indicates that the response in ova is an unreliable indicator of genetic resistance to cecal coccidiosis (Jeffers, 1978). Here, the property of resistance appears to be multifactorial with the genetic factors acting together to determine the susceptibility or resistance of an individual to an infection (Jeffers, 1978).

Rosenberg (1941) found that Barred Plymouth Rock and Jersey White Giant were more susceptible than White Leghorn, New Hampshire and Rhode Island Red chickens. Long (1968a) tested five strains of chickens for their susceptibility to five Eimeria species (E. acervulina, E. brunetti, E. maxima, E. mivati and E. tenella) using mortality, body weight gain and oocyst production to measure the effect on the host. He found that Light Sussex were more susceptible than Rhode Island Red chickens to E. acervulina, E. brunetti, E. maxima and E. mivati, but was not shown to be susceptible to E. tenella. On the other hand, Brown Leghorns and White Leghorns were more susceptible than the Rhode Island Red strain to all Eimeria species used. According to Jeffers (1978) these studies involved only a single strain of each breed of chicken, thus the results may not be generally applicable to the breed. Such differences in susceptibility between strains of a breed were confirmed by Buvanendran and Kulasegaram (1972) who found that the differences between strains within breeds were greater than those between breeds.

Jeffers, Challey and McGibbon (1970) measured the survival of 11-day old chicks of 13 non-interbred experimental laying bird lines after inoculation with 1×10^5 oocysts of E. tenella per chick. In this experiment the selected Wisconsin R (resistant) and S (susceptible) lines were also included, while none of the other lines had been intentionally selected for resistance to E. tenella infection. One of

these non-selected lines (D168sm) was more susceptible than the Wisconsin S line, while two (HN and RPL-15) were more resistant than the selected Wisconsin R line.

Studies on sex differences in resistance to coccidial infection done at the University of Wisconsin (Challey, Jeffers and McGibbon, 1968; Jeffers, Challey and McGibbon, 1969) with chickens of widely different genetic backgrounds showed little or no differential susceptibility to cecal coccidiosis. However, in tests with three generations of two inbred lines (H-299-ES-L) the females consistently showed significantly greater survival rates (Jeffers, 1978).

5. Gut flora

Although coccidia develop within the epithelial cells of the intestinal wall, several early investigators suggested that there is synergism between normal intestinal flora and coccidia (Visco and Burns, 1972a,b,c). Ryley (1975) has suggested that bacteria living in the intestinal lumen may influence the effect coccidia have on the host and that the therapeutic effect of sulphonamides may be related to this, especially when used later in the infection, rather than to its weak anticoccidial activity.

Ott (1937, cited by Visco and Burns, 1972b) was able to culture Escherichia coli, Staphylococcus albus and Salmonella pullorum from the liver of chickens infected with E. tenella, and suggested that secondary invasion by intestinal bacteria is an important aspect of the disease. Many recent investigators have shown that conventional chickens or chickens with mono or diflora infected with E. tenella develop more severe lesions than do their bacteria-free counterparts (Johnson, Reid

and Kemp, 1972; Bradley and Radhakrishnan, 1973; Viseo and Burns, 1972a, b). It was also reported that cecal coccidiosis enhances the growth of Clostridium perfringens and coliforms, especially E. coli, while the growth of Lactobacillus sp. was suppressed (Johnson and Sarles, 1948; Radhakrishnan, 1971, cited by Visco and Burns, 1972a). The reason of this bacterial fluctuation is not known (Bradley and Radhakrishnan, 1973). Decreased intestinal motility, intestinal injury and obstruction of the intestinal lumen have been shown to favour the growth of C. perfringens in various animals (Bradley and Radhakrishnan, 1973).

To determine if specific bacteria could be implicated in coccidial disease, Visco and Burns (1972b) introduced Streptococcus facealis, E. coli, C. perfringens and S. epidermidis to bacteria-free chickens in conjunction with E. tenella oocysts. They observed that the severity of the disease in bacteria-free chickens could be increased by introducing one or two species of these bacteria. Chickens receiving E. coli and/or C. perfringens in combination with E. tenella developed the most severe lesions of cecal coccidiosis.

Although several investigators believe that cecal microflora increase the severity of cecal coccidiosis, others (Clark and Smith, 1961, 1963; Clark, Smith and Dardas, 1962) have found that bacteria-free chickens are equally susceptible to E. tenella. According to Visco and Burns (1972c), these disparate results obtained by different investigators may be attributed to the different strains of chickens used and there susceptibility to coccidiosis. Using chicken lines highly susceptible to E. tenella, Visco and Burns (1972c) were unable to demonstrate differences in the severity of the lesions, irrespective of the presence or absence of gut flora.

6. Other Factors

Coccidial infections may also be potentiated by the presence of other disease agents (Long, 1973; Long 1978). Biggs, Long, Kenzy and Roots (1968) showed that infection with Marek's disease virus, a common lymphoproliferative disease of chickens, increased the susceptibility to Eimeria infections. The increased susceptibility is brought about by interference with the development of immune response to coccidial infection (Long, 1978). Similarly, chickens exposed to infectious bursal disease virus suffered more severely from a concurrent E. tenella infection (Giambrone, Anderson, Reid and Eidson, 1977).

The interaction of aflatoxin and coccidiosis has been investigated by many workers (Edds, Nair and Simpson, 1973; Wyatt, Ruff and Page, 1975; Ruff and Wyatt, 1978). Edds et al. (1973) and Ruff and Page (1975) found that aflatoxin increased the mortality from cecal coccidiosis. Mortality with the combination of E. tenella and aflatoxin began earlier and occurred at a higher rate than did mortality from aflatoxin or E. tenella alone (Wyatt et al. 1975). Chickens that received aflatoxin and E. acervulina gained significantly less weight than chickens receiving either aflatoxin or E. acervulina alone (Ruff and Wyatt, 1978).

The nutritional status of the host is documented to both increase and decrease the severity of coccidial infection (Fernando, 1981). Chickens fed 24% crude protein and infected with E. tenella had a higher mortality rate than those fed 16 or 20% crude protein (Sharma, Fernando and Summers, 1973). On the contrary, in E. acervulina the higher crude protein diet was protective against weight loss (Sharma et al., 1973).

Pathogenetic Mechanisms Operating in Coccidial Infections

Having reviewed some of the factors which affect the pathogenicity and outcome of a coccidial infection, the question as to why and how coccidia are harmful to their host will be discussed.

Some workers have suggested that toxins produced by the coccidia are responsible for many of the changes observed while others are convinced that hemorrhage, especially in E. tenella, is the major cause of death (Ryley, 1975; Ruff and Reid, 1977).

There is no doubt that the coccidia cause a variety of changes in their immediate environment, the host cell, on the structure and function of adjacent cells and tissues, and on extraintestinal tissue (Ryley, 1975).

1. Cytopathology

Several coccidial species cause cellular and nuclear hypertrophy, an increase in cytoplasmic components and displacement of host-cell organelles (Hammond, 1971; Sampson and Hammond, 1972; Fernando, 1973).

Fernando, Pasternak, Barrell and Stockdale (1974) observed an increase in DNA of the enlarged nuclei of E. tenella and E. necatrix infected cells. A six-fold increase in the DNA content of nuclei of chicken epithelial cells infected with second generation schizonts of E. tenella has also been reported by Beyer and Shibalova (1974, cited by Fernando et al., 1974). The developing schizonts of E. necatrix are very close to the host-cell nucleus and often indent it. The enlarged nuclei of cells containing mature schizonts have 2-4 very prominent large nucleoli and are very irregular in shape with many deep clefts and indentations (Fernando and Stockdale, 1974).

In addition to nuclear changes, an increase in the endoplasmic reticulum (Fernando and Stockdale, 1974) and number of mitochondria (Pal, 1967) have been documented. It was observed that the host mitochondria lined the parasitophorous vacuoles of schizonts of E. necatrix (Fernando and Stockdale, 1974), Toxoplasma gondii (Jones and Hirsch, 1972), E. alabamensis (Sampson and Hammond, 1972), E. perforans (Shoholyseck, 1963, cited by Fernando and Stockdale, 1974) and E. acervulina (Fernando, 1974).

Finger-like protrusions of host membrane surrounding parasitophorous vacuoles have been reported in E. necatrix by Fernando and Stockdale (1974) and in Toxoplasma gondii by Sheffield and Melton (1968). The function of these membranous infoldings is not well understood. They increase the surface area of host cell in contact with the vacuoles and may therefore play a part in the parasite's nutrition (Ryley, 1975; Fernando and Stockdale, 1974).

Thompson, Fernando and Pasternak (1979) showed that plasma membranes from cells harbouring 2nd generation schizonts of E. necatrix acquired an increasing proportion of gel-phase lipid during the later stages of schizont maturation. At the same time, the plasma membrane became more permeable and failed to exclude trypan blue (Thompson et al., 1979).

2. Enteropathology

Coccidia invade and multiply in individual epithelial cells in specific areas of the intestine and eventually destroy them. However, they seem to have no observable effect on immediately adjacent cells, but they do to a greater or lesser extent influence the overall

structure and function of the part of the intestine in which they develop (Pellerdy, 1974; Ruff and Reid, 1977; Ryley, 1975).

When a schizont matures, the actively motile merozoites rupture the schizont membrane and subsequently the host cell membrane. According to Ryley (1975) the destruction of isolated cells, well up in the villi, have little mechanical significance, except that adjacent cells will be slightly displaced. In severe infections of E. brunetti however, cells containing the mature schizonts penetrate the connective tissue of the villi leading to sloughing of epithelial cells covering the villi as well as the underlying villous core (Kheysin, 1972). In E. necatrix infections, parasitized cells harbouring second generation schizonts are not the cells destroyed. Development of this stage deep in the lamina propria leads to the loss of structural integrity of large areas of subepithelial tissue, including the muscularis mucosa and underlying muscle layers. Capillaries in these areas rupture and epithelial cells with no underlying support become detached (Stockdale and Fernando, 1975; Ryley, 1975). In calves infected with E. bovis, loss of mucosa can be quite spectacular in that pieces of the necrotic intestinal lining may be passed in the feces (Hammond, Davis, and Bowman, 1944; Boughton, 1942).

The infection of villous epithelial cells with coccidia is often accompanied by villous atrophy. This has been described in intestinal coccidiosis of lambs infected with E. crandallis (Pout, 1967a,b), chickens infected with E. acervulina (Fernando and McCraw, 1973), dogs infected with Isospora ohioensis (Dubey, 1978) and in man infected with I. belli (French, Whitby and Whitefield, 1964). Pout (1967b) reported that the ratio of villus height/total mucosal thickness reaches a

minimum, 4 days after infection of chickens with E. acervulina. Fernando and McCraw (1973) showed that in two-week old chickens infected with 2.5×10^5 oocysts of E. acervulina, minimum values of mucosal thickness and villous height were reached at 6 days, while crypt length and villous thickness increased to a maximum at 5 days post infection. Epithelial turnover time decreased from 5 in the controls to 3 days in infected chickens. These peak changes occurred during gametogony when parasites were present in greatest numbers.

Villous atrophy has been reported in rats infected with the nematode Nippostrongylus brasiliensis (Ferguson and Jarrett, 1975) and in mice infected with Trichinella spiralis (Manson-Smith, Bruce and Parrott, 1979). It has been shown that the villus atrophy and crypt hyperplasia associated with these infections is a hypersensitivity reaction and is thymus dependent (Ferguson and Jarrett, (1975).

Marked histological and chemical changes have been reported by Michael (1973) in association with villus atrophy due to coccidial infection. Brush border microvilli were considerably reduced in size and number, and this was associated with a weak Periodic Acid Schiff (PAS) reaction and diminished activities of alkaline phosphatase, ATPase (pH 7.2) and leucine naphthylaminase. There was also reduction in acid phosphatase and β-glucuronidase (lysosomal enzymes) and enzymes associated with the endoplasmic reticulum (glucose 6-phosphatase and non-specific esterase). Changes in the Golgi apparatus and mitochondria caused reduced activities of thiamine pyrophosphatase and succinic dehydrogenase. Michael (1973) concluded that intestinal malabsorption resulting from coccidiosis is due not only to the reduction of villi and microvilli but also to the lowered absorptive and digestive capacities

of the absorptive enterocytes. These changes observed were related to the species, the level of infection, the area of the intestine examined and the day of infection. The most severe changes occurred during second generation schizogony in E. necatrix and during gametogony in the case of E. acervulina (Michael, 1974).

More interest in recent years has been directed towards studying the effect of coccidial infection on brush border enzymes in chicken intestine (Syke and Walters, 1970; Enigk and Dey-Hazra, 1976; Major and Ruff, 1978a,b,). Major and Ruff (1978a) reported that coccidial infection caused some decrease in luminal and surface bound amylolytic activity in broiler chickens. According to Major and Ruff (1978b) the site of infection is important in determining whether or not a particular species influences digestion. Species like E. acervulina, E. maxima and E. necatrix, which parasitize the duodenal and jejunal regions, had the most effect on digestion while E. acervulina had the most consistent effect on surface bound and luminal enzymes. On the contrary, E. brunetti had no effect and E. tenella only showed a mild reduction in surface bound enzymes (Major and Ruff, 1978b). Major and Ruff (1978b) also observed loss in pancreatic weight and an overall decrease in amylolytic activity in the pancreas in broilers infected with E. acervulina, E. maxima and E. necatrix. Major and Ruff (1978a) found that the activity of maltase and sucrase in the intestines of broilers inoculated with E. acervulina, E. maxima, E. necatrix and E. brunetti decreased in the region in which these species maximally parasitized. Interestingly, the maximum reduction occurred on the 1st or 2nd day after injection and was followed by a rapid recovery. Enigh

and Dey-Hazra (1976) also reported a decrease in disaccharidase activity with E. necatrix infection in chickens.

Decrease in enzyme activity is perhaps responsible for nutrient malabsorption seen in coccidial infections. In E. acervulina infection there was a decrease in the rate of absorption of glucose (Preston-Mafham and Sykes, 1967, 1970), vitamin A and carotenes (Kouwenhoven and Van Der Horst, 1967, 1970), zinc and oleic acid (Turk and Stephens, 1967). Besides the decrease in the amount of nutrients absorbed the time required for maximum blood concentration was prolonged; in the case of oleic acid, maximum blood levels were noted at 1-2 hours with controls and 8 hours with infected chickens (Turk, 1974). In the case of Eimeria necatrix which mainly parasitizes the jejunum, zinc absorption and protein digestion and absorption were markedly reduced, while calcium and oleic acid absorption were less affected and amino acid uptake was unaffected (Turk and Stephens, 1970a,b; Turk, 1973, 1974). Infection of the lower part of the intestine with Eimeria brunetti depressed calcium absorption, but had only slight inconsistent effects on the other nutrients studied (Turk, 1973, 1974). Cecal coccidiosis (E. tenella infection) resulted in minor changes in absorption (Turk, 1974).

Humphrey and Turk (1974) correlated changes in nutrient absorption in E. acervulina infection with changes at the ultrastructural level. Mitochondrial swelling and loss of internal structure, vacuoles, vesicles, cellular edema, dilated Golgi cisterna, abnormal endoplasmic reticulum and increased number of lysosomes were found in parasitized cells.