Malaria still remains a world wide public health problem, both in tropical and subtropical countries causing a considerable morbidity and mortality, especially in rural areas near the hilly regions and semiforest area. Its impact is so high that in sub-saharan Africa only about 100 million infections and one million annual deaths amongst children occur (Bruce-chwatt, 1987). Malaria, a protozoal infection is caused by the parasite belonging to the genus 'Plasmodium' (Laveran 1880). Sternberg (1884), defined malaria as an unknown poison of telluric origin, that causes periodic fevers. Human beings are infected by four species of Plasmodium, among which P.falciparum, poses the greatest danger by causing death due to its life threatening complications like cerebral malaria, black water fever and pulmonary oedema. Mostly children, pregnant women and unexposed travellers from non-malarious areas are affected with P.falciparum in endemic area. The bite of female anopheles mosquito acts as the mode of transmission to the man. Infected human beings may carry the organism from endemic areas to areas where further transmission may occur via blood transfusion, shared needles among drug addicts and to the fetus through materno-fetal circulation in pregnant women.
at the time of delivery or maternal fetal transfusion, (Dover and Shultz 1971, Singal et. al. 1977, Lefavour et. al. 1980).

The life cycle of human malarial parasite is complex and involves two phase of development namely invertebrate (mosquito) and vertebrate (human) hosts. The infective forms (sporozoites) are injected into the host by the bite of female anopheles mosquito. The sporozoites migrate to and invade the parenchymal hepatocytes, multiply and result in the development of exo-erythrocytic or pre-erythrocytic stage. Merozoites thus, released either reinfect liver cells or enter red blood cells (rbc), followed by asexual stage of the parasite i.e. gametocytes which are infective to mosquitoes.

MALARIA AND PREGNANCY:

Malaria infection, particularly P. falciparum during pregnancy is associated with many years along with fetal complications (Goth 1881).

Malaria during pregnancy, apart from causing acute morbidity, chronic illness or ill health and anaemia, can also cause abortion, preterm labour, intrauterine fetal death and low birth weight (Clark 1915; Blacklock and Gordon 1925b; Bruce-chwatt 1952;
Malarial morbidity and mortality is higher in pregnant women than in nonpregnant women (Walton 1949; Gilles et al. 1969; Brabin 1972; Bruce-chwatt 1983), particularly primigravidae are more susceptible to *P. falciparum* than multigravidae (Kortman 1972; Campbell et al. 1980; McGregor et al. 1983). Transmission of malaria to pregnant women may be stable or unstable.

**Unstable Malaria:**

This is characterised by a marked variability in incidence and is found in regions like India, South East Asia, Western Pacific and South America. *P. falciparum* and *P. vivax* are the important and frequent parasites. Malaria during early pregnancy is generally associated with high rate of abortion and fetal death, whereas if acquired during third trimester still birth, premature labour and maternal death. Women of all parities are equally susceptible to malaria. Since transmission of disease is intermittent so immunity is poorly developed (Bray and Anderson 1979, Brabin 1983, McGregor 1984, WHO 1986).
Stable Malaria:

This refers to the heavy transmission of malaria and occurs all round the year. *P. falciparum* is the important parasite causing repeated attacks, resulting in the development of considerable amount of immunity. Even then, pregnant women remain at high risk. Primigravidae are more susceptible than multigravidae. Incidence of infection is higher during 4th and 5th month of pregnancy (W.H.O. 1986).

Maternal Malaria:

The impact of unstable malaria on pregnant women was first studied by Wickramasuriya (1937). Malaria occurs frequently in pregnant women leading to deleterious effects like maternal death, high rate of abortion, still birth, and premature delivery (Wickramasuriya 1937; Vanhung 1951).

Lawson (1967), reported that pregnancy exerts an adverse effect on the course of malaria or during malaria. Acquired immunity against malaria is liable to break down as marked by decreased ability to limit parasitaemia. Both parasite rate and densities were higher during pregnancy and febrile attacks were common during third trimester. Pregnant women do suffer from
cerebral malaria. It was also reported that anaemia was the prime cause of morbidity in pregnant women which in turn was aggravated by malaria. Malaria assumes an extraordinary severe form in pregnant women leading to abortion, premature labour, intrauterine fetal death or growth retardation while transplacental infection of fetus is extremely rare in indigenous population of endemic areas.

Menon (1972), analysed 37 pregnant Malaysian women suffering from malarial infection. He observed abortion in 60% of infection in early pregnancy whereas late pregnancy results in maternal death, premature or still birth. Hyper-pyrexia and anaemia were the dominant clinical features found in pregnant infected women and were the precipitating cause of abortion. They further observed that depression of haemoglobin levels in association with parasitaemia were substantially higher in first pregnancy and diminishes progressively as parity increased (Gilles et al. 1969; Menon 1972). Menon (1972) also described two congenitally acquired infections in new borns within 24 hours after birth each due to P. vivax and P. falciparum (McGregor 1983). However, Clark and Chaudhari (1988b) found TNF (Tumor Necrosis Factor) to an important factor for anaemia in malaria. It (TNF) also causes erythrophagocytosis and dyserythropoiesis, a
components of anaemia. The differential response of pregnant women to malaria is due to loss of age dependent or acquired immunity against it. This hypothesis seems to be attractive but needs further information.

There have been relatively few attempts to establish a convenient animal model of malarial pathogenicity associated with pregnancy. VanZon (1984) and his colleagues and Odoula et.al. (1982) have used P.berghei in the pregnant mice and indicated that as in human, malaria was more severe in pregnant mice and was associated with high rate of abortion. The offsprings were of low birth weight and had enlarged spleen but did not come to know the precise reason for such observations.

VanZon et.al. (1982) documented that malaria infection was more virulent in pregnant mice. This was due to loss in previously existing immunity during pregnancy, particularly in the second half of pregnancy which was due to increase in plasma corticosterone. This fact, production of corticosterone during pregnancy was further confirmed by adrenalectomy (before pregnancy) which prevented the production of maternal corticosterone. Thereby, abrogating the loss of immunity during pregnancy.
It has been observed that large variation exists regarding the loss of acquired immunity. VanZon et al. (1985) demonstrated that a considerable proportion of mice loose their acquired immunity against P. berghei during first pregnancy. Immune parous mice had better immune status than virgin mice. The risk of loss of immunity during subsequent pregnancy was greatly reduced as marked by reduced parasitaemia and maintenance of immunity was less dependent on spleenic functions. The establishment of improved immunity was due to the presence of proliferating parasites in subsequent pregnancy. Immunity or immune reactivity was improved even after chemotherapeutically treatment. Improved immunity after pregnancy was a consequence of a reconfontration. VanZon and his co-workers (1986) have demonstrated that spleen cells from immune mice exhibited significantly enhanced proliferative response to parasitized reticulocytes as compared to normal spleen cells. The specific response of spleen cell to malarial antigen was decreased in pregnant immune mice as compared to non-specific response to the PHA. Further, it was observed that addition of normal mouse serum to spleen cell cultures of immune mice depressed both PHA and specific proliferative response whereas serum of pregnant mice exerted stronger inhibition than
nonpregnant mice. Charcoal adsorption of mouse sera, eliminated the serum dependent immunosuppression from normal as well as pregnant serum. This decreased response to malarial antigen was due to serum corticosterone.

Several studies have indicated the profound influence of malaria during pregnancy both in human (McGregor et al. 1983; McGregor 1984, 1986) and P. berghei mice model (VanZon et al. 1980a, b, 1984, 1986; Odoula et al. 1986) resulting in high degree of abortion. The offspring of malarious mice were of low birth weight and had enlarged spleen.

Incidence of Malaria During Pregnancy:

Prevelance rate of malaria in pregnant women is different as compared to non-pregnant women. In Sierra Leone alone the prevelance rate was 30% in pregnant women as compared to 12% in non-pregnant women (Walton 1949). Pingoud (1969), from West Nigeria observed 47% of prevelance rate of parasitaemia in pregnant women as compared to 22.7% in nonpregnant women.

Gilles et al. (1969) from Nigeria have reported 22.2% parasite rate in pregnant women than 8.6% in nonpregnant women. It was also reported that 31.8% prevelance rate of parasitaemia in pregnant women in
Kenaba (Gambia) as compared to 25.9% in nonpregnant women during 1961 to 1975. During an investigation in a hyperendemic area of Western Kenya with known prevalence of chloroquine resistant parasite, Steketee et al. (1987) demonstrated that primigravid women had parasite prevalence rate twice that of multigravid women (32%), whereas multigravid women aged between 14-18 years had an intermediate prevalence rate of 50%. Studies by Vleugels et al. (1987 and 1989) from Kenya (holo endemic area) reported higher parasite rate and density in primigravidae as compared to multigravidae. They found 59% parasite rate in primigravidae as compared to 40% in multigravidae, thereby indicating further the susceptibility of primigravidae to malaria, having higher prevalence rate and parasite densities, more profound anaemia and more marked reduction in birth weights of infants as compared to multigravidae (Lawson 1969; McGregor 1978; McGregor et al. 1983, McGregor 1984, 1986; Brabin et al. 1988). Recently, Brabin et al. (1988) from Papua, New Guinea, reported 40% parasite rate in pregnant women as compared to 33% in nonpregnant women.

The study conducted by Lehner and Andrew (1988) in highly endemic area of Papua New Guinea, have shown entirely a different observation which was not in consistent with previous studies. They found that
The prevalence rate of malaria in pregnant women (29.4%) was not significantly greater than in nonpregnant women (24.7%).

Further most important question arises that, is there any difference in the susceptibility to malaria according to gestation or gestational period? Brabin (1983) observed that pregnant women mainly primigravidae were more susceptible to malaria infection in early second trimester and after 24 weeks of gestation. It was also observed that there was either increased or severe malarial infection at the time of delivery. Kortmann (1972) and Bray and Anderson (1979) observed that in puerperium period both the parasite prevalence rate as well as density remained same and no further increase in susceptibility occurred. Study by McGregor (1984) from Western Kenya revealed that prevalence of malaria infection in both primigravidae (85.7%) and multigravidae (51.7%) occurred at 13 to 16 weeks of gestation while infection rates at delivery and immediate postpartum remained or became equal to levels in nonpregnant women. He also concluded that the pattern of infection in pregnancy was comparable to that observed in infants or young children.
Parasite Density:
Malarial immunity largely depends on the number of parasites in the blood (Brabin 1983). In most of cases the number of parasites per unit volume of blood was greater in pregnant than in nonpregnant group. It is clearly known that primigravidae have highest densities as compared to multigravidae and it decreases progressively with increasing parity (Bray and Anderson 1979). Pingoud (1969) and Kortman (1972) observed that its density occurred before 24th or 25th week of gestation and it varied between 1500-3200 parasites/cubic-mm. This corresponds to the period of high infection rates. Similar findings were also observed by Campbell et.al. (1980). In P.falciparum infected pregnant women the parasite density was 68960/cubic-mm than in nonpregnant women (3808/cubic-mm). In P.vivax infection also, it was significantly higher in pregnant women (3564/cubic mm) than in nonpregnant women (1949/cubic-mm).

Placental Parasitation or Placental Malaria:
Placental malaria has been found to be relatively frequent even in malarious endemic areas. Earlier workers have shown that placental malaria and peripheral malaria were entirely different from each
other and no correlation existed between two (Reinhardt et al. 1978, McGregor 1984). One of the oldest study on placental malaria has clearly demonstrated that parasitaemia in maternal placental blood were twice in number as could be found in peripheral maternal blood (Clark 1915). It was also observed that heavy placental malaria could even occur in the absence of febrile illness in Nigerian women.

Blacklock and Gorden (1923) in Sierraleone observed that placental parasitaemia was more frequent than in peripheral blood. McGregor et al. (1983) suggested that new placental vasculature that develops in association with pregnancy offers the malarial parasite especially *P. falciparum*, to bind to endothelial cells during late intra erythrocytic development, a means of evading immune response at least until the new vasculature develops its own parasite killing mechanisms.

Various placental incidences have been reported from south Africa were: In Kenya 27% (Garnham, 1938), Uganda 16% (Jelliffe 1968), Gambia 31% (Logie et al. 1979), Senegal 21% (Anthonjiuz et al. 1979). High rate of placental malaria has been reported from primigravidae as compared to multigravidae (Archibald 1956, Spitz 1957, Cannon 1958, Reinhardt et al. 1978). McGregor et al. (1983) also investigated the incidence of placental
malaria and found it to be 20.2% in singleton birth, 18.6% in twins and none in triplets. The highest incidence of several placental infection occurs among semi-immune primigravidae. Placental malaria was less frequent in urban (12%) than in rural communities (27.1%) (McGregor 1983).

Placental Pathology:

Placental malaria has clearly documented the heavy infection in the placentae. The mechanism by which the aggregated parasites induce the abnormal structural changes in the placentae are not fully understood. However, the observations indicate that whilst intact malarial parasites did not cross the placental barrier under normal condition or circumstances they might none-the-less damage this organ and thereby jeopardize the matereno-fetal relationship. Bruce-chwatt (1954) demonstrated only parasite in infected placenta of pregnant women. Faulk et.al. (1978) have demonstrated a nonspecific trophoblastic damage in infected placentae. Studies carried by Galbraith et.al. (1980a) have visualized the malarial pigment in placental tissue mainly in the cytoplasm of trophoblast, intervillous spaces of placentae using either white light or modified flourescence microscopy. In the same year, Galbraith et.al. (1980b) also revealed the accumulation of large
number of monocytes in intervillous spaces, loss of syncitial microvilli and proliferation or thickening of trophoblastic cells. Later, Odoula et al. (1982) demonstrated similar findings in the placentae obtained from *P. berghei* infected mice. Walter et al. (1982) demonstrated malarial parasites and macrophages in the intervillous spaces of *P. falciparum* infected placentae along with deposition of malarial pigments. They also demonstrated presence of parasite in the intervillous spaces of placentae.

Odoula et al. (1986) studied both the histological and ultrastructural changes occurring in infected placentae at or near the term that revealed disruption of architecture with gross thickening, necrosis of cells in the labyrinthine zone and fibrosis of trilaminar trophoblast along with accumulation of inflammatory masses. Immunological studies on placentae have documented that in terms of IgG, IgM or IgA, no clear difference exist between infected or uninfected placentae.

In brief, the pathological changes induced by placental infection included large intervillous accumulations of parasitized erythrocytes malarial pigment, macrophages and monocytes in the intervillous
spaces of the placenta along with irregular thickening of the trophoblastic basement membrane with profusion of syncytiotrophoblasts into the basement membrane (Garnham 1938, Galbraith et al. 1980 a,b; Odula et al. 1982, 1986; Walter et al. 1982). It has also been reported that numerous macrophages and fibrinoid deposits occur in intervillous spaces (Watkinson et al. 1985), that were involved in the damage of syncytiotrophoblast (Walter et al. 1982). Placental pathology in malaria have been attributed to P. falciparum.

**Fetal Development:**

Localisation of parasites within placenta may jeopardize the materno-fetal relationship. Placental malaria or placental damage compromises fetal blood supply and leads to intra-uterine growth retardation. It has been reported that birth weight was significantly lowered if placenta contained malarial parasites or malarial pigments as compared to normal placenta (Cannon 1958, Kortmann 1972). However, the birth weight defects associated with placental malaria were greater in first born than in subsequent pregnancies (Reinhardt et al. 1978). Mean birth weights of singletons born to mothers with parasitized placenta were 55-310 gm less than those born to mothers without placental malaria (McGregor et al. 1983). No clear association has been established
between still birth and placental malaria in stable malarious areas (Bruce-chwatt, 1952). Clark and Chaudhari (1988a) observed that small doses of TNF caused fetal death in 16 day pregnant mice.

Till now, not even a single report is available which has demonstrated parasite in fetuses, because the placenta acts as a selective barrier. Studies conducted on congenital malaria are against this observation or hypothesis. Emajuowe et.al. (1979), Diallo et.al. (1983) and Marshall (1983), have revealed that the infected placentae might not be so impervious barrier and that although congenital malaria might be rare yet congenital infection might be relatively common. Therefore, suggesting that sequestration of *P. falciparum* in deep vasculature of placentas might actually be a beneficial adaptation (Miller 1969). The exact mechanism for sequestration of *P. falciparum* is not known. However, Udeinya et. al. (1981) demonstrated that "Knobbed" infected erythrocytes adhere to the endothelial cells by means of as yet unidentified receptors, wherein placental vascular bed contains a greater number of such receptors or receptors of greater affinity than do the endothelial cells of other organs like brain or kidney. The damaged, compromised placenta may allow passage of the parasite (or other factors such as immune complex) to prime the
fetus and give it the immune potential to survive the early post-natal malaria infection. Recently, Lehner and Andrew (1988) have reported malarial parasite in 14.6% cord blood samples of pregnant women and in 7.7% in the peripheral blood of infants.

**Malarial Immunity During Pregnancy:**

Relatively very few or scanty information is available pertaining to pregnancy induced immunological indices relevant to acquired antimalarial immunity. Even pregnancy is generally considered to be associated with immunosuppression and especially its cell mediated response which is altered characteristically than humoral immunity (Beer and Bellinghan 1972, Fabris et.al. 1977, Loke 1978). It was observed that pregnant women were capable of mounting both antibody and cell mediated immune responses to antigenic stimulation (Lederman 1984, Lewis et.al. 1986). The immunological alterations or interventions that explain the increased susceptibility to malaria infection during pregnancy, particularly first exposed pregnancy have not been determined.

**Humoral Immune Response:**

McGregor et.al. (1965) found no difference in the titres of malarial antibodies in the sera of pregnant and nonpregnant women further supported by the studies of
Gilles et al. (1969), Campbell et al. (1980) and Ibeaiako and Williams (1980). While Bray and Anderson (1979) recorded lower mean titres in association with pregnancy; the fall in antibody level, however, tended to be small and did not seem to occur in primigravidae. McGregor et al. (1970) noted that while mean concentrations of IgG and IgA (but not of IgM) were significantly lower in association with pregnancy, the sera of the gravid women still contained demonstratable precipitins to malarial antigens. Due to reduced level of immunoglobulins (Ig), these authors concluded that reduced immunity to malaria exists. However, Logie et al. (1973) observed higher concentrations of immunoglobulin in the plasma of Gambian parturient women associated with malaria - an observation suggesting that in pregnancy, women remain immunologically reactive to the stimulus of plasmodial parasitaemia. McGregor and Wilson (1971) examined sera from parturient women and their offspring resident in rural areas of the country found precipitin activity towards malarial antigens in 98% of maternal samples and in 97% of samples from newborns. Specific malarial antibody responses were not depressed in pregnant as compared to nonpregnant women (McGregor 1985). However, observations on antibody responses to infectious agents during pregnancy showed that the specific humoral response was generally normal (Brabin 1985). McGregor
(1984) observed higher levels of specific serum malaria (fluorescent) antibody levels in pregnant women than pregnant uninfected women. In addition to all these, the fluorescent antibody titres were also found to be depressed in pregnant, parasitaemic women (McGregor 1965, Bray and Anderson 1979). Stimson (1980) found that \( \alpha \) glycophosphoprotein inhibited the transformation of lymphocytes in mixed lymphocytes cultures as well as in PHA stimulated cultures. It was also found that sera of pregnant women too inhibited both chemotactic and phagocytic activity of phagocytes i.e. cells. Inspite such observation, the biological importance of diminished immune responsiveness in the pregnant women remains either unclear or ill understood.

Recently, Deloron et.al. (1989) investigated potential mechanism for pregnancy associated alterations in the immune response to malaria. The lowest antibody titres to RESA (Ring infected Erythrocyte Surface Antigen) in primigravid, intermediate titres in nulligravid and highest titres in multigravid \textit{P. falciparum} infected women but these titres were not associated with either parasite density or response to chloroquine treatment. However, levels of antibody to the synthetic peptides of the circumsporozoite protein (CS) increased with age and were higher in gravid than in
nulligravid women.

**Cellular Response or Cell Mediated Immunity:**

It is well established that cell mediated responses are dampened during pregnancy which prevents the rejection of allograft, i.e. fetus. This immune modulation in pregnancy is either due to rise in serum hormones like corticosterone cortisol levels or due to cellular changes. In primipara *P. falciparum* infected pregnant women, the level of cortisol has been found to be elevated as compared to multipara infected women (Vleugels 1984 & 1987). These hormones like cortisol / corticosterone would dampen immune responsiveness probably by redirecting T and B cell traffic from the circulation to the bone marrow from where they remain inertly unresponsive. The immuno deficency during pregnancy, especially that of the cell mediated arm would allow for higher parasitaemia and the consequent higher mortality and morbidity. VanZon et.al. (1982, 1985 a,b) have also shown that serum cortisol has a role in the regulation of malaria immunity during pregnancy in the murine malaria model. Only report available on cellular immune response is of VanZon et.al. (1986). They found that spleen cells from mice immune to *P. berghei* exhibited a significantly decreased response to malaria antigen in contrast to nonspecific response to a phytohaemagglutinin
Steroid in Malaria

Vleugel et al. (1989) demonstrated higher serum cortisol concentrations in women with patent malaria during pregnancy and the levels were higher before, during and after the malaria episode. They have observed that higher concentration of cortisol in primigravidae with patent infection was responsible for the cortisol related loss of immunity during pregnancy. This was in consistent with the observations made by Vanzon et al. (1982, 1985a) in P. berghei mouse model, wherein they showed that the serum glucocorticoid level could be responsible for loss of immunity during pregnancy and this was further confirmed in the Tanzanian's study (Vleugel et al. 1987).

Vleugel et al. (1986) revealed a linear increase of serum cortisol level during pregnancy which was higher in primigravidae than in multigravidae with a patent infection. In contrast, Vleugels et al. (1984) found cortisol concentration to be dependent on patent infection in both primigravidae and multigravidae, whereas in nulliparous the cortisol concentration was independent of with or without patent infection.
VanZon et al. (1985b) studied the role of ACTH in modulation of malarial immunity in mice and found that ACTH in mice induced a dose dependent increase of plasma corticosterone levels which resulted in loss of malaria immunity even in the immunised group of mice. This was equivalent to loss in immunity during pregnancy, suggesting thereby that the effector function of malarial immunity was sensitive to corticoides, at least during pregnancy. The naturally occurring serum corticosterone level appears to be an important regulator of malaria immunity, suggesting that plasma corticosterone was an effective regulator of the effector function of malarial immunity.

Recrudescence of Malarial Infection:

VanZon and Eling (1980) found that mice immunized against P. berghei by drug treatment of an initial infection tended to experience recrudescence (some proportion only) during pregnancy. They also observed that a portion of drug treated mice were resistance to P. berghei challenge infection and never experienced recrudescence during pregnancy, whereas some had recrudescence in the later period of pregnancy.

VanZon et al. (1980b) also observed recrudescence in majority of immunized mice prior to...
pregnancy had a fatal course of malaria. They also found that malarial immunity was improved after pregnancy.

VanZon et al. (1985) reported improved immunity after pregnancy, and was a consequence of a reconfrontation of a suppressed or convalescent immune system with proliferating parasites.

Prophylaxis:

Chemoprophylaxis is the main stay for residents in malarious areas free of chloroquine resistance for prevention of malaria in the travellers. Drugs like chloroquine phosphate, an Fansidar (pyrimethamine and sulphadoxine) quinine, primiquine, mefloquine are used as standard drugs for prophylaxis for all but are contraindicated during pregnancy. Wolfe and Cordero (1985) reported their experiences of a chorat of women who used chloroquine for chemosuppression of malaria during pregnancy. They observed that infants born to such women had birth defects like tetralogy of fallot and congenital hypothyroidism but the relative risk was only 1.34 with a 95% confidence limit of 0.25-7.3 (P=0.52).

Retinal damage and other defects have been reported with higher doses of chloroquine than recommended for malarial prophylaxis (Roes and Maibach...
1963) as observed during pregnancy. Hart and Naunton (1964) reported that treatment with higher dose of chloroquine during pregnancy resulted in spontaneous abortion or with a congenital defect, like hemihypertrophy, neonatal convulsions, cochleovestibular paresis, retinal pigmentary.

Lindqvist and Ulberg (1922) showed that chloroquine administered intravenously to pregnant mice crosses the placenta and accumulates in the eyes of the fetus at both early and late stages of development.

However, Kaseje et.al. (1987) tried to study the effect of malaria chemoprophylaxis during pregnancy, but did not succeed because women did not take the chloroquine due to fear of toxic reactions like pruritis and chloroquine related abortions or still birth. Spencer et.al. (1987) have observed that antimalarial chemoprophylaxis to pregnant women reduces the parasitaemia and increases haemoglobin (Hb) levels in both, infants as well as in mothers but this chemoprophylaxis could not prevent the transmission of parasitaemia to infants. Taufa (1978) observed that maternal chemoprophylaxis during pregnancy resulted in increased infant birth weight in malaria endemic areas. Whereas Odoula et.al. (1982) found that chloroquine
treatment of pregnant mice early after initiation of infection promptly reduced maternal parasitaemia, but pups birth weights were less than those of pups from uninfected mice. No adverse effect of drug treatment was observed in pups from uninfected mice that received equivalent chloroquine treatment.