Attachment 2.4.1 (a) : 2

and other monokines have been hampered by artefactual stimulation during cell separation.

42 A DETRIMENTAL ROLE FOR IL-5 DURING ACUTE TOXOPLASMA GONDII INFECTION

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The role of IL-5 during *T. gondii* infection was examined. IL-5-/- mice infected orally with *T. gondii* were less susceptible to infection than WT mice as demonstrated by reduced mortality rates and pathology changes in their small intestines 8 days post-infection. Splenocytes and mesenteric lymph node (MLN) cells derived from IL-5-/- mice produced similar levels of IL-12, IFN-???IL-4, IL-10 and nitric oxide (measured as nitrite) as those derived from WT mice when stimulated with TLA (*Toxoplasma* lysate antigen). WT mice, but not IL-5-/- mice had raised levels of eosinophils in their peripheral blood between days 5-8 post infection. Administration of L-NAME, (from day 4 post infection), increased mortality rates in both IL-5-/- and WT mice, indicating a protective role for nitric oxide during the early stages of oral *T. gondii* infection. These results demonstrate a detrimental role for IL-5 during the early stage of oral infection with *T. gondii* which is associated with increased small intestine pathology and eosinophilia.

43 STRAIN SPECIFICITY OF ANTI-PFEMP1 ANTIBODIES IN A COHORT OF GHANAIAN CHILDREN

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Antibodies directed against parasites derived-erythrocyte surface antigens (PfEMP1) during and following clinical malaria episodes are very important protective immune responses that may control *Plasmodium falciparum* infections. Individuals respond to Plasmodium falciparum infection by making antibodies to PfEMP1 that agglutinate infected erythrocytes in a variant specific manner.From a longitudinal cohort study of malaria in children from Dodowa in the Dangbe West district of the Greater Accra region of Ghana, where malaria transmission is perennial with considerable seasonal variations, peaking during and immediately after the rains, parasites obtained over the ten months period were cultured until they reached the schizont stages and used to analyse specificity of anti-PfEMP1 specific antibodies in the plasmas using flow cytometer. The results revealed anti-PfEMP1 specific antibody levels to be lower and remained stable over the study period against the heterologuos parasites as compared to the levels against the homologous parasites. The anti-PfEMP1 specific antibody levels were found to correlate with age and there were common and rare isolates in the study area. These results thus suggest anti-PfEMP1 antibodies to be specific and with common and rare isolates in the study area.

44 ROLE OF ANTIOXIDANTS IN FILARIAL INFECTION

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Introduction: *W. bancrofti* is a multicellular organism and its elimination is most likely to be by extracellular mechanisms mediated by free radicals. Changes in blood levels of free radicals may therefore account for the wide spectrum of clinical manifestations observed in this infection.

Objective: Measure levels of antioxidants in the blood (as a measure of oxidants), in asymptomatic microfilaraemics (*mf* +ve cases), endemic normals (EN), and non-endemic controls(NEC).

Methods: Blood levels of catalase, glutathione peroxidase (GPX) and superoxide dismutase were assayed in 29 *mf* +ve cases, 29 matched endemic normals defined by negative micropore filtration and ICT tests, and 29 non-endemic controls. Endemic normals were selected from the same household as the cases, and blood samples of cases and endemic normals were obtained at the same time. Analysis of blood was done within 6 hours of collection.

Results:

Mf+ve cases			*EN*			*NEC*		
M:F	*Age;mean(SD)*		*M:F*	*Age;mean(SD)*		*M:F*	*Age;mean(SD)*	
12:17	38yrs (16)		16:13	34yrs(14)		16:13	33yrs(14)	
Mean	*SD*	*Range*	*Mean*	*SD*	*Range*	*Mean*	*SD*	*Range*
Catalase(x 103ku/l)								
0.82	0.17	0.5-1.15	0.89	0.24	0.51-1.27	0.61	0.19	0.31-1.1
NEControl vs mf +ve: p<0.001*, NEControl vs EN: p<0.001*, mf+vs EN: p=0.2*								
Superoxide dismutase(x 102u/ml)								
2.2	0.52	1.6 - 3.4	2.02	0.58	1.3 - 2.9	2.2	0.2	1.7-2.5
NEControl vs mf +ve: p=0.7*, NEControl vs EN: p=0.2*, mf+vs EN: p=0.2*								
Glutathione peroxidase(x103u/l)								
5.6	1.9	3.1-10.8	7.8	2.1	4.6-12.4	5.7	1.8	2.9-10.2
NEControl vs mf +ve:p= 0.8*, NEControl vs EN: p<0.001*,mf+ve vs EN: p <0.001*								

Conclusions: Serum GPX levels were significantly higher in endemic normals (reflecting high GPX related oxidant levels in their blood) when compared to levels in asymptomatic microfilaraemics and non-endemic controls. This may enable endemic normals to resist filarial infection.

45 A ROLE FOR NITRIC OXIDE IN TRANSMISSION-MODULATING IMMUNITY TO MALARIA

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Immunity to the sexual stages of malaria may operate against both intraerythrocytic gametocytes in the mammal and extracellular forms in the invertebrate, but little is known of cellular involvement. Previous work *in vitro* has shown nitric oxide (NO) to exert a concentration-dependent modulation of *Plasmodium falciparum* exflagellation, the production of male gametes that occurs in response to the lower temperature and increased pH of the ectothermic *Anopheles* midgut. At concentrations of NO generated by activated macrophages, 50-150 μM, which are largely cytostatic to asexual malaria parasites *in vitro*, NO reversibly suppresses male gamete development. Levels of NO produced constitutively by endothelial cells, 0.1-0.5 μM, increase the rate and total number of exflagellations. We have now determined directly the effect of NO on infectivity for the mosquito by allowing *An. stephensi* to feed on gametocyte-rich cultures of *P. falciparum* through a membrane feeder. Dissections immediately after the infective blood feed, and at 10 and 17 days post infection, allowed