●961 DELETERIOUS EFFECT OF IMMUNE GLOBULIN IN THE TREATMENT OF H. INFLUENZAE B INFECTION IN INFANT RATS.

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Despite optimal antibiotic therapy, H. influenzae b (Hib) meningitis often causes permanent sequelae and occasionally death. We examined the efficacy of immune globulin (IG) therapy alone or in combination with antibiotic therapy in the infant rat model of Hib infection. Two IG preparations were used: (1) Sandoglobulin (IVIG), at 5% protein, containing 25µg PRP Ab/ml and (2) Bacterial Polysaccharide Immune Globulin (BPIG) prepared from donors immunized with Hib vaccine, at 16% protein containing 450 µg PRP Ab/ml. Infant rats were challenged with 10^3 Hib ip resulting in 99% bacteremia and 88% meningitis at 18h. Therapy (Rx) given sc was Ceftriaxone (CEF; 75mg/kg qd), IVIG (15ml/kg qd), BPIG (15ml/kg qd) and combinations of CEF + IG's. Blood and CSF were cultured 24h and 72h after Rx.

Therapy(n)	HIB Ab# (ng/ml serum)	Bacteremia (after Rx)	Meningitis (after Rx)	Death (time after Rx) (<24h)	(3d)
Saline(24)	<25	22/22	22/22	2/24	14/24
CEF(25)	<25	0/25*	0/25*	0/25	2/25*
IVIG(20)	34	11/13 }	12/13 }	7/20 }	13/20}
BPIG(19)	2800	5/13* }	10/13 }	6/19 }	10/19}
CEF+IVIG(21)	84	0/15*	0/15	6/21}	8/21}
CEF+BPIG(19)	1500	0/17*	0/17	2/19	2/19*

24h after Rx by RIA * $p<0.05$ vs saline group }$p<0.05$ vs CEF group

CEF was highly efficacious at clearing bacteremia and meningitis and reducing mortality ($p<0.01$). BPIG alone but not IVIG alone cleared bacteremia; neither cleared meningitis. Both IG's produced more early deaths than saline, and IVIG + CEF resulted in higher mortality than CEF alone. We conclude that IG alone had poor efficacy in the therapy of Hib infection and may increase the early mortality rate. In addition, IVIG + CEF is less efficacious than CEF alone in the treatment of Hib infection in rats.

●962 PEDIATRIC HUMAN IMMUNODEFICIENCY VIRUS (HIV) INFECTIONS: FACTORS INFLUENCING CASE IDENTIFICATION AND PROGNOSIS.

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Since 1981, 131 children with HIV infection have been diagnosed at Jackson Memorial Hospital in Miami, Florida. 123 cases are perinatally acquired. 55 of these children meet the CDC criteria for diagnosis of AIDS. Only 3 children are clinically asymptomatic.

The number of cases has dramatically increased over the past year, representing 42 cases or 32% of our total population. Screening of family members of infected adults or children have resulted in 15 new cases. Twenty one cases are younger siblings of the infected index child. Twenty four women have delivered 42 subsequent infants between October 1981 and December 1986. 21 (50%) of these infants are infected and account for 17% of our total cases. 50 children have died, with 50% of deaths occurring in the first 12 months of life. Longitudinal investigation of these children reveals that development of Pneumocystis carinii penumonitis, decreasing immunoglobulin G levels and depletion of T4 cells were associated with a poorer prognosis. Children with LIP*alone have a better prognosis than those with opportunistic infection. Mortality is 25% versus 66% ($X^2=10.45$ p .005).

Prevention of pediatric HIV infection will depend on identification of infected women and appropriate education and counselling regarding risk of pregnancy.

*Lymphoid interstitial pneumonitis

† 963 IMMUNOLOGIC PRIMING OF INFANTS WITH A SINGLE DOSE OF H. INFLUENZAE TYPE B (Hib) POLYSACCHARIDE-N. MENINGITIDIS OUTER MEMBRANE PROTEIN (PS-OMP) CONJUGATE VACCINE.

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In a trial of its immunogenicity, 13 children from 2-6 months of age received a single dose of PS-OMP conjugate vaccine. Titers of antibody against Hib capsular PS(PRP) one month after immunization were determined at Merck Laboratories by radioimmunoassay with the use of ^{125}I extrinsic labelled antigen. All 13 children had <0.4µg of antibody/ml before receiving PS-OMP vaccine and 6/13 (46%) had ≥1.0µg/ml after a single dose (geometric mean: 5.2µg/ml).

Because additional PS-OMP vaccine was not available and previous work suggested that the conjugate vaccine may prime infants to respond to plain PRP we administered PRP vaccine to all 7 children with <0.1µg of antibody/ml after PS-OMP vaccine and to 4 children with >1.0µg of antibody/ml after PS-OMP vaccine. Of the 7 children with <1.0µg of antibody/ml (geometric mean: 0.4µg/ml), 4 (57%) developed ≥1.0µg of antibody/ml (geometric mean: 5.2µg/ml) one month after "boosting" with PRP vaccine. Of the four children with >1.0µg of antibody/ml after PS-OMP vaccine, the titers of antibody one month after "boosting" with PRP vaccine increased in one child (from 19.6 to 31.2µg/ml), changed little in one child (from 1.0 to 1.1µg/ml) and decreased in two children (from 1.3 to 0.4µg/ml and from 1.5 to 0.4µg/ml, respectively). We conclude that the antibody responses of young infants to a single dose of PS-OMP conjugate vaccine vary: titers of antibody ≥1.0µg/ml develop in some infants, others are primed to achieve ≥1.0µg/ml after subsequent "boosting" with PRP vaccine, while others fail to have a substantial response.

●964 RETICULOENDOTHELIAL CLEARANCE OF TYPE III GROUP B STREPTOCOCCI OPSONIZED WITH TYPE III SPECIFIC MONOCLONAL ANTIBODIES OF IgM OR IgG2a ISOTYPES IN AN EXPERIMENTAL RAT MODEL.

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We showed previously that type specific monoclonal antibodies of IgM and IgG2a isotypes afford excellent protection against group B streptococcal (GBS) infection in a neonatal rat model. The protective efficacy of these antibodies is associated with an enhanced neutrophil response in neonatal rats. In the present studies we investigated splenic, hepatic and lung uptake of type III GBS opsonized with ^{125}I labelled IgM or IgG2a monoclonal antibodies using neonatal as well as 8 and 17 day old rats. After inoculation of antibody treated GBS, 48 hour old rats demonstrated predominantly splenic uptake, greatest from 30 minutes to 4 hours. Little uptake occurred in the liver or lung at any time point. For infected 8 day rats, the spleen was the major site of uptake at 30 minutes but hepatic uptake predominated at 2 and 4 hours. Seventeen day rats, which are resistant to overwhelming GBS infection, demonstrated radiolabelled antibody treated bacterial uptake in equal amounts in the spleen, liver and lung at each time point. In contrast to younger rats, 17 day rats had peak uptake by 2 hours followed by a rapid decline at 4 and 8 hours postinfection. These studies indicate that the reticuloendothelial system is a major site for phagocytic clearance of GBS in neonatal rats and that it functions less efficiently than in older rats who do not die from GBS infection.

965 FATTY ACID METABOLISM IN REYE'S SYNDROME.

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We examined the oxidation of different chain length fatty acids in the leukocytes and the quantity of lipid peroxides in the plasma of Reye syndrome patients. We have found that the oxidation of [1-^{14}C] octanoic acid in homogenates of leukocytes from a patient with Reye syndrome (1.25 ± 0.09 nmol/mg protein/hr) was only 38 percent of the control (3.34 ± 0.07 nmol/mg protein/hr), whereas oxidation of [1-^{14}C] palmitic and [1-^{14}C] lignoceric acids was slightly increased. The rates of oxidation of [1-^{14}C] lignoceric and palmitic acids in Reye's Syndrome were 0.885 ± 0.004 and 0.032 ± 0.002 nmol/mg protein/hr respectively and for their controls were 0.661 ± 0.05 and 0.02 ± 0.004 nmol/mg protein/hr respectively. The level of lipid peroxides in the serum of two Reye syndrome patients in stage III was 4.42- and 3.04 times higher than the control level. Lipid peroxides and ammonia levels were higher in one patient during the period of active disease and subsequently came back to normal levels as the patient improved. These results suggest that impaired oxidation of octanoic acid and higher levels of lipid peroxides may contribute to the pathogenesis of cellular toxicity in Reye syndrome. Supported by grants from National Reye's Syndrome Foundation and NS 22476 from National Institutes of Health.

† 966 HAEMOPHILUS B OLIGOSACCHARIDE-CRM (HbOC) VACCINE: CONTINUING CLINICAL STUDIES.

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1347 injections of HbOC have been given to 784 children of 2-24 mos. Associated symptoms post-vaccination included T>38°C - 6%; local redness/warmth - 3%, swelling - 2% and were not affected by the child's age, ab titer or dose sequence. Ab assays include ^3H-HbPs RIA, anti-HbPs ab isotype, bactericidal (BC) activity. GMT of anti-HbPs ab titers, µg/ml (No. sera analyzed), after 25 µg dose(s) include:

Age (mos.) #1 Vax	Pre	2 mos. Post #1	2 mos. Post #2	1 mo. Post #3
1-4	0.17 (109)	0.51 (109)	10.36 (61)	22.14 (43)
	Pre	2 mos. Post #1	1 mo. Post #2	4,5 mos. Post #2
7-15	0.15 (212)	6.21 (212)	22.32 (176)	12.87 (76)
	Pre	1 mo. Post #1	3 mos. Post #1	6 mos. Post #1
16-23	0.21 (146)	16.11 (146)	15.04 (115)	10.44 (52)

Vaccination of children at 15-22 mos. substantially increased anti-HbPs IgG and BC activities; similar studies are being completed for vaccinated infants. It can be concluded that HbOC is a safe, effective vaccine against Hib disease for all aged children.