- 1141 PATHOGENESIS OF TOXIC SHOCK SYNDROME (TSS). Marian E. Melish, Kanitha S. Frogner, Shirley A. Hirata and Miko S. Murata. University of Hawaii School of Medicine, Department of Pediatrics, Honolulu, Hawaii.

Toxic Shock Syndrome Toxin I (TSST-I), a reliable marker for TSS staph, has not yet been proven to be the sole responsible toxin. We and others find that TSS staph, but not other *S. aureus*, inoculated in subcutaneous chambers in rabbits → shock and death with renal, hepatic, muscular and hematologic changes of TSS. TSST-I is produced in chamber by 4 hr, reaching peak of 7.4 µg/ml (≈120 µg total) at 47 hrs. TSST-I is disseminated to blood with peak of 3.4 ng/ml and excreted in urine over 48 hrs. To determine if TSST-I alone is responsible for changes seen in the infection model, we injected purified TSST-I into chamber and produced a syndrome indistinguishable from live infection and clinical TSS. Hypotension, renal impairment, hypocalcemia and death occurs by 25 hrs at dose of 300 µg and a chronic, ultimately fatal illness lasting 8 days with profound renal failure, hypocalcemia and multiorgan dysfunction occurs at a 150 µg TSST-I depot. At the higher dose, TSST-I peak conc. in chamber is 17 µg/ml, plasma levels peak at 9 ng/ml and cumulative urine excretion is 18 to 30 µg. Lower dose → peak chamber conc. of 10 µg/ml and peak plasma levels of 2 ng/ml. These plasma values equal those found in human TSS. Passive administration of TSST antibody blocks TSS in this model while anti-endotoxin (J5) does not. TSST-I is therefore the toxin responsible for the major physiologic changes of TSS and does not require host-derived endotoxin for its action. Anti-toxin therapy has promise in therapy of established human TSS.

- 1142 PHARMACOKINETICS AND DOSAGE REGIMEN OF TOBRAMYCIN IN NEWBORN INFANTS BELOW ONE KILOGRAM BIRTH WEIGHT. Milap C. Nahata, Dwight A. Powell, Diane E. Durrell, Marcia A. Miller, Ohio State University Colleges of Pharmacy and Medicine, Children's Hospital Department of Pediatrics, Section of Infectious Diseases, Columbus, Ohio.

Current dosing recommendation of tobramycin 2 mg/kg/12 hr, in newborn infants does not consider birth weight as a variable. Because of limited data, we studied tobramycin kinetics in eight infants (gestational age 24-30 wk; postnatal age 3-6 d; birth weight 600-970 g) receiving tobramycin, 2.5 mg/kg IV every 18-24 hr for presumed or proven sepsis or meningitis. After 2-4 days of therapy, the blood samples were collected at 0, 0.5, 1, 2, 4, 6, 8, 12, 18 and 24 hr and analyzed by EMIT. Tobramycin peak and trough serum concentration ranged from 6.0 to 8.4 and 1.3 to 2.4 µg/ml, respectively. Trough serum concentration exceeded 2 µg/ml in 75% at 12 hr and 20% patients at 18 hr. Total body clearance ranged from 0.55 to 0.81 (0.69±0.11) ml/min/kg; apparent volume of distribution ranged from 0.44 to 0.71 (0.56±0.12) L/kg; and elimination half-life ranged from 7.7 to 11.7 (9.5±1.4) hr. These data suggest that tobramycin, 2.5 mg/kg every 18-24 hr may be adequate to achieve effective and potentially safe serum concentration in low birth weight infants.

- 1143 LABORATORY ASSESSMENT OF PROTECTION AGAINST H. INFLUENZAE TYPE B (Hib). Valerio M. Novelli, Jean Taylor-Wiedeman, Philip Brunell, Lisa Frierson. Dept. of Pediatrics, U.T. Health Science Center, San Antonio, TX.

The protective level of anti-polyribosylribitol phosphate (PRP) antibodies has been estimated to be 0.15 to 1 µg/ml. An enzyme-linked immunosorbent assay (ELISA) to detect anti-PRP antibodies was used to test 20 cord sera treated with staphylococcal protein A to remove IgG. A seronegative range of <0.02 (delta optical density) was determined by adding 3 SD to the mean. 13/20 untreated cord sera were positive; 0/10 were seropositive by 7-14 months of age reflecting a loss of passively acquired antibody. 2/14 children 16-24 months of age were seropositive probably reflecting infection with Hib. 3/7 of the younger children were seropositive after a single dose of PRP conjugated to diphtheria toxoid (PRP-D) while all were positive after a booster dose. Following a single dose of PRP-D all 9 of the older group were seropositive while only 1/3 PRP recipients were positive. The ELISA value equivalent to 1 µg/ml of anti-PRP, was found in 4/7 younger vaccinees and 8/9 older vaccinees receiving PRP-D and only 1/4 older vaccinees receiving PRP. By defining the seronegative range it was possible to determine which vaccinees, who had lost maternal antibody and not experienced natural infection, had a T cell dependent (IgG) response. PRP-D appeared to be more effective in older than younger children and probably more effective than PRP (24/90 recipients have been tested). By comparing various methods of measuring immune response with protection, a more precise laboratory definition of "protection" can be developed.

- 1144 ACUTE MASTOIDITIS: DIAGNOSIS AND COMPLICATIONS. John W. Ogle, Brian A. Lauer. Departments of Pediatrics, University of Colorado School of Medicine and The Children's Hospital, Denver, CO.

30 patients with 31 episodes of acute mastoiditis (AM) were identified by discharge diagnosis and studied retrospectively. There were 17 females and 13 males. The age range was 3 months to 14 years, with 43% less than 24 months. All had abnormal tympanic membranes. 27/31 had swelling above or posterior to the ear which deviated the pinna. Findings on mastoid films were clouding-16, osteomyelitis-2, and normal-7. In 14 patients organisms were recovered from normally sterile sites. The most frequent were *Pneumococcus*-5, group A streptococcus-3, *Haemophilus*-2, and anaerobes-3. 15/30 patients did well without surgery. In 23/31 episodes the patients were afebrile and much improved within 24 hours of hospitalization. Of these 23 episodes, 8 were treated surgically and 15 medically. In 8 episodes fever lasted longer than 24 hours. In 3/8 an intracranial complication had occurred; in 2/8 fever responded to a change in antimicrobials. Complications which occurred in 11/30 patients were subperiosteal abscess-7, meningitis-4, osteomyelitis-2, facial nerve palsy-1, and subdural and brain abscess-1. Of 6 patients with neurological complications, 4 had no external sign of AM on physical exam. In the absence of a complication, most patients will respond to antimicrobials within 24 hours. The absence of mastoid swelling does not rule out AM.

- 1145 A GROUP B STREPTOCOCCAL (GBS) EXTRACT INDUCES NEUTROPHIL AGGREGATION AND NEUTROPENIA. Thomas A. Olson, Gerald W. Fischer, Val G. Hemming, and David A. May-bee, Dept of Peds, USUHS, Bethesda, MD and WRAMC, Washington, DC

Neutropenia has been commonly associated with neonatal GBS infections. The cause of the neutropenia, however, is poorly understood. The intravenous infusion of a trichloroacetic acid extract of GBS (GBS-TCA) into 1-6 day old lambs (dose 1 mg/kg), induced a rapid decrease in peripheral blood PMNs (0 time-3.1 X 10³/mm³ + 0.5 vs 2.2 x 10³/mm³ + 0.7, 5 min after infusion; p < 0.01, n=6). Neutropenia persisted throughout the 20 min post infusion period. Pulmonary histology demonstrated extensive accumulations of PMNs in the interstitial space after GBS-TCA administration. To determine if GBS-TCA could induce aggregation *in vitro*, PMNs were isolated from adult and cord blood specimens. Aggregation was measured using a Siencco aggregometer. The maximal change in light transmission (ΔT) over 1 min was obtained from aggregation curves. Serum alone did not aggregate PMNs. However, GBS-TCA incubated in serum (1 hr) induced prompt PMN aggregation. A typical dose response occurred and was maximal at 10 mg/ml (GBS-TCA in serum-mean ΔT 12.3% ± 2.8 vs GBS-TCA in PBS-mean ΔT 2.5% ± 2.1; p < 0.001, n=8). These data demonstrate that cell free GBS products may induce PMN aggregation in serum. PMN aggregates may be nonspecifically removed from the peripheral circulation by entrapment in the pulmonary vasculature. GBS induced PMN aggregation may play an important role in the neutropenia and pulmonary manifestations commonly associated with neonatal GBS infections.

- 1146 PNEUMOCOCCAL ANTIGEN DETECTION IN CHILDREN AT RISK FOR OCCULT BACTEREMIA. Edward O'Rourke, Pauline Martin, Ann Maccone, Alison Anderson, Donald Goldmann, George Siber, Donna Ambrosino. Children's Hospital and Dana-Farber Cancer Institute, Boston, MA

We prospectively evaluated latex agglutination tests for rapid detection of pneumococcal antigen in young children at risk for occult bacteremia. Using the Bactigen and Wellcogen kits, we examined serum and/or urine from 1153 children (ages 6-36 months) presenting to the CH emergency room for evaluation of fever ≥39°C.

None of the 16 children with pneumococcal occult bacteremia had antigen detected in their serum by either test. Six of these patients had urine available and one was positive by Bactigen. Urine was concentrated by minicon filters for two of these patients and did not increase the sensitivity. Eight additional patients with positive blood cultures and focal pneumococcal disease (3 meningitis, 3 pneumonia, 2 cellulitis) were evaluated. One child had detectable serum antigen by both tests and one child by Wellcogen alone. Quantitative blood cultures were available for 6 patients; antigen was present in the one patient with high grade bacteremia (>4000 cfu/ml) and absent in the five with low grade bacteremia (1-18 cfu/ml). We found no correlation between pneumococcal serotype and sensitivity of tests. Of 1153 children evaluated, 16 had positive antigen tests (6 serum, 8 urine, 2 both) without positive blood cultures. None of these children had evidence of pneumococcal disease by clinical evaluation or repeat cultures.

We conclude that neither pneumococcal antigen detection test was sufficiently sensitive or specific to recommend as a screening test for occult bacteremia.