Microbial invasion, tissue injury, immunologic reactions, and inflammatory processes induce a constellation of host responses collectively referred to as the acute phase response. The response is characterized by changes in metabolic, endocrinologic, neurologic, and immunologic functions. The purpose of this nonspecific acute phase response appears to be early protection and preparation for a prolonged defense. There is evidence that pre-exposure to some inflammatory cytokines, such as IL-1, protects by non-specific mechanisms against subsequent bacterial challenge. Mostly, investigations have involved bacterial or viral infections and there is little data describing parasitic diseases. It was therefore considered of interest to study the effect of parasitic infections on hepatic acute phase response during experimental malaria and filariasis.

**Experimental Malaria**

Malaria continues to be one of the major killer diseases inflicting human race in tropical countries. Malarial infection induced toxicity is associated with a number of structural and functional alterations in different organs of the host, viz., liver, spleen and kidney. Hepatotoxicity has very widely been studied, since liver is the primary organ of homeostasis in mammals. Several attempts have been made at structural and biochemical levels to understand the mechanism of hepatotoxicity in malaria infected hosts. However, its complications remain a prominent cause of morbidity and mortality in the developing
In the present study, experimental erythrocytic *P. berghei* malaria was induced in normal *M. natalensis* by intraperitoneal inoculation of 10 parasitized erythrocytes in a single injection. A parallel batch of healthy animals was used as control. Percent parasitaemia was evaluated by staining a thin smear of infected blood with Giemsa stain.

Animals with three different levels of parasitaemia, viz., 10-15%, 30-35% and 55-60% were sacrificed under light anaesthesia. A portion of liver was homogenized in cold for biochemical estimations of lipid, protein, carbohydrate and transaminases. Serum was collected for monitoring transaminases. The gross changes observed in *P. berghei* infected *M. natalensis* include: enlargement of liver (hepatomegaly) and change of colour from chocolate to dark brown or, even black at the peak parasitaemia (55-60%). A significant increase in wet liver weight (*P* < 0.001) and continuous decrease in body weight of *M. natalensis* during *P. berghei* infection was observed. Biochemical studies *in vivo* revealed that during *P. berghei* erythrocytic parasitaemia, the total protein content of liver decreased significantly by (13%), (26%) and (40%); total carbohydrate by (16%), (47%) and (77%); total glucose by (47%), (76%) and (81%); total glycogen by (51%), (80%) and (88%); GOT by (25%), (36%) and (45%); GPT by (8%), (13%) and (18%); cholesterol by (6%), (11%) and (21%) at 10-15%, 30-35% and 55-60%
parasitaemia, respectively.

Total lipid and lipid peroxide content of liver during *P. berghei* erythrocytic parasitaemia increased significantly. The total lipid content increased by (15%), (40%) and (82%) while lipid peroxide levels increased by (118%), (250%) and (334%) at 10-15%, 30-35% and 55-60% parasitaemia, respectively.

*P. berghei* erythrocytic parasitaemia also led to increased levels of serum transaminases: SGPT increased by (62%), (86%) and (188%) while SGOT increased by (21%), (66%) and (86%) at 10-15%, 30-35% and 55-60% parasitaemia, respectively.

The findings presented above showing loss of body weight, increased protein catabolism, glycogenolysis, hepatomegaly and fatty infiltration in the infected liver at higher parasitaemia suggest that *P. berghei* infection may lead to acute phase response. Sera from *P. berghei* infected mastomys, when analysed by crossed immunoelectrophoresis, showed presence of two major acute phase proteins viz., alpha-2 macroglobulin and alpha-1 acid glycoprotein. Since liver is the major organ for the synthesis of plasma proteins, synthesis of positive and negative acute phase protein markers by hepatocytes was monitored at > 40% erythrocytic parasitaemia. While synthesis of alpha-2 macroglobulin and alpha-1 acid glycoprotein increased, that of albumin was suppressed during *P. berghei* erythrocytic parasitaemia. These findings support the view that during *P. berghei* infection, an acute phase protein response is generated.
where synthesis of some proteins, termed positive acute phase proteins increases, whereas levels of the negative markers e.g., albumin and cytochrome P-450 decline.

**Experimental Filariasis**

More than 300 million people are affected with filariasis worldwide. The chronicity of filariasis influences a broad range of host's immune responses. *Acanthochaelonema viteae* infection in mastomys is an example of murine asymptomatic filariasis with distinct prepatent, patent and latent stages. *A. viteae* infection in mastomys was used to evaluate acute phase reaction during prepatent, patent (with circulatory microfilariae) and latent (amicrofilariaemic) stages. Acute phase proteins started to appear during prepatent stage, while patent stage infection showed peak levels of acute phase reactants. During latent stage, the level of acute phase reactants declined. These results were further confirmed by following the synthesis of acute phase proteins in vitro during patent stage of *A. viteae* infection. The results demonstrated induction of two major acute phase proteins viz., alpha-2 macroglobulin and alpha-1 acid glycoprotein, and decreased level of albumin. When some liver specific enzymes viz., cytochrome P-450, arylhydrocarbon hydroxylase (AHH) and glutathione-s-transferase (GST) were assayed during different stages of *A. viteae* infection, cytochrome P-450 levels were observed to decrease by (18%), (22%) and (37%) respectively during prepatent, patent and latent stages.
of infection, while AH and GST levels did not increase significantly. Thus, it may be concluded that during *A. viteae* infection, an acute phase response is generated where peak levels of acute phase proteins could be detected during patent stage, while cytochrome P-450 could be negative acute phase marker.

**In vitro model to monitor acute phase response**

In the present study efforts were made to design a suitable model for studying the differentiated functions of hepatocytes *in vitro* and to use this model to study the effect of conditioned medium (from the splenocytes isolated from *A. vitheae* and *P. berghei* infected mastomys) on the synthesis of acute phase proteins by hepatocytes *in vitro*. Mastomys hepatocytes were isolated by *in situ* perfusion technique described by Seglen and cultured in synthetic medium and DMSO. Maintenance of hepatocytes in primary culture was performed according to Enat, et al. Extra cellular matrices viz., collagen, poly-l-lysine and fibronectin were used as culture substrates to improve the attachment and survival of the cultured hepatocytes.

Hepatocytes, cultured during the present study, retained their differentiated characteristics for at least one week. It was observed that after 7 days culture in synthetic medium plus DMSO and Se, substantial number of hepatocytes remained viable and consumed measurable oxygen. The cells were found to synthesize and secrete albumin at a rate comparable to freshly isolated hepatocytes. Similarly, use of defined medium helped in
maintaining cytochrome P-450 activity for at least one week. Once these differentiated functions of hepatocytes were maintained, the studies were extended to follow the synthesis of acute phase proteins in vitro under different experimental conditions. Culture supernatants from splenocytes (prepared during patent stage of *A. vitearae* infection and at > 40% *P. berghei* erythrocytic parasitaemia when added to hepatocyte monolayers, led to increased synthesis of alpha-2 macroglobulin and alpha-1 acid glycoprotein and depressed the synthesis of albumin. Thus in light of the above findings, it may be concluded that an acute phase response is indeed generated during *P. berghei* and *A. vitearae* infections in mastomys.