†1147

THE ENHANCING EFFECT OF INTERFERON- β AND γ ON THE KILLING OF LEISHMANIA TROPICA MAJOR IN HUMAN MONOCYTES IN VITRO.

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Native human interferon (IFN) β or γ added to human monocytes in culture increased their leishmanicidal effect on intracellular Leishmania tropica major amastigotes. This effect was dose dependent and was apparent if the IFN was added either prior to or after infection of the monocyte cultures with the promastigote form of the parasite. IFN- γ was shown to be approximately three times more effective than IFN- β . Recombinant IFN- γ showed similar effects. In addition, IFN- γ increased H_2O_2 production from human monocytes in culture in a dose dependent manner. Monocytes which had been infected with L. major amastigotes produced less H_2O_2 than did the control uninfected cultures.

IFN- γ (i.u./ml)	% infected monocytes	n mol H_2O_2 /mg protein
		control infected
-	52 $\pm$ 4	46.8 $\pm$ 10.8 29.4 $\pm$ 1.3
50	22 $\pm$ 6	159.0 $\pm$ 14.7 34.7 $\pm$ 1.3
100	10 $\pm$ 2	192.4 $\pm$ 17.4 85.5 $\pm$ 14.7
250	6 $\pm$ 4	261.9 $\pm$ 8.0 17.4 $\pm$ 5.3

Monoclonal antibody to IFN- γ abrogated both its effect on the leishmanicidal capacity and its increase of H_2O_2 production by the monocytes. These results suggest that IFN- γ may be of therapeutic value in cutaneous leishmaniasis.

†1148

PLASMA FROM RABBITS WITH EXPERIMENTAL GROUP B STREPTOCOCCAL (GBS) SHOCK PROMOTES POLYMORPHONUCLEAR LEUKOCYTE (PMN) AGGREGATION (AGG) IN VITRO. Keith J. Peevy, Peter Panus, Stephen A. Chartrand, Robert C. Boerth, and Gesina L. Longenecker, University of South Alabama, College of Medicine, Departments of Pediatrics and Pharmacology, Mobile, Alabama.

The accumulation of PMNs in lung tissue in response to intradermal injection of heat-killed GBS has been previously demonstrated (Ped Res 17(4)338A(1810)). Non-specific accumulation of PMNs in the uninfected lung suggests that PMNs may be altered to enhance pulmonary trapping of PMNs. To study the possible contribution of PMN AGG to the evolution of pulmonary PMN trapping, we examined the aggregatory response of human PMNs to plasma from rabbits before (TIME I) and after (TIME II) a 50% fall in mean arterial pressure was induced by infusion of heat-killed GBS (10¹² organisms/kg). AGG was quantitated using a Payton aggregometer and Omniscrite recorder. Human PMNs were isolated from heparinized venous blood and resuspended in Hank's Balanced Salt Solution (10⁴ cells/ul) for AGG studies. The mean value of PMN AGG at TIME I was 5.8 units $\pm$ 1.7 (SEM), a value representing background AGG response in the system, which was not significantly different from saline controls. PMN AGG at TIME II (plasma from rabbits with GBS-induced shock) had a mean value of 17.3 units $\pm$ 3.8 (SEM) and was significantly greater than that at TIME I ($p < .05$). Our data 1) show that plasma from animals in septic shock promotes PMN AGG and 2) suggest that PMN AGG may contribute to non-specific pulmonary trapping of PMNs.

†1149

PERSISTENCE OF ANTIBODY IN CHILDREN IMMUNIZED WITH HEMOPHILUS INFLUENZAE, B POLYSACCHARIDE (PRP) COMBINED WITH DTP VACCINE (PRP-DTP) AT 18 MONTHS OF AGE.

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PRP-DTP vaccine given to children at 18 mos. of age who have previously received this vaccine results in enhanced serum anti-PRP responses at 19 mos. of age, as measured by RIA. To assess the duration of elevated serum anti-PRP concentrations, antibody titers at 36-42 mos. of age in 31 prior recipients of PRP-DTP at 18 mos., 17 of whom had also received PRP-DTP in infancy, were compared with those at 19 mos. The mean GMTs (ug/ml) in the two groups did not change significantly in the interval.

Vaccine Groups in Infancy:	A) PRP-DTP	B) DTP
GMT at 19 M (95% CL)	9.36 (4.67-18.75)	1.18 (0.49-2.85)
GMT at 36-42 M (95% CL)	7.78 (4.72-12.81)	1.18 (0.43-3.23)

In groups A and B, anti-PRP titer decreases of twofold or more occurred in 4/17 and 6/14 ($p = 0.44$), respectively. The frequency of anti-PRP concentration ≥ 0.15 and ≥ 1.0 ug/ml at 19 mos. and at 36-42 mos. in each group did not differ:

[Anti-PRP]	Group A: 19M	36M	Group B: 19M	36M
> 0.15 ug/ml	17/17	17/17	13/14	13/14
≥ 1.0 ug/ml	17/17	16/17	8/14	7/14

These findings indicate that anti-PRP titers in 3 to 3½ year old children immunized with PRP-DTP at 18 mos. of age reflect immunological responses at that age; and for those achieving high titers at 19 mos., subsequent doses of PRP may not be necessary to sustain protection.

†1150

EFFECTS OF INHIBITORS AND ANTIBODY ON THE PULMONARY HYPERTENSIVE EFFECTS OF BOLUS GRP B STREP IN CONSCIOUS PIGS. Joseph Phillips; Raymond Lyrene;

Guillermo Godoy; Gwen Graybar; Elaine Barefield; Barry Gray; Jep Sams; Dept. of Ped. and Anesth., UAB, Bham, AL.

We have shown that heat-killed Group B Streptococci (GBS) cause dose-related pulmonary artery hypertension in chronically instrumented piglets. These responses are similar to those seen with gram negative bacterial endotoxins. Prostanoids and endorphins have been implicated as mediators of these responses. We tested the effect of a cyclooxygenase inhibitor, indomethacin; a thromboxane synthesis inhibitor, dazmegrel (UK-38,485); a leukotriene synthesis inhibitor, BW 540C; and an endorphin antagonist, naloxone on the response to a bolus of 5 x 10⁷ heat-killed GBS Type III (M 732) /kg. We also tested the effect of pre-incubating the GBS with high-titer, type-specific rabbit antibody.

Rx	Control	Indo.	Daz.	540	Nal.	Anti.
Δ Ppa(torr)	16.7	0.3*	3.0*	20.5	18.2	28.0*
SD	5.7	0.5	1.4	5.2	4.2	7.0

* $p < .05$, Dunnett's test with 1-way ANOVA

Neither leukotriene nor endorphin blockade affected the response. In contrast, both cyclooxygenase and specific thromboxane synthesis inhibition markedly blunted the GBS-induced pulmonary hypertension. This suggests that thromboxane A₂ mediates this response. Antibody coated organisms increased the response, suggesting antibody participation in this reaction. Further work will increase our understanding of the response to sepsis.

1151

TIME-RELATED POTENTIATION OF THE PULMONARY HYPERTENSIVE RESPONSE TO BOLUS GROUP B STREPTOCOCCI IN CONSCIOUS PIGS. Joseph Phillips; Raymond

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Infusions of Group B Streptococci (GBS) cause pulmonary hypertension in acutely instrumented lambs. We developed a chronic piglet model to further study this response. We placed a pulmonary artery electromagnetic flow transducer plus pulmonary, aortic, left atrial and central venous catheters. After > 4 days recovery, animals were given 1 x 10⁸ heat killed GBS type III (strain M732)/kg as a rapid bolus each weekday for 10 days. The table shows the mean $\pm$ SD change in mean pulmonary artery pressure (Ppa) for each day.

DAY	1	2	3	4	7	8	9	10
Δ Ppa(torr)	8	9	8	9	15	19	21	18
SD	2	2	1	1	4	4	3	6

N=3; F=12.407; $P < .001$ by 2-way ANOVA

The average increase in Ppa on days 8, 9 and 10 was 230% greater than on days 1, 2 and 3. Other variables changed little, if any, and returned to baseline within 1-2 minutes while pulmonary pressure was elevated for 6 $\pm$ 1.5 minutes on days 8, 9, and 10. These data document a previously unreported time-related potentiation in the pulmonary hypertensive response to bolus GBS in conscious piglets. Investigations into the mechanism(s) underlying this response are under way. Further work with this model may improve our understanding of the host response to infectious challenge.

1152

ENHANCED RAT AND HUMAN NASOPHARYNGEAL (NP) COLONIZATION BY PILIATED (+) HAEMOPHILUS INFLUENZAE TYPE B (Hib). Michael E. Pichichero, Porter W. Anderson,

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The pili of Hib appear to increase adherence to human epithelial cells (EC) in vitro. Yet, previous experiments in rats have led some authors to suggest that piliation does not implement colonization by Hib. From 35 strains, + populations were selected by adherence to human erythrocytes (RBCs). One strain, H305, simultaneously acquired an increased adherence to rat RBCs (rHA+) and buccal EC. In contrast to other strains such as Eag +, which does not agglutinate rat RBC's, H305 in + form, was more effective than the - form in the NP colonization of 21-26 day old infant rats by intranasal inoculation. After the + inoculum, however, the organisms cultured in the nasal washes were found to be p-:

Inoculum	colonized rats/ total	cfu/20 μ l nasal wash	HA+ colonies/ total tested
10 ⁵ H305 p-	4/9*	----	0/40
10 ⁵ H305 p+	10/10*	----	0/100
10 ⁹ Eag p-	7/12	----	0/70
10 ⁹ Eag p+	5/12	----	0/50
10 ¹⁰ H305 p-	7/8	15+ (2.7-83)	0/58
10 ¹⁰ H305 p+	10/10	78+ (29-209)	0/100

* $p < .025$; †geometric mean ($\pm$ 1SD) $p < 0.02$

Human experiments, now ongoing, indicate that pili of Hib enhance NP colonization in vivo. Furthermore, human data suggest that + Hib resist being washed off EC while giving rise to progeny that are more likely to be cultivable by nasal washing.