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SIMULTANEOUS ADMINISTRATION OF TWO LIVE INFLUENZA VACCINES. P.F. Wright, M. Bhargava, J. Thompson, D.T. Karzon. Vanderbilt University, Nashville.

Live, attenuated, intranasally administered influenza A vaccines are being actively evaluated for influenza protection in children. For practical and theoretical reasons, it is important to know if two influenza vaccine strains can be administered simultaneously. Towards this end, cold-adapted H1N1 and H3N2 vaccines at an equivalent dose ($10^{6.5}$ TCID₅₀) were mixed and administered intranasally to 18 doubly seronegative children. Nasal washes were collected daily for 10 days to document virus shedding. Virus was grown in the presence of type specific antisera to determine strains being shed. Plaques were picked at a terminal dilution and hemagglutinins and neuraminidases were characterized to detect reassortant (H3N1 or H1N2) virus. Clinically the simultaneous administration of vaccine was well tolerated with no increase in respiratory symptoms when compared to 4 placebo controls in the trial or to previous studies in which each vaccine strain was given independently. H1N1 virus shedding predominated particularly between days 6-10 when there were 44 instances of H1N1 virus recovery vs 19 instances of H3N2. Reassortant plaques were recovered with 3 H3N1 and 21 H1N2 plaques among 97 analyzed indicating the potential for influenza reassortment (a mechanism for emergence of new strains) in the human host. An HAI serologic response was shown to H1N1 in 13 (72%) and to H3N2 in 12 (67%) by 6 weeks after vaccination. This compares to 57% (50/87) seroconversion with the H1N1 vaccine and 85% (40/47) with the H3N2 vaccine when each was given alone. Two influenza strains of similar attenuation (each contain identical cold-adapted A/Ann Arbor/6/60 internal genes) may be given simultaneously with only minimal interference with H3N2 virus shedding and serologic response. This observation greatly increases the potential utility of these vaccines.

†1159

A PROSPECTIVE SEROEPIDEMIOLOGICAL SURVEY OF HERPES SIMPLEX (HSV) INFECTIONS IN A COLLEGE POPULATION. E. Wu*, J. Sayre, E. Wiesmeier, D. Bernstein, B. Visscher, Y. Bryson; UCLA Sch. Med., Los Angeles, Ca.

The true incidence of HSV2 infections in a young, sexually active population and its relationship to prior HSV AB status is unknown. Acquisition of HSV1 AB increases with age, inversely correlates with socioeconomic status, and modifies HSV2 infections. A prospective seroepidemiologic survey of HSV infections in a predominantly upper and middle class college population (658 enrolled mean age 20.2 yrs, 76% sexually active) without a history of genital HSV infection was initiated. Students were followed by active clinical surveillance and by 6 mos serology. After screening for HSV AB by immunofluorescence (IFA), type specific AB responses were studied by western blot analysis (WBA). To date 36.6% of 562 students had previous HAV AB by IFA. Seventy-six % (237/371) of those <age 21 were seronegative. No significant differences of gender, ethnicity, geography, income, type of or frequency of sexual activity between seropositive and seronegative groups were found. Of 226 serological FUPs at 12 mos (125 initially seronegative), 2 (1.5%) seroconverted asymptotically by IFA with HSV type 1 AB by WBA. Over 12 mos FU (562 students), 4 confirmed first episode symptomatic genital HSV outbreaks occurred (0.7%). Two had primary genital HSV (1 HSV1, 1 HSV2); 2 had first episode nonprimary (prior HSV1 AB) genital outbreaks; 1 had HSV1 virus isolated. In 29 FU sera (2 with prior HSV2, 27 with prior HSV1 AB), none have seroconverted to the respective HSV type asymptotically by WBA. In a susceptible, sexually active population in 12 mos FU, the incidence of symptomatic, genital HSV disease, particularly HSV2 disease, appears to be low.

●1160

LOW DOSE ENDOTOXIN (EN) AND FIBRONECTIN (FN) DEPLETION IN RATS: A MODEL OF REYE'S SYNDROME. M.C. Yoder, M. Yudkoff, J. Chatten, C. Stanley, K. Hummeler, S.D. Douglas, R.A. Polin. Dept. of Peds., Univ. of Pa. Sch. Med., Philadelphia, PA.

Plasma FN concentrations are decreased in Reye's Syndrome. FN depletion in experimental animals potentiates the systemic effects of EN. The purpose of this study was to determine the effect of FN depletion on the response to endotoxin. Sprague-Dawley male rats (n=30) were entered into 4 groups: (C) Control (D5W IV), (F) FN depletion (1% gelatin 15 mg/kg IV), (E) E. coli EN (0.2 mg/kg IP), and (FE) 1% gelatin (15 mg/kg IV) followed in one hour with EN (0.2 mg/kg IP). Serum ammonia (NH₃), free fatty acids (FFA), lactate, glucose, SGOT and SGPT were obtained prior to fasting (baseline), 12 hours after onset of fast, and upon sacrifice (12 hr after test injection). At sacrifice, liver, spleen and brain specimens were fixed for fat staining, routine histology, and electron microscopy (EM). Plasma chemistry values were unchanged by fasting.

RESULTS:

Group	Baseline			12 Hrs After Test Injection		
	C	E	FE	C	E	FE
NH ₃ mM/L	62.0	64.1	65.5	84.1	124.5	207.8*
FFA mM/L	0.9	0.8	1.1	1.2	1.7*	1.6
Lactate mM/L	1.8	2.0	1.9	2.0	3.5	3.8

FE resulted in significant increases in NH₃ and FFA over control (p<.05*). FE and E revealed increased microvesicular hepatic fat (without necrosis) compared to fasting controls. EM demonstrated loss of cristae and matrix disruption in hepatic and splenic but not brain mitochondria. SGOT, SGPT, and serum glucose were unchanged from baseline levels in all groups. Thus, FN depletion and EN administration produces metabolic, histologic, and ultrastructural changes similar to Reye's Syndrome.

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ZOONOSIS IN EARLY INFANCY. Mary M. Zabala, Ranjendra Singh, Tahira Bokhari, Roger W. Cooper, Anthony Minnefor, James M. Uleske (Spon. by Franklin C. Behrle). University of Medicine and Dentistry of New Jersey. Department of Pediatrics. Newark, New Jersey.

Zoonoses during early infancy have been infrequently reported in the pediatric literature. The spectrum of the disease in such affected infants ranges from mild disease such as gastroenteritis to the unusual forms involving the CNS. During a 16 month period, 3 infants less than 3 months of age were seen; 2 patients ages 4 and 8 weeks respectively, developed septicemia and meningitis with blood and CSF cultures growing *Pasteurella multocida*. Their hospital courses were complicated by seizures and delay in the identification of the organism. They were both treated with 2 weeks of IV antibiotics. Both infants had an unremarkable recovery with no neurological sequelae. A 3 week old infant was diagnosed to have *Yersinia enterocolitica* sepsis and was treated with appropriate IV antibiotics. All 3 patients had close direct contact with pet dogs and one infant had a household adult contact whose nasopharynx grew *Pasteurella multocida*. Epidemiological, clinical and serologic data obtained emphasized the high degree of association with household pets, especially dogs. The 3 cases reported have provided documentation of the occurrence of zoonoses in normal, non-immuno-compromised infants and stresses the need to develop preventive measures in protecting the infant from exposure to such infectious agents.

●1162

AUGMENTED ANTIBODY (Ab) RESPONSES IN INFANTS ADMINISTERED A NEW HAEMOPHILUS INFLUENZAE TYPE B CAPSULAR POLYSACCHARIDE (PRP) DIPHTHERIA TOXOID CONJUGATE VACCINE (PRP-D). John M. Zahradnik and Lance K. Gordon, Baylor College of Medicine, Dept. of Microbiology & Pediatrics, Houston, TX Connaught Labs., Inc. Swiftwater, PA (Spons. by W.P. Glezen).

PRP-D, a hapten-carrier conjugate containing 20µg PRP/0.5cc, has previously been shown to be highly immunogenic in adults and young children (<18 mo.) given 2 doses. Ab responses in sera taken 1 mo. post-vac were evaluated in 90 infants administered PRP-D, PRP, or placebo at ages 3, 5 & 7 months. No significant adverse reactions occurred. Anti-PRP responses for the vaccinees shown (Farr assay with SK standard) developed in 14%, 53%, & 100% of PRP-D vaccinees respectively, following the first three doses as compared to 0, 7%, and 60% in PRP vaccinees respectively. A sequential increase in the mean anti-PRP titer was seen in the PRP-D group and final mean titers were 5-fold greater than that following PRP:

Vaccine	Mean anti-PRP titer 1mo. following vaccination:			
	Pre-vac	1st	2nd	3rd
PRP-D	66 ^a (14) ^b	92 (15)	200 (15)	1301 (5)
PRP	46 (14)	30 (14)	20 (14)	240 (5)
Placebo	59 (14)	57 (14)	33 (14)	48 (2)

a-Nanogram Ab/ml b-Number of volunteers

This new PRP-D conjugate vaccine appears to have resulted in an enhanced response since the seroconversion rate and Ab titers were higher than those seen following PRP.

METABOLISM

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EFFECT OF 1, 25 DIHYDROXYCHOLECALCIFEROL (1,25 D₃) ON LEUKOCYTE GAMMA GLUTAMYL TRANSPEPTIDASE (GGTP). Carolyn Abitbol, Michael Freundlich, Gaston Zilleruelo, Kersti Thodenius and Jose Strauss. Department of Pediatrics, University of Miami, Miami, Florida.

GGTP is a membrane enzyme necessary in the transfer of some amino acids into the cytosol as a primary event in protein synthesis. Mechanisms of 1,25 D₃ in promoting protein synthesis in corporal cells need further elucidation. Circulating leukocytes offer a readily accessible modality for assay of cellular enzyme activity. We, therefore, studied the effects of 1,25 D₃ on growth and GGTP activity in young male Wistar rats. The animals were allowed ad libitum feeding of standard Purina Lab Chow during a period of 21 days. Vitamin D supplemented animals received daily injections of 50 pMol 1,25 D₃ in 0.2 ml polyethylene glycol (PEG). Control animals were injected with 0.2 ml PEG alone. At sacrifice, leukocyte GGTP was assayed. Growth parameters and enzyme activity are shown below: (Mean±S.D.; *Indicates Difference p<0.05)

	Growth		GGTP
	ΔWeight/Body (g)	ΔTail Length(cm)	
Control (10)	128±20	4.5±.9	173±230
Vit.D (10)	149±15*	4.8±1.2	1160±1721*

A tenfold increase in GGTP activity was noted in 1,25 D₃ supplemented animals. Our study suggests an induction of GGTP activity in leukocytes by 1,25 D₃ which may, in turn, influence corporal protein synthesis.