for TLV. In ME patients with documented methicillin-susceptible *S. aureus* infection, the rates were 84.6% for VAN and 89.9% for TLV. The proportions of patients who died, experienced a serious adverse event, or who discontinued the study drug due to an adverse event were similar between the two groups. **Conclusion:** These data support the efficacy and safety of once-daily telavancin in the treatment of Gram-positive cSSSI.

LB-18 Controlled Trial: 5-day Course of Telithromycin versus Doxycycline for the Treatment of Mild to Moderate Scrub Typhus

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interval required to defervescence after drug administration in the telithromycin administration group was 20.45 ± 12.9 hours (mean interval \pm SD), and that in the doxycycline administration group was 22.60 ± 21.44 ($p > 0.05$). In addition, a statistically significant difference could not be observed in regard to the time required for alleviation of headache, myalgia, and rash. **Conclusions:** Ours is the first study reported in the English literature to confirm that for the treatment of mild to moderate scrub typhus without accompanying complications, 800 mg daily treatment of telithromycin for 5 days is a safe and effective treatment that is comparable to doxycycline 100mg bid for 5 days. The superior tissue kinetics profile of telithromycin and its low potential to induce resistance suggest that telithromycin is a promising new antibacterial agent that can be used for the treatment of scrub typhus and rickettsiosis.

LB-19 Methicillin Resistant versus Methicillin Sensitive *Staphylococcus Aureus* Adult Haematogenous Septic Arthritis

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Background: *Staphylococcus aureus* (SA) is the number one cause of septic arthritis. Methicillin Resistant *Staphylococcus Aureus* (MRSA) is increasing in incidence but how it differs from Methicillin Sensitive *Staphylococcus Aureus* (MSSA) septic arthritis is unclear. Our aim was to delineate the differences in clinical features and outcomes of MRSA septic arthritis. **Methods:** Retrospective review of adult patients presenting from 2000 to 2006 with native joint haematogenous septic arthritis. We identified 11 cases of MRSA and 29 cases of MSSA septic arthritis. Fisher's exact test and the Student's t-test were used in analysis. **Results:** MRSA and MSSA (79% vs 64%) predominantly affected males. MRSA cases were older ($p = 0.001$), with a mean age of 73.4 vs 45.8 years, and had more comorbidities with a mean of 2.55 versus 1.28 ($p = 0.009$). In MRSA and MSSA the main sources of sepsis were unknown (27.3% vs 55.2%), intravenous lines (36.4% vs 3.5%), soft tissue infection (27.3% vs 3.5%) and Intravenous Drug Use (9.1% vs 37.9%). MRSA was significantly more associated with intravenous line sepsis ($p = 0.01$) and nosocomial ($p = 0.0001$). Presentation was similar in both groups although MRSA was significantly more likely to be pyrexial ($p = 0.04$, 82% vs 44.8%) and to affect the shoulder ($p = 0.04$). Mean length of antimicrobial therapy was similar in both MRSA and MSSA patients (10.4 vs 12.6 days intravenous and 22.6 vs 39.7 days oral). As was number of surgical interventions required (2.5 versus 1.9). Outcomes were similar in MRSA and MSSA with no significant differences in recurrence (0% vs 11%) or sepsis related mortality (9.1% vs 6.9%). **Conclusion:** MRSA septic arthritis tends to affect older patients with multiple comorbidities and has a particular tropism for the shoulder. Surprisingly with appropriate antimicrobials and surgical intervention it does not have a significantly worse outcome than MSSA and does not require significantly longer periods of antimicrobials or more surgical interventions.

LB-20 Pantoprazole Co-treatment Increases Cecal Titers of *C. difficile* Cytotoxin B During Quinolone Therapy

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Background: The contribution of proton pump inhibitor (PPI) and quinolone use to rising *C. difficile*-associated disease (CDAD) rates is controversial. An animal model of quantitative *C. difficile* challenge was used to determine if cytotoxin B titers could be altered by pantoprazole co-treatment during quinolone exposure. **Methods:** Male Sprague-Dawley rats ($n = 80$) were housed individually and fed a chow/ beef diet for 20 days. On days 8–11, the food was contaminated with 10^3 *C. difficile* spores of a PCR-Ribotype 027 (NAP1) or 001 strain. From days 10–20, groups of animals received cefotaxime (15mg q8h), levofloxacin (5mg q12h), moxifloxacin (3 mg q12h) or gatifloxacin (3 mg q12h) s.c. Half of the animals in each group also received daily 2 mg i.p. pantoprazole. On day 21, the cecal contents were measured for pH, cytotoxin B titer and quinolone concentrations; *C. difficile* was quantitatively cultured. **Results:** Within each group, mean \log_{10} *C. difficile* counts were not significantly different between PPI-treated and-untreated animals (moxi= $10^{7.8}$, levo= $10^{8.5}$, gati= $10^{9.4}$ CFU/gm). The pH of the cecal contents was not altered by PPI therapy (Non-PPI: 6.42 ± 0.41 vs. PPI: 6.39 ± 0.36). Mean concentrations \pm SD of levo, moxi and gati were 77 ± 25 , 25 ± 10 , and 49 ± 21 ug/ml, respectively.

Antibiotic	Challenge strain	No PPI		PPI		p-value
		N	Toxin titer ^a	N	Toxin titer ^a	
Cefotaxime	027/NAP1	4	1300±436	4	6000±1155	<0.03
Levofloxacin	027/NAP1	8	702±238	8	1750±366	<0.04
Moxifloxacin	027/NAP1	8	680±246	8	3150±1131	0.0505
Gatifloxacin	027/NAP1	8	1375±183	8	7000±655	0.0002
All 027 Animals	027/NAP1	28	973±135	28	4257±577	<0.0001
All 001 Animals ^b	001	12	818±197	12	2750±329	0.0004
All animals (027 + 001)	027/001	40	927±110	40	3805±329	<0.0001

^a 1/cytotoxin B titer (fold dilution) \pm SE.

^b Includes 8 animals (4/4) for each of three quinolone/PPI pairings tested.

Conclusion: In a quantitative *C. difficile* challenge model of quinolone and PPI co-therapy, cytotoxin B titers were significantly increased by PPI exposure despite no difference in bacterial counts. CFU and toxin titers varied by

quinolone treatment, and were amplified by PPI exposure. *C. difficile* ribotype 027 appears to be more toxigenic in-vivo. These findings support a role for PPIs in the changing epidemiology of CDAD.

LB-21 Diagnosis of *Clostridium difficile* (CD) Colitis

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Background: Nosocomial CD colitis is increasingly prevalent and serious. Specific antimicrobial therapy is available, and prompt and accurate diagnosis is important. Early treatment reduces duration of diarrhea which, in turn, reduces spread of infection. A cytotoxicity assay (CYT) has long been regarded as the "gold standard." We compared results of CYT with those of enzyme immunoassay (EIA) and a rapid EIA card (REIA). **Methods:** We studied all fecal samples submitted to the diagnostic microbiology laboratory for CD toxin assay. CYT (Diagnostic Hybrids) used human foreskin fibroblasts. EIA was by PremierTM CD Toxins A&B (Meridian Bioscience) and REIA used ImmunoCard[®] (Meridian). **Results:** 201 samples were studied. 33 samples (16.4%) were positive and 168 (83.6%) were negative by CYT. Results are presented in the table.

n=201	CYT	EIA	REIA
31	+	+	+
1	+	+	-
1	-	-	-
1	-	+	-
1	-	+	+
166	-	-	-
Total positive	33	32 of 33	31 of 33
Total negative	168	166 of 168	167 of 168
Sensitivity		97%	93.9%
Specificity		98.8%	99.4%

CYT was positive within 12–16 hr in all cases, but requires a skilled technician and access to an inverted microscope. EIA is labor-intensive, takes a few hours to do and requires an EIA reader; batching of samples is efficient, but delays reporting of results. REIA is more costly per unit, but is simple to do, requires no additional equipment, and provides results in 25 minutes. When CYT was regarded as the "gold standard", sensitivity and specificity of EIA and REIA were very high. In fact, based on clinical data and repeated assays on the same and additional fecal samples, one CYT assay was regarded as falsely positive, and another as falsely negative, indicating even better sensitivity and specificity of EIA and REIA. **Conclusion:** Several laboratory techniques are available to diagnose CD colitis. The three we tested yielded similarly reliable results.

LB-22 Dual Color PNA FISH Assay for Simultaneous Identification of *Candida albicans* and *Candida glabrata* Directly from Positive Blood Culture Bottles

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Background: *Candida* is the most frequently isolated fungus from blood cultures (BC). Since antifungal selection relies on species determination, conventional, multi-day identification methods may lead to a period of sub-optimal therapy. **Methods:** Fluorescent labeled PNA probes targeting specific 26S rRNA sequences of *C. albicans* (CA) and *C. glabrata* (CG) were developed and evaluated by fluorescence *in situ* hybridization (PNA FISH). The probe reagent was applied to smears made directly from positive BC bottles. After incubation for 90 min. at 55°C, unbound probe was removed by washing at 55°C for 30 min. Smears were then examined by fluorescence microscopy. CA and CG were identified as bright green or red fluorescent cells, respectively. Results were compared to identification by conventional methods. The method was also tested on lab strains of *Candida*, phylogenetically related species and other organisms frequently recovered from BC. **Results:** Five clinical microbiology laboratories tested 162 yeast-positive BC (representing 14 species). Positive and negative predictive values for identification of CA were 100% (68/68) and 98.9% (93/94) and 100% (29/29) and 100% (133/133) for CG. *Kluyveromyces delphensis*, a species closely related to CG, was detected by the test, all other lab strains were negative. **Conclusions:** Dual color PNA FISH is a rapid (<3 hr) and accurate method for identification of both CA and CG directly from positive BC bottles. Rapid identification of these species should lead to improvements in antifungal therapy while reducing hospital drug expenses.

LB-23 A pilot study of enfuvirtide (ENF) once daily (180mg QD) v twice daily (90mg BID) for 48 weeks

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Background: ENF is a BID SC administered HIV-1 fusion inhibitor (FI) approved for treatment-experienced patients. QD dosing would offer improved convenience. Previously it has been shown that overall exposure (AUC₂₄) was similar for 180 mg QD v 90 mg BID but QD had a higher C_{max} and lower C_{min}. We evaluated the W48 efficacy and safety of ENF given QD v BID. **Methods:** FI-naïve patients on a stable failing pre-study regimen with viral load (VL) ≥5000 c/ml, prior triple-class experience/resistance were randomized to ENF 180 mg QD (2 SC injections QD) v ENF 90 mg BID (1 SC injection BID) both in combination with a new OB. The primary endpoint was the % of patients with a VL <400 c/ml at W48. All data are ITT unless specified. **Results:** Sixty-one patients were randomized (30=QD/31=BID). For QD and BID respectively, median BL VL was 4.9 log₁₀ c/ml (both arms), CD4 was 120 v 105 cells/mm³, % of patients with GSS ≤1 was 57% v 52%. At W48 for QD and BID respectively, the % of patients with a VL <400c/ml was 23% in both arms (OT 64% v 47%) and the % of patients with <50c/ml was 13% v 23% (OT 36% v 47%). At W48 using LOCF for VF+DC the LSM decrease from BL in VL was 1.428 and 1.085 log₁₀ c/ml for QD and BID respectively. Using BLCF for VF+DC the LSM decrease from BL in VL was 0.726 and 0.835 log₁₀ c/ml and increase in CD4 cell count was 47 v 36 cells/mm³ for QD and BID respectively. High level ENF adherence (≥95% by 4 day recall) was reported by 80% of QD and 58% of BID patients. Week 48 VF was similar for QD (40%) and BID (36%). Injection site ecchymosis, induration or erythema were moderately less severe on BID. The most common AE (diarrhea, upper respiratory tract infection) were more frequent on BID. **Conclusion:** Both ENF QD and BID were similar, but adherence was better on QD. However, the study was not designed or powered to assess non-inferiority of QD dosing.

LB-24 Diagnosis of Coccidioidomycosis by Antigen Detection Using Cross-Reaction with *Histoplasma* Antigen

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Background: Coccidioidomycosis is a common cause of pneumonia in endemic areas and may be difficult to diagnose. Patients with coccidioidomycosis with positive tests for *Histoplasma* urinary antigen were recognized in 2005. **Methods:** We performed a retrospective review of patients with coccidioidomycosis cared for by the authors who underwent testing for *Histoplasma* urinary antigen in 2005 and 2006. **Results:** The *Histoplasma* urinary antigen test was positive in 11 of 19 patients (58%) with pulmonary coccidioidomycosis. In one patient with a negative result in urine, antigen was detected in bronchoalveolar lavage fluid. The sensitivity was highest in acute coccidioidomycosis, where antigenuria was detected in 11/14 cases (79%), and in a 12th (86%) following 10-fold concentration of the urine. **Conclusions:** Physicians should be alerted that coccidioidomycosis is a cause of positive *Histoplasma* urinary antigen. The diagnosis of coccidioidomycosis may be facilitated by taking advantage of cross-reactivity in a *Histoplasma* antigen assay.

LB-25 HSV suppression with valacyclovir reduces rectal and blood plasma HIV-1 levels in HIV-1, HSV-2 seropositive men

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Background: Herpes simplex virus type 2 (HSV-2) is common among HIV infected persons. HSV-2 reactivation is associated with increased plasma and genital HIV-1 levels and *in vitro*, HSV upregulates HIV transcription. Our objective was to assess whether HSV suppression reduces rectal and plasma HIV-1 levels in HIV-1, HSV-2 co-infected men who have sex with men (MSM). **Methods:** We randomly assigned 20 ART-naïve HIV-1 and HSV-2 seropositive MSM in Lima, Peru with CD4 >200 to receive valacyclovir (VAL) 500 mg bid or placebo (PLC) for 8 weeks, then a 2 week washout, followed by the alternative regimen for 8 weeks. Men collected daily home swabs of anogenital skin for HSV DNA PCR, had thrice weekly anoscopy for collection of rectal mucosal secretions for HIV-1 RNA, HSV DNA, and weekly plasma HIV-1 RNA by PCR. The primary outcome was rectal HIV level and secondary outcome was plasma HIV-1 level by study arm. **Results:** Median CD4 count was 406 [range, 232–869]. HIV-1 was detected in 99% of 288 plasma and 73% of 844 rectal specimens. HSV was detected on 29% of days on PLC and 4% of

days on VAL. Participants had a significant decrease in both rectal and plasma HIV-1 levels during the VAL compared to PLC arm: mean log₁₀c/mL of rectal (5.00 vs. 4.80; p < 0.0001) and plasma (4.50 vs. 4.14; p < 0.0001) HIV-1 levels. In multivariate analysis, the mean within-subject rectal HIV-1 was 0.16 log₁₀ (95% CI [0.07, 0.25]; p < 0.0001) lower during daily VAL, a 31% decrease, and plasma HIV-1 was 0.33 log₁₀ (95% CI [0.23 0.42]; p < 0.0001) lower, a 53% decrease. VAL had a greater effect on reducing plasma HIV-1 levels at higher CD4 count (p=0.018). **Conclusion:** Valacyclovir significantly reduces both rectal and plasma HIV-1 levels in HIV-1, HSV-2 co-infected men. HSV suppression may potentially decrease the risk of sexual HIV-1 transmission and provide clinical benefits to co-infected persons not on HAART.

LB-26 Association of Androgen Receptor Gene Polymorphism with HIV But Not HCV Infection in Women

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Background: Androgen deficiency is a common endocrine abnormality among men and women with human immunodeficiency virus (HIV) infection. Studies have shown the significant association of low testosterone and low circulating androgen concentrations in HIV infected men and women particularly with a reduction in lean body mass. In this study we report the association of Androgen receptor gene polymorphism with HIV infection but not with HCV infection. **Methods:** DNA was isolated from 77 HIV, 26 HCV with mono-infection, 10 combined infections and 233 normal healthy subjects. Polymerase chain reaction followed by HAE III restriction enzyme digestion was used to identify androgen receptor (AR) gene polymorphism SPSS version 10.0 for Windows software was used for data analysis. **Results:** A significant increase in homozygous 11 genotype(mutant) was observed in HIV individuals with mono (19.5%) and combined infections (30%; p < 0.0001). Individuals with HCV mono infection did not show any variation (3.8%) in comparison to controls (3.1%). This data also shows that females with HIV mono and combined infections had no heterozygous genotype as expected and such variation was not found in HCV females. **Conclusion:** Adrenal androgen is reduced in association with disease severity in HIV-infected women. The significant association of the homozygous mutant genotype-11 in HIV infected men and women could be a valuable marker to the treatment. Further studies are necessary to define the therapeutic role of androgen therapy in this population.

LB-27 Increased Incidence of Musculoskeletal Disorders (MSDs) in Children within One Year of Levofloxacin Therapy: A Large (n=2,223), Comparative, Prospective Trial Experience

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Background: Fluoroquinolones (FQs), including LVX, cause lesions in cartilage of juvenile lab animals during acute exposure. The occurrence of these lesions in FQ-exposed children has not been demonstrated. A large trial assessing the occurrence of MSDs in children treated with LVX was conducted to define the incidence of events plausibly associated with lesions in cartilage. **Methods:** Children completing both LVX and comparator-treated arms of recently completed efficacy trials were evaluated during and at the end of therapy, and up to 60 days to assess relation between acute exposure and joint disorders. In addition, children were evaluated at 6 and 12 months. The incidences of 4 specific MSDs (arthritis, arthralgia, tendinopathy, gait abnormality) and of failure to achieve 80% expected height after 1 year for LVX- and comparator-treated children were compared (by Fisher's exact test). **Results:** The incidence of MSDs within 60 days in LVX-treated children (2.2%) was significantly greater than those in C-T children. This difference was largely attributable to reports of arthralgia.

Disorder	Levofloxacin (n=1340)		Comparator (n=893)		P value
	N (%)	95% CI	N (%)	95% CI	
MSDs within 60 d	29 (2.2)	(1.5; 3.1)	8 (0.9)	(0.4; 1.8)	0.027
Arthralgia within 60 d	24 (1.8)	(1.2; 2.7)	7 (0.8)	(0.3; 1.6)	0.063
MSDs in wt bearing joints within 60 d	25 (1.9)		6 (0.7)		0.025
MSDs within 30 d	24 (1.8)	(1.2; 2.7)	7 (0.8)	(0.3; 1.6)	0.063
Failure to achieve 80% of expected height	101(8.7)		66 (8.4)		0.89

Conclusions: In this experience, the incidence of 4 MSDs was higher in LVX-treated children compared to children receiving non-FQs. These disorders appeared transient and not associated with persisting joint disease or growth failure during the 1-yr period of evaluation. These observations underscore the need to consider a potential effects on cartilage in prescribing LVX to children.

LB-28 Emerging *Clostridium difficile*-associated Disease in the Community and the Role of Non-antimicrobial Risk Factors

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LB-29 Herpes Zoster is Not Associated with Past Exposures to Varicella or Children

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Background: Exogenous exposure to varicella-zoster virus (VZV) may reduce the incidence of herpes zoster (HZ) due to immune boosting. We conducted a case-control study to determine if HZ is associated with exposure to varicella or frequency of contact with children. **Methods:** Cases and controls were identified from a geographic and managed care cohort served by Marshfield Clinic, a multi-specialty clinic in Wisconsin. Cases of incident HZ were identified from August 2000 to July 2005 using ICD9 codes (053) and confirmed with record review. Controls were frequency matched to cases on age and year of HZ onset. Cases and controls were 40–79 years old and had ≥ 6 months in the cohort prior to diagnosis. Participants were interviewed to ascertain frequency, duration, and type (e.g., household) of contact with persons who had varicella, HZ, or with young children in the previous 10 years. Multivariable models assessed the association between exposures and HZ. **Results:** Interviews were obtained from 633 cases and 655 controls. Cases and controls were similar demographically, but controls had higher refusal (29% vs. 21%) and loss to follow-up rates (14% vs. 9%, $p < 0.001$). Cases and controls reported similar exposures to persons with chicken pox (18% vs. 16%). The odds ratios (OR) for the total number of varicella contacts in the past 10 years were 1.2 (95%CI 0.8–2.0) for 1 contact, 0.9 (95%CI 0.5–1.5) for 2 contacts, and 1.4 (95% CI 0.8–2.2) for > 2 contacts, controlling for age and gender. The full multivariable model identified no significant associations between HZ and exposure to chickenpox or HZ. Exposures to children in the occupational (OR=0.5, 95% CI 0.1–1.7) and social (OR=1.1, 95% CI 0.4–2.7) settings were also not significantly associated with a reduced risk of HZ. **Conclusion:** These results provide no evidence to support external immune boosting in this population. Other factors that may be influential include internal boosting and possible nondifferential misclassification of exposure to VZV.

LB-30 Possible Human Infections Due to Spotted Fever Group Rickettsiae Other than *Rickettsia rickettsii* in North Carolina

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collected around home sites, speciated, pooled and assayed by polymerase chain reaction and sequence analysis for *Rickettsia* spp. **Results:** Of 29 patients with paired sera available, 18 (62%) were seronegative, 5 (17%) had confirmed *Ehrlichia chaffeensis*, and 6 (21%) had ambiguous titers to *R. rickettsii*. These 6 patients had a mild acute febrile illness with headache and myalgia, 5 recalled tick exposure or had ticks removed at their initial clinic visit and 1 had a diffuse maculopapular rash. All 6 had higher IFA titers to *R. amblyommii* antigen: 6 with at least one serum IgM titer > 64 , and 2 with ≥ 4 -fold rises in IgG. 6,502 ticks collected at 32 sites were speciated as *Amblyomma americanum* (99.6%), *Dermacentor variabilis* (0.4%), and *Ixodes scapularis* ($< 0.1\%$). Of 51 tick pools tested, 21 (41%) were positive for *Rickettsia* spp. Sequence analysis of 17 pools identified *R. amblyommii* in 11 *A. americanum* pools and in 2 *D. variabilis* pools. **Conclusion:** The serologic results combined with the preponderance of *A. amblyomma* ticks in the environment, many harboring *R. amblyommii*, suggests that human illness due *R. amblyommii*, resembling mild RMSF or ehrlichiosis, may be occurring in NC.

LB-31 *Anaplasma phagocytophilum* and *Rickettsia rickettsii* Seroprevalence in US Military Personnel

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Background: Most epidemiologic studies of tick-borne rickettsial diseases are small with limited demographic scope. We conducted a serological study of 10,000 US military to estimate exposure to *A. phagocytophilum* (*Ap*) and *R. rickettsii* (*Rr*), agents of human granulocytic anaplasmosis (HGA) and Rocky Mountain spotted fever (RMSF), respectively, in a geographically diverse population. **Methods:** Specimens were selected randomly from personnel on active duty in 1997 using the DoD Serum Repository. Testing included enzyme linked immunosorbent assay (ELISA) for antibodies to *Ap* and *Rr*. *Ap*-positive specimens were tested by Western blot (WB). **Results:** Subjects were mostly male (84%), young (mean [standard deviation] = 28.2 [7.6] years), diverse ethnically (White 68%, Black 20%, Hispanic 11%) and from all US states. *Ap* ELISA and WB positivity were 2.6% and 0.11% (95% confidence interval [CI], 0.05–0.18%), respectively. *Ap* WB positivity was not significantly associated with demographic characteristics. *Rr* ELISA positivity was 6.0% (95% CI, 5.5–6.4%). *Rr* positivity was significantly ($P < 0.01$) associated with older age (by quartile: 5.0%, 5.4%, 6.0%, 7.5%), male sex (6.5%; female, 3.3%), ethnicity (White 5.6%, Black 8.7%, Hispanic 3.6%, other 1.6%), ground combat specialty (9.5%; other, 5.5%), and home state with RMSF incidence $\geq 5/1,000,000$ /year (9.8%; other states, 5.2%). Associations were significant in multivariate logistic regression for oldest vs. youngest quartile, sex, Black vs. White, ground combat specialty, and home state with high RMSF incidence. **Conclusion:** Compared to previous US cross-sectional studies, seroprevalence was lower for *Ap* and similar for *Rr*. Small samples and less specific tests in earlier studies may explain discrepancies. HGA risk in the general US population may be lower than previously suspected.

LB-32 Identifying Opportunities for Improving Environmental Hygiene in Cruise Ship Restrooms

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ships suggesting that suboptimal cleaning of these sites may play a role in AGI pathogen transmission in this setting.

LB-33 HE2100 (5-AED): A Potential Candidate for the Prevention of Nosocomial Infection

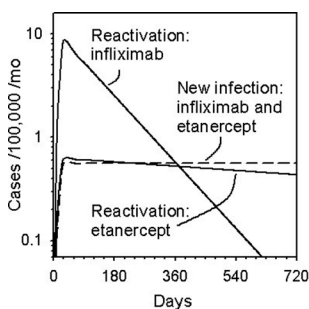
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Background: Nosocomial infection (NI) is a major cause of morbidity and death in hospitalized patients and is currently compounded by the increasing emergence of antibiotic resistant bacteria. The innate first line protection against NI includes the activation of neutrophils (NT) and platelets (PLT). HE2100 (5-AED), an immune stimulatory hormone, induces trilineage hematopoiesis and significantly decreases mortality due to gram negative infections in both healthy and irradiated mice. HE2100 given at 15mg/kg for 5 in lethally irradiated myelosuppressed rhesus monkeys decreases antibiotic requirements and reduces deaths by 20 percent (mid-pvalue = 0.048). **Methods:** A randomized, double-blind, 3:1 placebo-controlled safety study of 5 daily IM injections of HE2100 was performed in 39 healthy human volunteers (18–65 years). Placebo equivalent or 50 mg, 100 mg, 200 mg, or 400 mg HE2100 were administered intramuscularly. Subjects were followed for 56 days for safety, pharmacokinetics and evidence of drug activity. **Results:** HE2100 produced a significant dose-response increase in NT and PLT in peripheral blood. NT increased by 85% (200mg group) and PLT increased by 171% (400 mg group) as compared with placebo controls. NT reached peak levels at days 4–5 ($p < 0.001$) and PLT peak levels occurred at day 14 ($p < 0.001$). A dose-response increase in PLT was still significant at study day 56 ($p = 0.03$). HE2100 was safe and well tolerated and all subjects completed the study. **Conclusion:** In healthy human volunteers receiving 200 mg/day HE2100 for 5 days, pharmacodynamic responses of NT and PLT were comparable to that dose which resulted in decreased antibiotic use and increased survival in irradiated rhesus monkeys ($p < 0.05$). We conclude that HE2100 stimulates innate immunity, suggesting that its use in hospitalized patients may reduce risk for NI. Studies are underway to further test this hypothesis.

LB-34 Contribution of New Infection to Tuberculosis during TNF Blockade

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Background: Tumor necrosis factor (TNF) antagonists greatly increase tuberculosis (TB) risk. Efforts to reduce this risk have focused exclusively on preventing reactivation of latent TB infection (LTBI). This study used mathematical modeling to examine the contribution of progression of new infection to TB due to TNF blockade. **Methods:** Iterative methods were used to identify the parameters of a hidden state transition (Markov) model that reproduce US TB incidence and time to onset data reported to the US Food and Drug Administration Adverse Event Reporting System. **Results:** Modeling revealed a monthly rate of reactivation of LTBI by infliximab (TNF monoclonal antibody) of 22%, whereas that of etanercept (soluble TNF receptor) was 1.6% (below). 75% of infliximab-associated cases were due to reactivation, whereas slightly more than half of etanercept-associated cases were due to progression of new infection. The apparent annual rate of TB infection (ARTI) was 0.007%, close to that estimated in the US using other methods. Over half of new infections progressed to disease. New infection became increasingly important for both drugs as the duration of treatment increased. **Conclusions:**



The contribution of new infection to TB during TNF blockade is greater than is presently appreciated. New strategies to prevent tuberculosis will be required as these therapies become available in regions of high TB prevalence.

LB-35 A Natural History Model Estimating the Clinical Benefits Associated with HPV Vaccination and Cross-Protection among US Females 12–26 Years of Age

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Background: This study assessed the clinical benefits of vaccinating 12–26 year-old US females against HPV-related cervical disease. **Methods:** A natural history model simulated the lifetime effects of pap screening plus vaccination and compared the benefits in 13–26 year-old versus 12 year-old females. Three scenarios, combined with screening, were evaluated: (1) no vaccination; (2) vaccination against HPV 16/18 only; and (3) vaccination against HPV 16/18 with cross-protection against other oncogenic HPV types. Published literature and clinical trial data were used to model HPV natural history, vaccine efficacy, practice patterns, and patient outcomes. Outcome measures included abnormal pap tests, CIN3, cervical cancer and related deaths. **Results:** Compared with no vaccination, model results estimated that vaccination of 13–26 year-olds against HPV 16/18 reduced abnormal paps, CIN3, cervical cancer and related deaths by 10%, 16%, 42% and 39%, respectively, while vaccination of 12 year-olds produced reductions of 12%, 23%, 51% and 51%, respectively. An HPV 16/18 vaccine with cross-protection reduced these clinical endpoints in 13–26 year-olds by 14%, 21%, 45% and 42%, respectively, and in 12 year-olds by 16%, 29%, 55% and 55%, respectively. Among 13–26 year-olds, an HPV 16/18 vaccine with cross-protection prevented an additional 41% abnormal paps, 27% CIN3 cases, 8% cervical cancer cases and 8% cervical cancer deaths than a vaccine against HPV 16/18 only. **Conclusion:** While results indicated immunization generated the greatest benefits in females aged 12 years, vaccination was estimated to provide substantial protection to 13–26 year old females. Model results further suggested efficacy against non-16/18 oncogenic HPV types provided additional benefit in preventing cervical disease across all ages evaluated.

LB-36 Safety of Mass Immunization with Tetanus-Diphtheria-Acellular Pertussis Vaccine (Tdap) During a NH Hospital Pertussis Outbreak

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Background: Tdap is recommended for health-care personnel (HCP) aged <65 yrs who received Td/TT ≥2 yrs earlier (routine HCP). After a hospital Tdap campaign during a pertussis outbreak, we assessed adverse event (AE) rates in routine HCP and 3 non-routine HCP groups: <2 yr interval (received last Td/TT <2 yrs earlier), aged ≥65 yrs, or pregnant. **Methods:** We surveyed (paper/electronic) HCP vaccinees to assess time since last Td/TT (≥2 yr vs <2 yr), age, pregnancy status, and local AEs and subjective fever during the 2 wks after Tdap. We calculated AE rates by group. Routine HCP rates were compared with rates in <2 yr interval or age ≥65 yrs groups. Rates in routine non-pregnant HCP women aged <45 yrs were compared with rates in pregnant HCP. We calculated 95% confidence limits (CL) on rate differences. **Results:** Overall, 4524 (72%) HCP received Tdap; 2518 (56%) completed surveys (79% female). Median age was 45 yrs (range 17–83). Most AE rates in non-routine groups were similar to or lower than rates in routine groups (Table).

HCP Group	N	Percentage reporting AEs			
		Pain ^a , M/S [S]	Redness, >1 [>2] in	Swelling, >1 [>2] in	Subjective fever
All	2518	19 [1]	8 [4]	11 [5]	13
Routine HCP ^{b,c,d}	1660	19 [1]	8 [4]	11 [5]	13
<2 yr interval ^{c,d}	266	16 [2]	7 [3]	9 [4]	15
Age ≥65 yrs ^{b,d}	26	4	8*	0	4
Routine women HCP ^{b,d,e}	708	29	11	16	18
Pregnant ^{1,2}	18	11	0	6	17*

^aM/S, moderate/severe; S, severe. ^b≥2 yrs TT/Td to Tdap interval; ^cAge <65 yrs; ^dNon-pregnant; ^eAge 18–44 yrs. *Upper 95% CL on rate difference (non-routine minus routine) ≥10%.

Conclusion: Local AE rates in HCP vaccinated with Tdap who received Td/TT ≥2 yrs (routine HCP) and <2 earlier were similar and consistent with pre-licensure results. Our findings suggest Tdap reactogenicity in HCP who received Td/TT <2 yr earlier may be acceptable. More data are needed to assess Tdap safety at short intervals and in older and pregnant HCP.

POSTER ABSTRACTS
Late breaker posters

LB-37 DNA-based Anthrax Vaccines Induce Rapid, Potent Anamnestic Responses

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Experimental design: vaccination and pseudochallenge of *Cynomolgus* macaques

Group (no. of animals)	Intramuscular vaccination (no. of Days 0, 7 and 14 (0.6 mg/ml))	Intramuscular pseudochallenge (Day 56 (12.5 µg/0.5 mL))	Days serum taken for anti-PA antibody and toxin neutralization activity (TNA) analysis (days)	
			Pre-pseudochallenge	Post-pseudochallenge
1 (2♂/2♀)	PA pDNA ^a formulated with PBS administered with EP ^b	rPA ^c	0, 7, 14, 21, 56	58, 60, 62, 65, 68, 77
2 (2♂/2♀)	PA pDNA ^a formulated with CRL1005 poloxamer administered with EP ^b	rPA ^c	0, 7, 14, 21, 56	58, 60, 62, 65, 68, 77
3 (2♂/2♀)	PA pDNA ^a formulated with CRL1005 poloxamer administered by needle and syringe	rPA ^c	0, 7, 14, 21, 56	58, 60, 62, 65, 68, 77
4 (1♂/1♀)	None	rPA ^c	0, 5	58, 60, 62, 65, 68, 77

^apDNA encoding *B. anthracis* protective antigen. ^bAdministration by needle and syringe with electroporation (EP) using the Medpulsor[®] DNA Delivery System (Inovio Biomedical Corporation). ^cRecombinant PA (rPA) in Alhydrogel[™] (VaxGen Incorporated).

Results: Irrespective of formulation, anti-PA antibodies increased more rapidly and reached higher magnitudes with EP-assisted delivery. Peak geometric mean concentrations (GMC) reached 204 µg/mL and 234 µg/mL for Groups 1 and 2 respectively by Day 28 and only 13 µg/mL by Day 56 for Group 3. By Day 28, geometric mean titer (GMT) for TNA peaked for Groups 1 (56 ED₅₀) and 2 (157 ED₅₀); no TNA was seen in Group 3. Post-pseudochallenge, GMT TNA increased rapidly by ~1 log₁₀ (Groups 1 and 2) to ~3 log₁₀ (Group 3), typical of anamnestic responses, with Group 3 levels reaching the same order of magnitude as Groups 1 and 2 by Day 9 (~2000 ED₅₀). Group 4, antibody and TNA kinetics were: anti-PA GMC=699 µg/mL by Day 21; TNA GMT=353 ED₅₀ by Day 21. **Conclusion:** These results corroborate previous findings of anamnestic responses and demonstrate that 1) EP-assisted delivery increases the magnitude and accelerates the kinetics of post-vaccination immune responses and 2) irrespective of administration method, vaccination with PA pDNA elicits a potent priming response that can be activated to full effector function rapidly upon exposure to the antigen.

LB-38 VACCINATION TO PREVENT INVASIVE PNEUMOCOCCAL DISEASE: WHAT AGE TO START AND HOW OFTEN? A DECISION ANALYSIS

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Background: Pneumococcal polysaccharide vaccine (PPV) to prevent invasive pneumococcal disease (IPD) has been recommended for all persons aged ≥65. Routine vaccination of younger adults and scheduled revaccinations are being considered. Recent changes in the epidemiology due to the childhood conjugate vaccine complicate vaccine policy decision making. **Methods:** We used a Markov model to examine seven strategies: no vaccination, one vaccination (age 50 or 65), two vaccinations (50/65 or 65/80), three vaccinations (50/65/80) or four vaccinations (50/60/70/80) in US population cohorts. We used NHIS data to segment cohorts into comorbid illness groups to model differential vaccine effectiveness and IPD rates based on age and comorbidity. CDC data (Active Bacterial Core surveillance) were used to model serotype specific IPD rates. A Delphi panel supplied estimates of PPV efficacy based on age of and time since vaccination, number of previous PPV, and comorbidities. We report preliminary results here, with effectiveness measured as the relative proportion of IPD cases prevented.

Strategy	IPD/10 ⁵	RR	IRRR
No PPV	790	1.0	–
65 only	736	0.93	6.9%
50 only	716	0.91	2.7%
65/80	703	0.89	1.8%
50/65	662	0.84	6.0%
50/65/80	629	0.80	4.9%
50/60/70/80	593	0.75	5.8%

Results: With no vaccination, IPD risk from age 50 onward was 0.79%. The table gives the number of IPD cases, relative risk (RR), and the incremental relative risk reduction (IRRR) associated with each PPV strategy. Results were sensitive to the experts' low end estimate of vaccine effectiveness, significantly decreasing incremental RRR's, particularly for revaccination at age 80. The cost effectiveness for two doses at age 50 and 65 is \$38,851 and for four doses at ages 50/60/70/80 is \$54,451. **Conclusion:** Routine PPV starting at age 50 with a second dose age 65 is indicated by this analysis due to the reduction in IPD burden. Additional revaccinations at 10 intervals further reduces disease but at a higher price.

LB-39 Vaxfectin[™] as an Adjuvant for Plasmid DNA-based Pandemic Influenza Vaccines and for Protein-Based Inactivated Influenza Vaccines

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Background: Inactivated vaccines against H5N1 influenza viruses are poorly immunogenic in humans without an adjuvant. We are developing plasmid DNA (pDNA)-based vaccines formulated with Vaxfectin[™] which target H5 and conserved proteins. In addition, we are testing whether Vaxfectin[™] can enhance the immunogenicity of a conventional trivalent inactivated influenza vaccine (TIV). **Methods:** For pDNA studies, lethal challenges were conducted using highly virulent H3N2, H1N1, and H5N1 viruses. Consensus sequences for M1, M2, and NP were created as vaccine representatives of contemporary human influenza strains. For TIV studies, a range of Vaxfectin:protein ratios were tested. **Results:** Both NP and M2 plasmids were required for protection and formulating with Vaxfectin[™] provided superior protection at low pDNA doses. H5N1 lethal challenge studies were conducted to assess the protective efficacy of Vaxfectin[™]-formulated pDNA vaccines encoding NP + M2, H5, or all three pDNAs. H5-containing vaccines conferred complete protection against death and weight loss in both mice and ferrets. NP + M2 alone conferred 88% protection against death with moderate weight loss. Our initial experiments with TIV + Vaxfectin[™] show enhanced efficacy as measured by higher HI antibody titers compared with TIV alone. **Conclusion:** The heterosubtypic protective effects of Vaxfectin[™]-formulated NP + M2 against H1, H3, and H5 viral challenges support the inclusion of NP + M2 as the foundation of a pandemic vaccine that also includes an HA component to optimize protection. With these supporting data, preparations are underway for Phase 1 clinical testing. In addition, Vaxfectin[™] appears to be a promising adjuvant for conventional inactivated influenza vaccines and may fulfill the critical need to dose spare H5 vaccines in the event of a pandemic.

LB-40 A Prototype Immune Complex Vaccine Platform Successfully Adapted to Hemagglutinin (H5) as a Potential H5N1 HPAI Vaccine

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Background: Previously, we have produced and tested a highly protective prototype vaccine platform directed against anthrax (Prototype Anthrax Lethal Toxin Vaccine Technology Provides Protection From Death In The Anthrax-Sensitive Fisher 344 Rat Model; IDSA 2004, Martin et al.). We now report this technology adapted to H5 as a prototype against H5N1 highly pathogenic avian influenza. **Method:** To create the vaccine, an immune complex was constructed around a baculovirus-produced rH5 immunogen. White Rock poultry strain chicks were hatched, placed in barrier units at 14 weeks of age and immunized at 15 weeks. 48 birds were immunized by either intramuscular injection (IM) or intranasal infusion (IN) of the vaccine in 300 µL aliquots. Within each of the two groups, doses of vaccine containing either 0.5, 2, 5 or 15 µg of H5 immunogen was administered to six birds in each group. Total N=48 birds plus 4 sham controls. Plasma samples were collected before and 30 days after vaccination. Samples were evaluated for anti-H5 antibodies by ELISA. **Results:** By day 30, 20/24 IM birds showed positive for anti-H5 antibodies, compared to 9/24 IN birds. Reproducible and robust antibody titers were detected in birds immunized with the lowest 0.5 µg H5 inoculum. Based on the ELISA used, positive birds vaccinated with the lowest dose, 0.5 µg, reported 1.5 to 22.5 µg of anti-H5 antibodies per mL plasma. **Conclusion:** This prototype vaccine appears potent against the H5 antigen, as was its precursor against anthrax, thus demonstrating wide application potential. Hemagglutination inhibition assays will determine if the baculovirus glycosylated H5 provides the proper antigen recognition for the vaccine platform. Regardless of this outcome, the efficacy of this technology has once again been demonstrated and warrants close investigation since this dose is some 15 times less than previously reported to produce detectable antibodies. Egg antibody determination will enhance and refine these results.

LB-41 Characteristics and Vaccine Coverage Related to Medical Indications for Pneumococcal Vaccination among Adults Aged 18–64 years, United States, 2004 National Health Interview Survey

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Background: Persons with certain underlying conditions are at increased risk of hospitalization or death associated with pneumococcal infection. The pneumococcal polysaccharide vaccine (PPV) is recommended for persons aged ≥ 65 years and 2–64 years with high-risk conditions. **Methods:** We analyzed data from the 2004 National Health Interview Survey to identify adults in the U.S. aged 18 to 64 years with high-risk conditions. The association of selected socio-demographic and access-to-care variables with high-risk status was assessed. PPV coverage by individual high-risk conditions was evaluated. **Results:** Approximately 29.6 million adults aged 18–64 years (16.4%: 95% confidence interval = 15.9%, 17.0%) reported high-risk conditions indicated for PPV; the prevalence of high-risk conditions was higher among persons aged 50–64 years (29.1%) compared to those aged 18–49 years (12.5%). Heart diseases were the most common high-risk conditions for persons aged 18–49 years (6.5 million) and 50–64 years (7.0 million). PPV coverage among high-risk persons aged 18–64 years was 29.2% for diabetic adults, 19.1% for persons with heart disease, 26.9% for persons with chronic lung diseases excluding asthma, 32.4% for persons with renal disease, 22.6% for adults with liver disease, and 21.3% for persons with cancer vs. 6.4% for adults with no identified high-risk condition. **Conclusions:** PPV coverage varies among persons with different high-risk medical conditions, but is uniformly unacceptably low for all high risk groups. The results of this study underscore the importance of designing and implementing effective strategies for improving PPV coverage.

LB-42 Successful Treatment of Hospital-Acquired Acute Hepatitis C

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Background: Treatment of hepatitis C virus (HCV) infection results in high rates of sustained virologic response (SVR) when initiated in the acute phase of infection. Healthcare-acquired clusters of HCV infections offer an opportunity to learn more about efficacy of therapy in acute HCV infection. **Methods:** Seventeen cases (16 patients and one provider) were identified in an outbreak investigation of a cluster of HCV infections among patients who had received perioperative anesthesia care from an HCV infected provider. Patients without contraindications were offered 24 weeks of treatment with pegylated interferon $\alpha 2a$ (PEG-IFN- $\alpha 2a$) 180 μ g SQ weekly (7 patients) or PEG-IFN- $\alpha 2b$ 1.5 μ g/kg SQ weekly (8 patients), with ribavirin 800mg to 1200mg daily. The mean time from the date of surgery until treatment was 179 days (range: 77 to 373 days). The primary endpoint was undetectable HCV RNA 24 weeks after termination of treatment (SVR). **Results:** The median age was 29 (range 15–82). Twelve were Caucasian (71%), 5 were African-American (29%), 13 were male (76%) and 4 were females (24%). Six had acute hepatitis, and 11 were asymptomatic. One patient who was treatment-eligible except for pregnancy had no evidence of HCV infection when reevaluated after delivery. Fourteen patients with acute HCV infection and the HCV-infected provider (86% genotype 2a, 7% genotype 1b, 7% mixed infection) initiated treatment. Two patients discontinued therapy after 30 days due to side effects; one achieved SVR in spite of this (genotype 1b), while the other (genotype 2a) had a late relapse following early spontaneous clearance. Two were lost to follow-up, and treatment is planned in one. Eleven of 15 patients completed 24 weeks of therapy, and 10 of these achieved SVR (all genotype 2a). **Conclusions:** Identification of persons with hospital-acquired HCV infection allowed early intervention with antiviral therapy which can effectively limit progression to chronic hepatitis C.