Chapter 1 Review of the Literature

1.1. Overview of the Australian lamb industry

Traditionally, wool production has been the governing force behind the Australian sheep industry; however over the past two decades there has seen a shift in enterprise with many producers diversifying production systems away from primarily wool-producing operations to include cropping, beef or meat-breed lamb production enterprises. Increases in lamb prices and decreases in micron premiums for fine wool are considered factors behind these enterprise changes. Other factors have also affected sheep numbers over this period such as the effects of drought, wild dogs, increased numbers of sheep slaughtered and an increase in live exports. As a consequence of these changes, Australian sheep numbers have declined by 54% since 1991 (163 million to 76 million sheep) (Table 1-1). Despite declining numbers, Australia remains a world leader in wool production, with 21% of world production originating from Australia (ABARES, 2014).

Table 1-1 Australian sheep numbers (million) and percentage (%) reduction in sheep numbers between 1991 and 2013.

Year	NSW	Vic	Qld	SA	WA	Tas	ACT	Australia: Overall
1991	59.8	27.5	17.4	17.2	36.5	4.8	0.1	163.2
2013	27.8	16.1	2.9	10.8	15.5	2.4	0	75.5
% reduction	53%	42%	83%	37%	58%	50%	61%*	54%

* The values for this territory were 0.118 and 0.046 million sheep in 1991 and 2013 respectively for calculation of percentage reduction. Source: (ABARES, 2014)
NSW: New South Wales, Vic: Victoria, Qld: Queensland, SA: South Australia, WA: Western Australia, Tas: Tasmania, ACT: Australian Capital Territory

In contrast to the decline in wool production, the Australian lamb industry has thrived with the number of lambs slaughtered increasing by 38% since 1991, and has been accompanied by substantial growth in the export market with lamb meat exports increasing by 495% (Figure 1-1) (ABARES, 2014). This transformation may be accredited to substantial investment by industry and government bodies into research and development, and marketing to redefine and relaunch lamb in both domestic and export markets. Investment into research and development has focused on four key elements; genetics, health and reproduction, nutrition and on-farm management and adoption. Objectives were to produce heavier, leaner carcasses through genetic improvement, increase lamb marking percentages and turn-off rates, ensure a consistent supply of lamb throughout the year, and increase on-farm profitability (Pethick *et al.*, 2006; Meat and Livestock Australia, 2009).

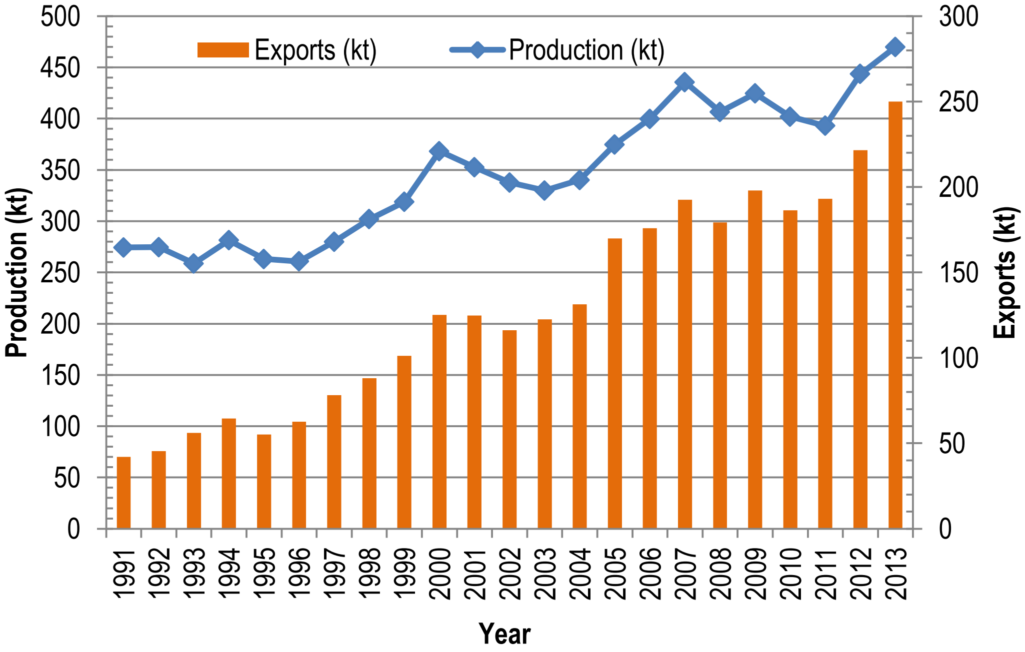


Figure 1-1 Production and export of Australian lamb (carcass weight; kt) between 1991 and 2013. Source: (ABARES, 2014)

1.2. Cost of gastrointestinal nematodes to the Australian sheep industry

Despite substantial investment into research and development over the past twenty years, gastrointestinal nematodes (GIN) continue to impose significant economic constraints on the Australian sheep industry. The annual cost of GIN has increased from an estimated $222 million (McLeod, 1995) in 1994 to $369 million (Sackett *et al.*, 2006) in 2006 with the most recent estimate of $436 million in 2015 (Lane *et al.*, 2015). Production losses account for the majority of losses associated with GIN with 78% of the cost of GIN attributed to production losses (2015), which is comparable to previous estimates of 87% by Sackett *et al.* (2006) and from the 1980’s (83%) and 1990’s (63%) (Beck *et al.*, 1985; McLeod, 1995). GIN are ranked the second highest endemic sheep disease in Australia however the effects of GIN also contribute to the cost of disease for fly strike and post-weaning mortality, highlighting that parasitism due to GIN is the highest management cost factor affecting sheep production systems.

In high rainfall regions, the cost of GIN is estimated at $28.29/head (Lane *et al.*, 2015) which is significantly higher than the previous estimate of $5.93/head in 2006 (Sackett *et al.*, 2006). This increase could be attributed to; differences in modelling designs, shift in production enterprises, improved wool and greatly improved lamb prices, increasing prevalence of drench resistance and a change in the distribution of sheep within regions (ABARES, 2014; Playford *et al.*, 2014; Lane *et al.*, 2015). Recently the effects of GIN were compared between two different GIN management systems; integrated parasite management (IPM) using regional WormBoss strategies (Kelly *et al.*, 2010) and farms managed in accordance to regionally typical (TYP) GIN management strategies on commercial Merino farms on the Northern Tablelands, NSW. Kelly *et al.* (2010) showed that the effects of GIN were reduced on farms implementing IPM strategies. To validate this finding, Kelly (2011) calculated the annual cost of GIN on

IPM farms to be $5.80/Merino ewe while it was $11/Merino ewe on TYP farms. The implementation of IPM strategies reduced the cost of GIN by 47%, and was largely due to lower mortality rates due to haemonchosis on IPM farms.

Research into the effects and costs of GIN on sheep has typically focused on Merino sheep with few reports for meat-breed lamb production. In southern Australia, where *Trichostrongylus* spp. and *Teladorsagia circumcincta* predominate, GIN reportedly reduced growth rate of meat-breed lambs by 19 g/day (Carmichael, 2009).These breed types and sheep operations differ markedly from that of Merino sheep and the lack of literature in this area highlights the importance of better defining the effect of GIN control on lamb performance, and the need to develop GIN control strategies appropriate to these breeds and operations.

1.3. Epidemiology of three important gastrointestinal nematodes affecting sheep on the Northern Tablelands, New South Wales

The Northern Tablelands of New South Wales is located in a temperate climatic zone, characterised by cool, dry winters and a high, summer dominant rainfall (Figure 1-2). The Northern Tablelands are located between the latitudes of 28°15’S and 31°30’S with an average elevation of 800 m (Alford *et al.*, 2003). These conditions make it a conducive environment for development and survival of three of the most ‘economically’ important GIN species affecting sheep; *Haemonchus contortus* (Barber’s Pole), *Trichostrongylus* spp. (scour worms) and *Teladorsagia circumcincta* (Small Brown Stomach worm). These GIN are considered to be the most pathogenic species of nematodes affecting production, well-being and welfare sheep on the Northern Tablelands, NSW (Donald *et al.*, 1978).

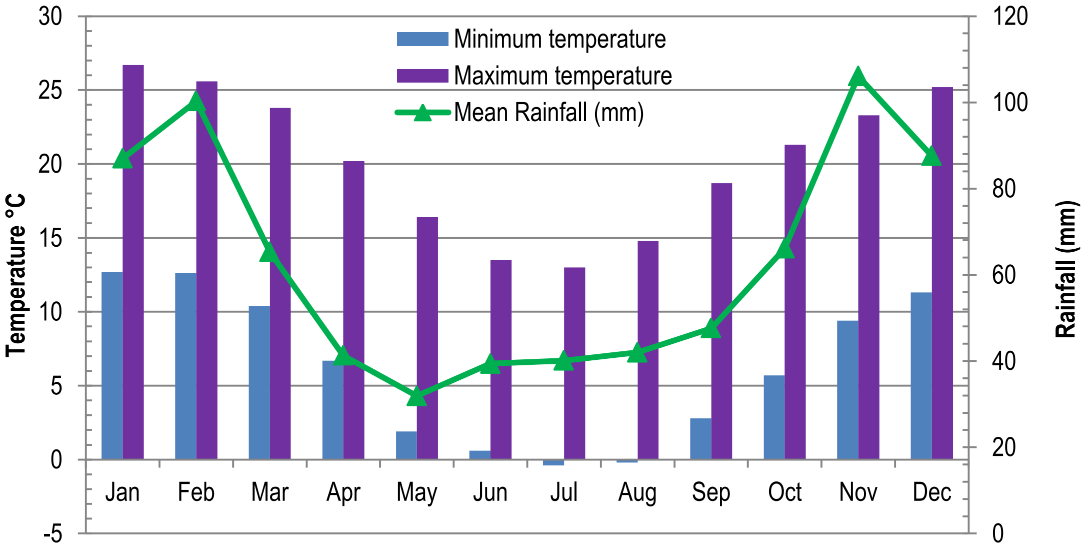


Figure 1-2 Mean monthly rainfall and mean minimum and maximum temperatures for Armidale between 1997 and 2015.
Source: http://www.bom.gov.au/climate/averages/tables/cw_056037.shtml

1.3.1. Macro and microclimatic variables and impact on development and survival of free-living larvae with emphasis on *H. contortus*

Ecology of the free-living stages (see Figure 1-3) and population dynamics of GIN have been extensively studied in a diverse range of environments (Crofton, 1965; Donald, 1968; Callinan, 1978; Besier & Dunsmore, 1993) and findings from these experiments have been used to design suitable management strategies for regional and seasonal GIN control. Conditions prevailing within the macro and microclimatic systems are important elements which contribute significantly to the developmental success and survival of GIN. Faecal and soil moisture, temperature, solar radiation, wind speed, evaporation rate, precipitation, sward height, pasture type and relative humidity all influence the microclimatic conditions and play a role in developmental success of the free-living larval stages (Thrusfield, 1995). However it is temperature and moisture that have greatest influence on development and survival of eggs and free-living larval stages (Figure 1-4) (Levine & Andersen, 1973; O'Connor *et al.*, 2006).

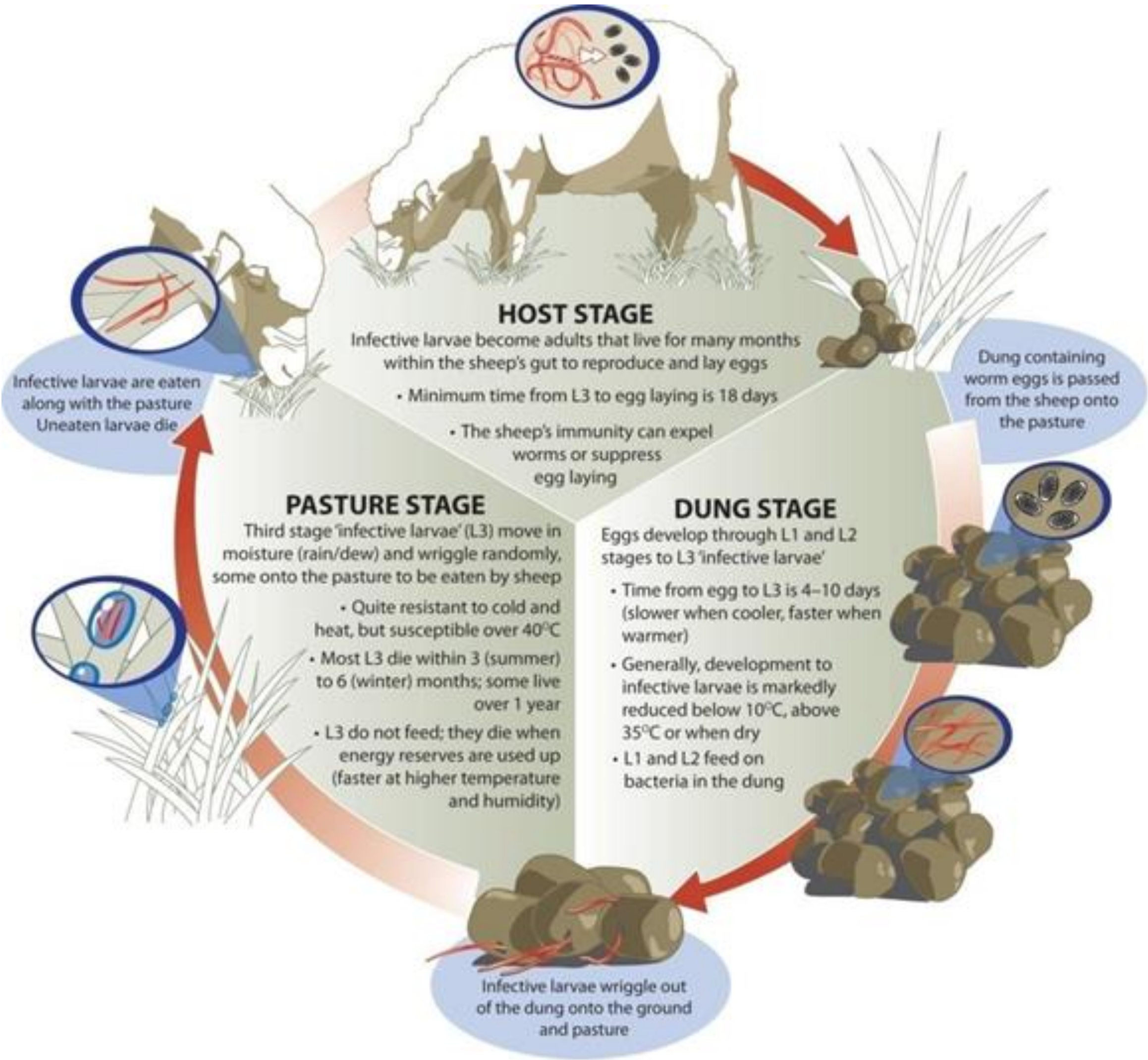


Figure 1-3 Common lifecycle of gastrointestinal nematodes.
Source: http://www.GINboss.com.au/GINs/roundGINs/roundGIN-life-cycle.php (WormBoss).

The optimum temperature ranges for development of the unembryonated egg to infective third stage larvae for the three important gastrointestinal nematode species are shown in Figure 1-4.

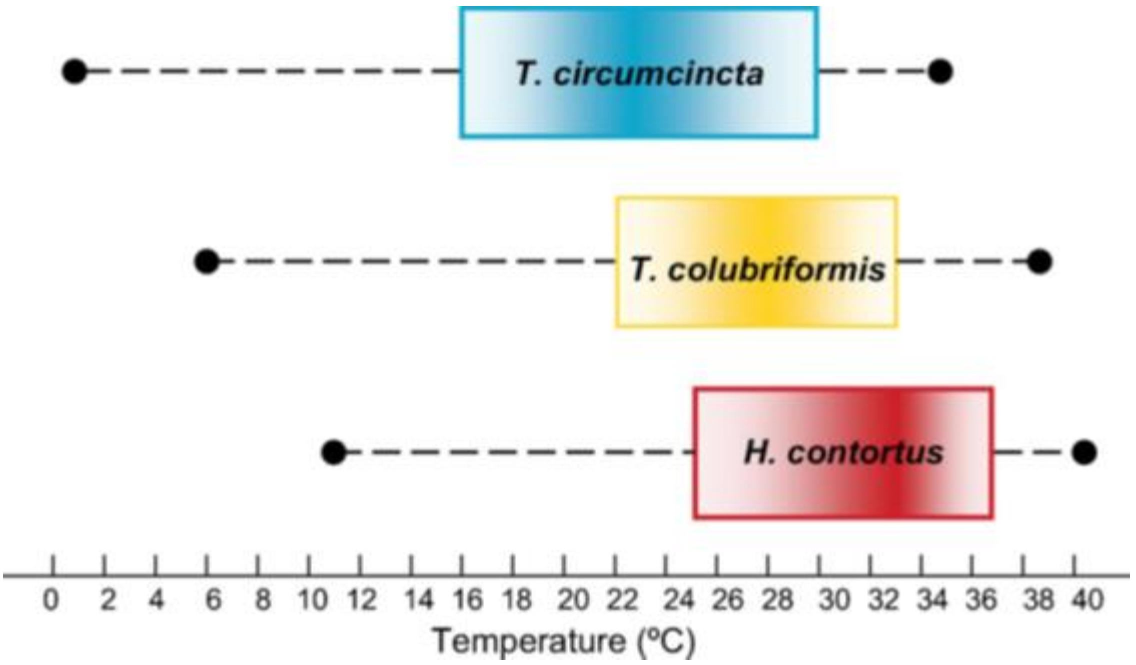


Figure 1-4 Optimum temperature range (indicated by box with most optimal temperature marked by high colour intensity) for development of the unembryonated egg to infective third stage larvae of three important gastrointestinal species on the Northern Tablelands, NSW. The dashed lines (—) extend to the upper and lower temperature limits for development. Source: (O'Connor *et al.*, 2006).

Temperature influences development rate with eggs hatching more rapidly as temperatures increase (Coyne & Smith, 1992; Rossanigo & Gruner, 1995) while at lower temperatures there is a greater disparity between GIN species with *T. circumcincta* and *Trichostrongylus* spp. able to develop at lower temperatures than *H. contortus* (Crofton, 1965; Jasmer *et al.*, 1986; O'Connor *et al.*, 2006) (Figure 1-4). Survival of the free-living stages of *H. contortus* and *T. colubriformis* is prolonged when maintained at a constant temperature of 4°C, while at temperatures above and below this threshold survival declines at accelerated rates (Andersen *et al.*, 1966; Todd *et al.*, 1976b) (Figure 1-5). Differences also exist in survivability of the egg and free-living stages with the unembryonated egg being most susceptible, and having the shortest survival time, while L3 larvae survive for the longest. When maintained at a constant temperature of 4°C, survival of L3 *T. colubriformis* and *H. contortus* was >90% and 20% respectively at 256 days, while survival of unembryonated eggs was <1% at 16 and 8 days for *T. colubriformis* and *H. contortus* respectively. While there is little difference in survival between L1 and L2 larval stages, there is difference between GIN species with <1% of L1 and L2 *H. contortus* larvae surviving by day 64, while approximately 15% of L1 and L2 *T. colubriformis* larvae were still alive by this time point, confirming the susceptibility of *H. contortus* at lower temperatures (Andersen *et al.*, 1966; Todd *et al.*, 1976b).

As temperatures increase so does the metabolic rate of L3 larvae, depleting energy reserves at an accelerated rate. Due to the inability to feed and replenish energy stores, the survival period of L3 larvae is shortened (Andersen *et al.*, 1966; Dunn, 1969; Todd *et al.*, 1976b) (Figure 1-5). At temperatures of 4 and 25°C, survivability of L3 *H. contortus* was 63 and 7% respectively at day 64 and at 45°C, only 7% of L3 survived to day 2 (Todd *et al.*, 1976b).

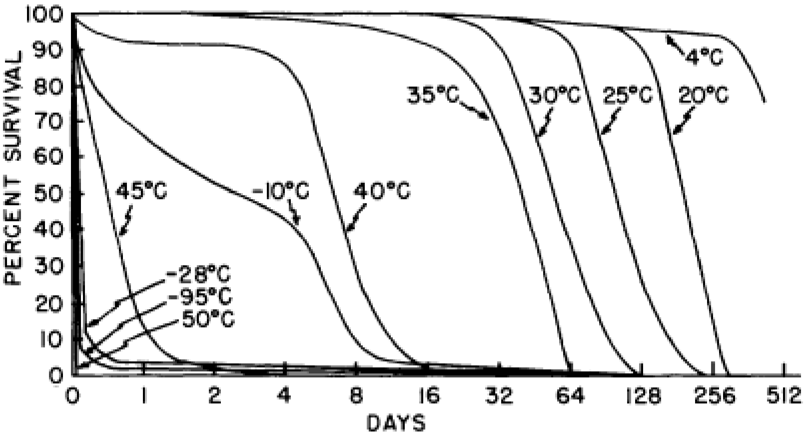


Figure 1-5 Declining rate of survival of infective *Trichostrongylus colubriformis* L3 larvae in water as temperature increases from 4°C. Source: (Andersen *et al.*, 1966)

Development of free-living stages of GIN is also significantly influenced by rainfall activity and faecal and soil moisture content. Recovery rates of L3 *H. contortus* increased as rainfall levels increased and was also enhanced when rainfall occurred within the week of faecal deposition (O'Connor *et al.*, 2007) and on the day of faecal deposition (Khadijah *et al.*, 2013b). Soil and faecal moisture content play important roles in the successful development of eggs to the infective L3 stage. Faecal moisture content of 60% and temperatures of 23 and 28% are optimal for egg development to infective larvae for *T. circumcincta* and *T. colubriformis* respectively (Rossanigo & Gruner, 1995). Soil moisture influences development of *H. contortus* and *T. colubriformis,* with recovery of L3 increasing as soil moisture content increases. Soil moisture can also compensate for lower rainfall amount as observed when events of 12 and 24 mm of simulated rainfall produced equal L3 recovery rates when soil moisture was at 10 or 15%, indicating that adequate soil moisture was present for larval development (2013c). On pasture, variables such as wind speed, temperature, evaporation and pasture coverage affect the microclimate and influence the rate of decline in soil and faecal moisture content and are important when considering development and survivability of the free-living stages on pasture (Krecek *et al.*, 1992; Khadijah *et al.*, 2013c, 2013d).

Relative humidity (RH) can significantly influence the rate of larval recovery with greater numbers of L3 recovered from grass swards at 95% RH as opposed to 56% RH (Silangwa & Todd, 1964). The main effect of RH occurs on lower herbage segments and soil (Krecek *et al.*, 1992) with larval recovery increasing as relative humidity increases. Hsu and Levine (1977) established a greater recovery of *H. contortus* L3 larvae when faeces were incubated at 100% relative humidity (RH) rather than 85%. However, if samples were stored at a constant temperature of 23°C, then a similar recovery of L3 larvae would occur when RH fluctuated between 70% and 100% (1977). Evaporation rates are also an influencing factor on L3 recovery with higher rates of recovery occurring at lower rates of evaporation (O'Connor *et al.*, 2008). These results suggest that dense, lush pastures afford protection for both eggs and larvae against potentially high rates of evaporation which would otherwise lead to desiccation.

L3 larvae also react to moisture, temperature, light and possibly gravity (Gordon, 1948) and migrate away from soil or faecal pats. Larvae typically migrate vertically a distance of <15 cm up grass swards (Holasová *et al.*, 1989; Amaradasa *et al.*, 2010) although >

20 cm can also be achieved when greater levels of herbage moisture is present (Silva *et al.*, 2008; Amaradasa *et al.*, 2010). Larvae can migrate up to 25 cm horizontally from the faecal pat however distances of <13 cm are more commonly observed (Goldberg, 1970; Holasová *et al.*, 1989; Amaradasa *et al.*, 2010). This process is facilitated by moisture and often occurs in early morning dew droplets and coincides with early morning grazing activities of the host, however reports indicate that there is little effect of time of day on larval migration with no trend observed for the number of larvae recovered at different times of the day (Silangwa & Todd, 1964).

1.3.2. *Haemonchus contortus*

Haemonchus contortus (H. contortus) is commonly referred to as barber's pole worm and considered to be one of the most pathogenic GIN species. It is of significant economic importance for producers particularly in the summer rainfall regions of northern New South Wales and south-east Queensland. *H. contortus* are one of the largest GIN in the Trichostrongylidae family with females ranging in length between 25 to 34 mm and males between 19 to 22 mm (Dunn, 1969). They reside within the abomasum and penetrate pits and glands of the mucosa (Sutherland & Scott, 2010). *H. contortus* are haematophagous feeders and have a tiny lancet contained within a small buccal capsule which pierces small blood vessels in the wall of the abomasum (Boughton & Hardy, 1935; Dunn, 1969). L4 and adult *H. contortus* can potentially consume up to 0.05 mL blood/GIN/day (Clark *et al.*, 1962; Rowe *et al.*, 1988). Adults can feed for up to 12 minutes with haemorrhaging occurring for a further seven minutes once the GIN has detached (Boughton & Hardy, 1935). It is unknown how much blood is consumed at each time. Developmental success of the free-living stages of *H. contortus* are affected by both temperature and moisture with the optimal mean daily temperature range for development of free-living *H. contortus* between 28 - 37°C, however development can occur, albeit at low rates, when mean temperatures are as low as 11°C (O'Connor *et al.*, 2006) (Figure 1-4). As temperatures increase, development is more rapid (Crofton, 1965). *H. contortus* are susceptible to desiccation with larval survival declining within 24 hours (Todd *et al.*, 1976a).

Once ingested it takes approximately 18 days for L3 to develop to mature egg-laying adults and eggs being observed in faeces. Mature adult females are prolific egg layers and lay between 5,000-10,000 eggs/day (Gordon, 1950; Gordon, 1967; Coyne *et al.*, 1991; Le Jambre, 1995). A significant challenge in controlling *H. contortus* is during haemonchosis outbreaks in the warmer months following recent rainfall when pasture larval challenge is very high (Cohen *et al.*, 1972; Colvin *et al.*, 2012). A large *H. contortus* burden (e.g. 35,000 *H. contortus*) can result in severe haemorrhaging and as a result the erythropoietic system is unable to manufacture sufficient quantities of erythrocytes to replace those lost either by *H. contortus* ingestion and/or haemorrhaging at the site of attachment (Dargie & Allonby, 1975).

Clinical effects associated with haemonchosis include; anorexia, anaemia, hypoproteinaemia, oedema, depression and mortality (Cohen *et al.*, 1972; Pradhan & Johnstone, 1972a; Abbott *et al.*, 1988; Rowe *et al.*, 1988; Albers *et al.*, 1989; Yacob *et al.*, 2009), while reduced growth, milk yields and wool growth are considered subclinical effects of *H. contortus* infection (Barger & Cox, 1984; Albers *et al.*, 1989; Cobon & O'Sullivan, 1992). Despite evidence of production losses due to the subclinical effects of infection, it is the effect of mortality that is of greatest economic importance for producers (Barger & Cox, 1984).

1.3.3. *Trichostrongylus* spp.

Trichostrongylus spp. (commonly referred to as scour worms) are most prevalent in the winter rainfall regions of Victoria, Tasmania, southern areas of South Australia and south-west Western Australia and in non-seasonal rainfall areas of central and southern New South Wales (Besier & Love, 2003) and also in the summer rainfall region on the Northern Tablelands, NSW. The four main *Trichostrongylus* spp. found in

Australia are *T. colubriformis*, *T. vitrinus*, *T. axei* and *T. rugatus* with *T. colubriformis* the most prevalent species on the Northern Tablelands (Bailey *et al.*, 2009a). *T. vitrinus* is the most pathogenic of the *Trichostrongylus* species while *T. colubriformis* is considered to have intermediate pathogenicity (Beveridge *et al.*, 1989). The adult female is capable of laying between 100 – 200 eggs/day (Gordon, 1967; Coyne *et al.*, 1991; Hansen & Perry, 1994), which is significantly less than the egg-laying capabilities of the *H. contortus* adult female, however in contrast eggs of *Trichostrongylus* spp. have a greater tolerance to cold and dry conditions (Urquhart, 1996). Infection causes damage to the lining of the small intestine and associated swelling, blood spots and excess mucous. Unthriftiness and scouring of sheep are common signs of mild to moderate *Trichostrongylus* spp. infection, while rapid liveweight loss, scouring, dehydration and an accretion of dark green to black faeces around the breech is commonly observed in sheep harbouring heavy infections. Mortality may occur in sheep with moderate to heavy infections. Effects of *Trichostrongylus* spp. infection are often observed in sheep (namely lambs) which have had little exposure to this species. Reduced growth rates and wool growth are common effects of *Trichostrongylus* spp. infection, caused by decreased efficiency in utilisation of metabolisable energy, impaired protein deposition, mineral deficiencies, loss of endogenous protein into the gastrointestinal lumen and reduced nitrogen retention (Coop *et al.*, 1976; Sykes & Coop, 1976; Steel *et al.*, 1980; Kimambo *et al.*, 1988b; Bown *et al.*, 1991a; Greer *et al.*, 2005b). These effects of parasitism are commonly observed during the initial twelve weeks of infection (Steel *et al.*, 1980; Kimambo *et al.*, 1988b) after which time sheep have developed an effective immunological response to GIN infection (Kimambo *et al.*, 1988a; Greer *et al.*, 2005b).

1.3.4. *Teladorsagia circumcincta*

Teladorsagia circumcincta, referred to as the small brown stomach worm, are prevalent in the winter rainfall regions of southern Australia but are also present in the summer rainfall regions of Australia. They are more tolerant of cold, dry conditions than *H. contortus* and *T. colubriformis* and L3 have the capacity to survive 'over-winter' (Waller *et al.*, 2004) and are a significant source of GIN infection for lactating ewes and their lambs in early spring. Optimal mean daily temperatures for development are between 15 - 30°C (O'Connor *et al.*, 2006) with few eggs hatching when maximum temperatures fall below 10°C (Vlassoff *et al.*, 2001) and only 0.5% of *T.circumcincta* eggs developed to the infective L3 larval stage when maintained at a constant temperature of 5°C (Leathwick *et al.*, 1999). Optimal faecal moisture content for developmental success is between 60 - 70% at 23°C (Rossanigo & Gruner, 1995). Adult *T. circumcincta* are considered to have a low egg-laying capacity with females producing <200 eggs/day (Gordon, 1967; Elsheikha & Khan, 2011). Pathological effects of infection are characterised by raised nodules on the surface of the abomasal mucosa. Emergence of immature adults from the nodules produces mechanical and biochemical disturbances, which increases the permeability of the abomasal epithelium and causes leakage of proteins into the gut lumen and sheep can potentially become hypoalbuminaemic (Urquhart, 1996; Vaughan *et al.*, 2006). Survival of future *T.circumcincta* generations is enhanced when development is inhibited (hypobiosis) at the 4th larval stage. This phenomenon is poorly understood but thought to occur when free-living *T.circumcincta* larval stages "sense" unfavourable microclimate conditions for imminent development and survival of future generations (Armour *et al.*, 1966; Urquhart, 1996).

Common clinical effects associated with infection include; decline in voluntary feed intake, liveweight gain, milk yield, wool growth and wool fibre diameter, diarrhoea, dehydration and possible death (Coop *et al.*, 1982; Leyva *et al.*, 1982; McNeilly *et al.*, 2009). These effects are consequences of physiological disturbances and morphological changes in the abomasa causing an increase in abomasal pH, thickening of mucosal tissue, decreased efficiency in utilisation of metabolisable energy, impaired protein deposition, mineral deficiencies and loss of endogenous protein into the gut lumen (Coop *et al.*, 1982; Scott *et al.*, 1998; Scott *et al.*, 2000). An effective immunological response to *T. circumcincta* is often attained 6 – 8 weeks after continuous challenge and coincides with a rapid decline in WEC and an increase in voluntary feed intake (Symons, 1981; Coop *et al.*, 1982).

1.4. Effects of gastrointestinal nematodes on sheep

The adverse effects associated with parasitism are not only associated with feed intake but also the functions of motility, digestion and absorption (Holmes, 1986) within the gastrointestinal (GI) tracts. The degree of impairment is influenced by the species of GIN present and the magnitude of the infection (van Houtert & Sykes, 1996). The degree to which these effects vary is in accordance with breed, age, immunological status and nutritional factors. The main effects GIN impose on the host are: i) a decrease in voluntary feed intake (VFI) causing reductions in total energy, protein and mineral intake; ii) an increase in endogenous protein losses into the gut lumen (van Houtert & Sykes, 1996); (iii) repartitioning of amino acids towards the gut (Yu *et al.*, 2000) and (iv) impaired rumen function (van Houtert & Sykes, 1996). Literature detailing the mechanisms of protein, energy and mineral metabolism as affected by GIN parasitism has been well reviewed elsewhere (Steel, 1972; Reveron *et al.*, 1974a; Sykes & Coop, 1976, 1977; Steel *et al.*, 1982; Poppi *et al.*, 1986; Kimambo *et al.*, 1988b; Bown *et al.*, 1989, 1991b) and only a brief summary is provided.

Efficiency of nutrient utilisation is compromised due to the adverse effects of GIN in the gastrointestinal tract with the effects of infection reducing the availability of metabolisable protein (MP) and energy (ME) to the host for production (e.g. muscle, bone and wool growth). Retention of nitrogen is necessary to ensure amino acids are available to host tissues for development and production (Bown *et al.*, 1991b). However availability is often reduced due to; (i) loss of endogenous proteins (plasma protein, erythrocytes, mucin and sloughed epithelial cells) (Bown *et al.*, 1991b; Sykes, 2000) into the gut lumen due to increased permeability of the epithelium caused by the feeding activities of mucosal browsers (Poppi *et al.*, 1986; Urquhart, 1996) and local inflammatory responses; (ii) diversion of protein away from productive purposes to repair damage to the gut (Yu et al., 2000) and (iii) blood loss due to the haematophagous activities of *H. contortus* and associated haemorrhaging into the gut lumen (Boughton & Hardy, 1935; Urquhart, 1996). Inflammatory lesions and physical disruption to the gut wall caused by immature and mature GIN causes loss of enteric plasma and erythrocytes into the gut lumen. Although these losses are significant, approximately 87% of the plasma protein lost into the gut lumen is digested and reabsorbed distal to the site of infection (Bown *et al.*, 1991a), however increased levels of nitrogen in urinary and faecal output are often observed (Sykes & Coop, 1977). Salvaging this protein does not compensate however for inefficiencies associated with extra cycling of amino acids or the energy expended due to increased metabolic demands.

1.4.1. Reduction in voluntary feed intake

A widely recognised and typical consequence of GIN parasitism in sheep is a reduction in VFI, defined also as anorexia and this depresses growth rates in young, susceptible sheep and results in bodyweight losses in mature animals. Reductions in VFI between 20 – 30% are often associated with sub-clinical GIN infections (Reveron *et al.*, 1974b; Coop *et al.*, 1976; Greer *et al.*, 2005b) but depressions of up to 60% have been reported (Bown *et al.*, 1989). The degree of pathogenesis depends largely on the species of GIN present, level of infection, immunological status of the host and quality of nutrition available (Sykes, 1994; van Houtert & Sykes, 1996). Acute or complete inappetance is often associated with clinical infections and may potentially lead to death. The effects of sub-clinical GIN infections on VFI are often difficult to observe, however a reduction in VFI is often associated with animals infected with *T.*

circumcincta and *T. colubriformis* (Sykes & Coop, 1977; Steel *et al.*, 1980; Coop *et al.*, 1982).

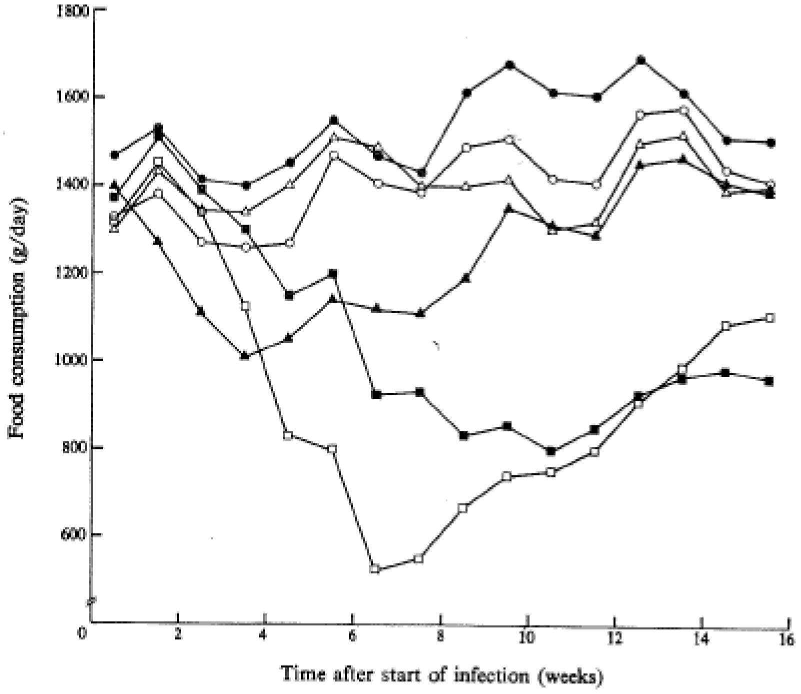
The mechanisms associated with depression in VFI are not completely understood however the host's immunological response to infection is a known factor (Greer *et al.*, 2005a; Greer *et al.*, 2008). The influence of the host's immunological response to GIN infection on VFI was investigated using lambs infected with either *T. colubriformis* (80 L3/kg liveweight/day) or *T. circumcincta* (4,000 L3/day) or remaining uninfected and either immunosuppressed (using a corticosteroid) or non-immunosuppressed. VFI was reduced due to GIN infection however abrogation of the immunological response removed this effect with VFI of infected/immunosuppressed lambs similar to that of uninfected control lambs (Greer *et al.*, 2005b; Greer *et al.*, 2008). These observations support the assertion that it is the mechanisms associated with the host's immunological response to GIN infection that contribute to production loss. It has also been proposed that the host's defense mechanism in response to GIN may include pro-inflammatory cytokines which induce anoretic effects in the parasitised animal however Dynes *et al.* (1990) dismissed this assumption since there was no effect on feed intake for parasitised (infected with 4,000 *T.colubriformis* L3/day) and uninfected sheep when an antagonist of peripheral cholecystokinin was administered. It was then suggested that central satiety signals may be involved as feed intake increased in GIN parasitised sheep following the blocking of the satiety effect of the ventromedial hypothalamus (Dynes *et al.*, 1990).

The effect of GIN on VFI is a function of both L3 developing to adult stage and established adults. Coop *et al.* (1982) infected crossbred lambs with either 1,000, 3,000 or 5,000 *T. circumcincta* L3/day for 12 weeks and as a consequence of infection, VFI was reduced by 5.6, 7.5 and 12.2% respectively compared with uninfected control lambs when offered an a*d lib* diet. In the same experiment, the effect of immature larvae on VFI was also examined (lambs administered 5,000 *T. circumcincta* L3/day for

12 weeks and drenched every 21 days). VFI declined by 12.5% and highlights the negative effect of immature GIN on VFI of the host. To distinguish between the effects of exposure to L3 larvae and the development and effects of L4 and L5 on the host, the inclusion of an additional group (lambs administered larvae daily and treated on a weekly basis) in this experiment would have provided a complete picture of the effects of each stage of larval development on VFI. Kelly *et al.* (2012) recently reported no effect of L3 challenge on VFI of Merino lambs, which had been treated with a controlled release albendazole capsule to prevent larval development and establishment. This suggests that the L4 and L5 stages are primarily responsible for causing depression in VFI with little effect of L3.

Earlier experiments identified threshold limits for *T. colubriformis* and *T. circumcincta* where production was adversely affected in crossbred lambs. Infection reduced VFI and impeded growth when weekly larval intakes were between 950 and 3,000 for *T. colubriformis* and between 12,000 and 37,500 for *T. circumcincta* (Steel *et al.*, 1980; Symons, 1981). The threshold limit for *T. circumcincta* may be further reduced as Coop *et al.* (1982) reported production losses (live-weight gain was only 90% of that of uninfected lambs) in crossbred lambs infected with 7,000 *T. circumcincta* L3/week. Although these losses were not statistically significant, it infers that the degree to which *T. circumcincta* adversely affects production may be more accurately defined between 7,000 – 12,000 *T. circumcincta* L3/week.

Many experimental studies have investigated the effects of parasitism on the host using monospecific infections; however in a typical grazing scenario it is more common for sheep to acquire mixed GIN infections. Steel *et al*., (1982) infected Merino x Border Leicester lambs with a concurrent infection of 3,000 *T. colubriformis* and 38,000 *T. circumcincta* L3/week for 16 weeks and reported a decline in VFI from week 3 onwards and to a greater degree than for the monospecific infections. The effect of concurrent GIN on VFI is shown in Figure 1-6. As a consequence, growth was significantly lower for lambs infected with mixed infection of *T. colubriformis* and *T. circumcincta* than for lambs infected with monospecific infections of *T. colubriformis* and *T. circumcincta* or uninfected.



Food consumption of sheep continuously infected with weekly doses of: (○) 0; (●) 900 and (△) 3000 *T. colubriformis*, (▲) 38 000 *O. circumcincta*, (□) 900 *T. colubriformis* + 38 000 *O. circumcincta*, and (■) 3000 *T. colubriformis* + 38 000 *O. circumcincta*. Each point represents the mean value of three sheep.

Figure 1-6 Effect of a concurrent *T. colubriformis* and *T. circumcincta* infection on voluntary feed intake of Merino X Border Leicester wether lamb (GIN species and infection rates described above). Retrieved from: (Steel *et al.*, 1982).

Depressed VFI persists until the host has acquired an effective immunological response to GIN (Kyriazakis *et al.*, 1996a), and coincides with an observed decline in WEC (Steel *et al.*, 1982; Greer *et al.*, 2005b). Thereafter, VFI of parasitised sheep is comparable to their uninfected counterparts. *H. contortus* has little influence on VFI (Abbott *et al.*, 1986b; Wallace *et al.*, 1998; Doyle *et al.*, 2011) except on low protein diets where it can reduce VFI (Abbott *et al.*, 1986b).

1.4.2. Direct damage to the gastrointestinal tract

The activities of the mucosal browsers, *T. circumcincta* and *T. colubriformis* cause significant impairment to the mucosal surface of the abomasum and small intestine respectively. This results in increased permeability, loss of protein and disruption to the digestion and absorption functions of the organs. *T. circumcincta* enter the gastric glands of the abomasum (Urquhart, 1996) and cause considerable disruption to the functioning of the gland and as a result alter the pH level in the abomasum. The rise in abomasal pH is a result of loss of parietal cell function and this in turn decreases acid production and as a result the enzyme, pepsin is not activated (Miller & Horohov, 2006). Consequently, the breakdown of proteins into constituents of peptides and amino acids for absorption by the intestinal lining is compromised.

T. colubriformis cause considerable damage to the duodenal section of the small intestine following the rupture of GIN from tunnels formed beneath the epithelium and between the epithelial glands of the mucosa. At the site of rupture, there is haemorrhaging and oedema and plasma proteins are lost into the lumen of the gastrointestinal tract. The villi in the proximal section of the small intestine (site of infection) are damaged reducing the surface area for protein absorption and this leads to inefficiencies in absorption of peptides and amino acids (Urquhart, 1996).

Petechias (small red or purple spots) are commonly observed on the abomasal mucosal membrane in acute and chronic stages of haemonchosis. They develop due to the haematophagic activity of *H. contortus* and associated haemorrhaging which occurs once the parasite has detached (Boughton & Hardy, 1935). The abomasal mucosa may also appear oedematous with fluid accumulating within the mucosa (Dunn, 1969). Abomasal contents are often dark brown due to blood loss into the lumen (Urquhart, 1996).

1.4.3. Anaemia

Typical clinical signs of anaemia in sheep include; pale gums and conjunctivae, lethargy and submandibular oedema. Anaemia in sheep is most commonly associated with infections of *H. contortus* and the haematophagic behaviour of this parasite (effects of *Fasciola hepatica* are outside the scope of this review and will not be reported)*.* The 4th and 5th larval stages induce a progressive and considerable decline in packed cell volume (PCV). *H. contortus* attach and feed from the abomasal mucosa and each can consume up to 0.05 mL blood per day (Dargie & Allonby, 1975; Rowe *et al.*, 1988; Urquhart, 1996), and equates to 200 mL blood lost/day in sheep burdened with 4,000 *H. contortus* (Rowe *et al.*, 1988).

Haematocrit level is therefore of particular importance and ranges between 30 – 45% are considered normal for typical Australian bred sheep (Sheriff & Habel, 1976). A tolerance level of $\geq$28% PCV has been reported for Merino lambs after which *H. contortus* negatively effects growth (1990). Strong negative correlations between WEC and haematocrit (Roberts & Swan, 1981; Albers *et al.*, 1987; Albers *et al.*, 1990; Le Jambre, 1995) and GIN burdens and haematocrit (Roberts & Swan, 1982) have been reported for both natural and experimental infections. The severity of anaemia is dependent upon the number of *H. contortus* present and subsequent changes in haematocrit levels which occurs between 1 – 2 weeks post infection (Dargie & Allonby, 1975; Zajac, 1990). The lowest haematocrit level before clinical effects are observed is 15% with sheep considered critically ill at values below 10% PCV (Malan *et al.*, 2001).

Anaemia in sheep can be clinically identified using the FAMACHA® system where the colour of the ocular mucus membrane of sheep is classified and graded. Sheep graded 1 or 2 are not anaemic (red; >28% to red-pink; 23-27%), grade 3 is mildly anaemic (pink; 18-22%), and sheep graded 4 and 5 are anaemic and severely anaemic respectively (pink-white; 13-17% to white; <12%) (Malan *et al.*, 2001; Burke *et al.*, 2007). This system is considered a reliable and valid measure for assessing anaemia by trained technicians (van Wyk & Bath, 2002; Burke *et al.*, 2007).

Development of anaemia in sheep is described in three stages (Dargie & Allonby, 1975; Donald *et al.*, 1978). The first stage commences between days 7 and 25 of infection with considerable blood loss prior to the mobilisation of the erythropoietic system to produce and replace erythrocytes. Acute haemonchosis can lead to death. Continuous loss of blood persists during the second stage (between weeks 3 and 8), however erythropoiesis has increased and red blood cells are able to be manufactured at a similar rate to that of blood being lost. The final and terminal stage is defined when the erythropoietic system is depleted of iron and unable to compensate for the continual loss of blood due to the effects of *H. contortus.*

1.4.4. Diarrhoea

Diarrhoea (scouring) is commonly associated with moderate to heavy infections of *T. circumcincta*, *Trichostrongylus* spp. and *Nematodirus* spp. in lambs and is most prevalent in the high winter rainfall areas of southern Australia (Larsen *et al.*, 1999), although scouring is not uncommon in the summer rainfall regions. Diarrhoea causes an accumulation of faecal matter ‘dags’ around the breech area and soiling of the wool (Sutherland & Scott, 2010) and can cause an increase in incidence of fly-strike in sheep (Williams *et al.*, 2010a). There are significant production losses associated with fly-strike, including mortality, poor growth along with costs associated with treatment and control. There are also increased risks of carcass contamination due to faecal microbes which may potentially be a threat to consumer health. These microbes can cause meat spoilage and carcass value declines as the affected tissue is trimmed (Jacobson *et al.*, 2009).

Causes of diarrhoea remain poorly understood and often associated with nutrition however causes have been linked to the effects of GIN and are most commonly observed in GIN susceptible sheep (i.e. lambs, weaners and pregnant ewes) (Larsen *et al.*, 1994). Common associations in the pathogenesis of diarrhoea are abomastis and enteritis, which causes mucosal damage, observed through inflammation and a reduction in the number of villi present (Jacobson, 2006). Diarrhoea may also be linked to hypersensitivity responses of GIN immunocompetent sheep as large numbers of larvae ingested from pasture can trigger a sudden increase in eosinophils and inflammation of small intestinal tissue (Larsen *et al.*, 1994; Williams *et al.*, 2010a). In immune-mediated scouring, *T. colubriformis* are considered the species of greatest importance as the increased flow of protein and minerals from the small intestine compromises water absorption in the caecum which in turn decreases faecal dry matter (Williams *et al.*, 2010b).

Dag scores are not considered a reliable indicator for determining existing GIN burdens in sheep (in particular adult sheep) as there is a poor relationship between WEC and dag score (Larsen *et al.*, 1994; Jacobson *et al.*, 2009). Scouring decreases faecal dry matter and WEC is likely to be an underestimate of the actual number of eggs per gram of faeces (Le Jambre *et al.*, 2007) and hyper-sensitivity syndrome occurs following ingestion of high intakes of larvae by ‘immune’ mature stock. This is however challenged by Brougham *et al.* (2007) who reported lamb dag scores could provide some indication of corresponding degree of GIN burden but this is dependent on the species of larvae present and stage of development as scouring in lambs often occurs 3 – 4 weeks after establishment of adult GIN (Le Jambre *et al.*, 2007).

1.4.5. Growth

One of the most significant consequences of GIN infection is a reduction in VFI which leads to reduced growth and bodyweight losses in sheep (Coop *et al.*, 1982; Kyriazakis *et al.*, 1996b). A significant proportion of available resources (protein and energy) are diverted away from normal physiological and productive processes, such as muscle accretion, to mounting an immunological response against GIN. These reductions will vary in accordance with the level of larval uptake, GIN species, age and immunological status of the host as well as the quality and quantity of available pasture (Holmes, 1987).

Sykes et al. (1977) quantified the effects of a subclinical infection of *T. circumcincta* on the growth rates of crossbred lambs infected with 4,000 *T. circumcincta* L3/day for 14 weeks. GIN infection reduced growth rate of lambs by 40 g/d of which 25 g/d was the direct result of a decline in VFI of lambs. Sykes and Coop (1977) hypothesised that prolonged inappetance of infected lambs may be caused by the continual presence of *T. circumcincta* immature larvae within the abomasal glands. A similar scenario or prolonged inappetance was observed in lambs infected with 2,500 L3 *T. colubriformis*/day (Coop *et al.*, 1976).

A number of experiments have reported the adverse effects of *H. contortus* on lamb growth (Pradhan & Johnstone, 1972b; Barger & Cox, 1984; Morley, 2006; Yacob *et al.*, 2009), however on many occasions when lambs are fed a high protein diet, the negative effects of *H. contortus* on growth are negated. In a longitudinal experiment, conducted for 9 weeks/year over three years, using a total of 1,078 Merino lambs, a difference in growth of 38% occurred between lambs infected with a single infection of 11,000 L3 *H. contortus* and those which remained uninfected (Albers *et al.*, 1989). While the effects of *H. contortus* on growth is evident in this experiment, the author did report that pasture conditions were variable and pasture quality was poor due to drought and this may have inflated the effects *H. contortus* in this experiment. In a housed experiment, Merino lambs were infected on day 0 with approximately 3,500 L3 *H. contortus* and thereafter weekly with 750 L3 *H. contortus* for 8 weeks. The diet in this experiment was formulated (crude protein (CP): 12.7%, metabolisable energy (ME): 8.6 MJ/kg DM) such that lambs had the capacity to achieve moderate growth rates and no effects of infection on lamb growth was reported (Morley, 2006). In another experiment with a similar level of infection (infected on day 0 with approximately 2,800 L3 *H. contortus* and thereafter weekly with 600 L3 *H. contortus* for 17 weeks), Finn Dorset or Dorset Horn lambs were fed either a high (17% CP, ME: 10.3 MJ/kg DM) or low (8.8% CP, ME: 10.3 MJ/kg DM) protein diet. GIN reduced VFI intake of lambs on the low protein diet and lambs lost weight during the experiment, while VFI was unaffected by GIN for lambs on the high protein diet. Liveweight of lambs on the high protein diet increased and overall there was a 4.4 kg growth advantage for lambs on the high protein diet (Abbott *et al.*, 1986a). In experiments where higher levels of infection (infected on day 0 with approximately 4,600 L3 *H. contortus* and thereafter three times weekly at 300 L3 *H. contortus*/kg for 13 weeks) were used, growth of infected Chokla lambs on high (15% CP, ME: 10.0 MJ/kg DM) and moderate (11.5% CP, ME: 10.0 MJ/kg DM) protein diets were greater than for lambs on a low protein (9.5% CP, ME: 10.3 MJ/kg DM) diet. VFI was higher for both infected and uninfected lambs on the moderate and high protein diets than for groups of lambs on the low protein diet. Despite a growth advantage for infected lambs on high and moderate protein diets, there was a cost of GIN as uninfected lambs on the same respective diets had higher growth rates. The difference in growth between the two levels of protein in diets was not analysed (Khan *et al.*, 2012). It might be considered that diets higher in protein provide additional resources (i.e. amino acids) to the erythropoietic system which would allow the system to respond and resume manufacture of erythrocytes to replace those lost in the abomasum (Abbott *et al.*, 1985b).

Coop *et al.* (1982) investigated the effects of different levels of *T. circumcincta* (1,000, 3,000 & 5,000 *T. circumcincta* L3/day for 12 weeks) on growth of crossbred lambs and confirmed that the negative effect of GIN on growth increased as the level of infection increased. GIN reduced growth of lambs administered 3,000 and 5,000 *T. circumcincta* larvae by 75% and 53% respectively. The effect of routine drenching (every 21 days) to remove adults did not alleviate the effects of infection with growth rates 66% of that of uninfected control lambs. These results indicate that developing GIN larval stages impede growth in lambs; however the effect of adult GIN stages on lamb growth remains unclear since they were not measured independently. . While the effects of each of the immature stages were not separately investigated, recent reports indicate that L3 stage larvae do not affect growth. Young Merino wethers and mixed sex meat-breed lambs were serially treated with effective anthelmintics to prevent larval development and establishment and challenged weekly with mixed larval infections (Merino's: initial dose, 150 L3/kg/BW *H. contortus, T. circumcincta* and *T. colubriformis* and thereafter weekly doses of 500 *H. contortus,* 2,000 *T. circumcincta* and 2,000 *T. colubriformis,* Meat-breed lambs: weekly doses of 300 *H. contortus* and 2.000 *T. colubriformis*). Larvae were administered as equivalent doses either twice or three times weekly and there was no production loss due to L3 challenge (2012; Dever *et al.*, 2015). GIN parasitism can reduce growth and is often associated with a decrease in VFI which diminishes the availability of nutrients for metabolic processes for repair of damage to gastrointestinal tracts, growth and immunological responses to infection. Providing additional protein in the diet and reduce these effects.

1.4.6. Milk production

Ewe milk production is an integral element of lamb performance with a strong correlation between milk intake and growth rate of lambs during the first 4 – 6 weeks of life (Wallace, 1948). Mule and Poll Dorset ewes were infected with 2,500 *H. contortus* L3/week and 4,000 *T. circumcincta* L3/day respectively for 6 weeks pre and post parturition. GIN infection reduced milk production by 23 and 17% for *H. contortus* and *T. circumcincta* respectively (Leyva *et al.*, 1982; Thomas & Ali, 1983). *T. circumcincta* reduced VFI by 16% and liveweight losses were greater for the lactating, infected Poll Dorset ewes (Leyva *et al.*, 1982) and alludes to reason for a decline in milk production. Interestingly, the decline in VFI was primarily associated with the period postpartum as little difference was observed in VFI during the prepartum period between infected and uninfected ewes, indicating that dietary components (14.5% crude protein and 18.3 MJ gross energy) were adequate for ewes to remain immunocompetent up to parturition while the demand for nutrients was greater postpartum during the lactational period. The effect of ewe GIN burden on lamb performance was unable to be assessed as the feed ration offered to ewes was easily accessed by lambs and indicates that VFI of ewes may be an overestimate. There was no effect of *H. contortus* on VFI of Mule ewes; however uninfected ewes had a significantly higher four hour mean milk yield with the mean difference of 145g over the six week sampling period (Thomas & Ali, 1983). Similarly, twin-bearing Merino ewes infected with 1,000 *H. contortus* L3/week had a lower daily milk yield six weeks postpartum than uninfected ewes (1,303 vs 1,575 g/day) (Macarthur *et al.*, 2014).

Diet quality has been shown to be influential in regulating immunocompetence and milk yields of pregnant and lactating Merino ewes infected with 8,000 *T. colubriformis* L3/week (Beasley *et al.*, 2012a). A high quality diet, formulated to provide between 80 - 100% metabolisable protein (MP) and metabolisable energy (ME) requirements for single-bearing ewes, prevented a prepartum rise in WEC, however a subtle postpartum effect was detected with a slight increase in WEC (<400 epg) five weeks after parturition. Conversely, ewes consuming a diet formulated to provide only 50 – 70% of MP and ME requirements experienced in a typical postpartum rise, with WEC increasing shortly after parturition and no evidence of an immunological response to infection by week 5. Ewes consuming the high quality diet had a higher mean milk yield, producing an average of 2.2 kg/day while ewes on the low quality diet produced 1.2 kg/day (Beasley *et al.*, 2012a). Higher milk yields as expected influenced lamb performance with higher growth rates (373 vs 224 g/day) for lambs reared by infected ewes on the high and low quality diets respectively.

1.4.7. Mortality

One of the most significant economic consequences of GIN infection is mortality. McLeod (1995) reported that the annual cost of GIN nematodes to the Australian sheep industry was $222 million of which $41 million (18.5%) was attributed to mortality. While Sackett *et al.* (2006) did not report the contribution of mortality for the cost estimate in 2006, the rate of mortality is not expected to have decreased between 1995 and 2006 particularly given the increase in the prevalence of drench resistance during that time. Similarly in 2015, mortality rate assumptions were provided (Merino weaners and adults (summer rainfall): 6.4 and 3.2% respectively, prime lambs 1.9%), however the actual cost attributed to mortality was not reported (Lane *et al.*, 2015).

On the Northern Tablelands, NSW, death due to haemonchosis is most frequently observed during autumn, following months of warm temperatures and rainfall which are conducive for larval development. The level of infective larvae on pasture increases rapidly under these favourable environmental conditions and due to the high fecundity rate of the female *H. contortus* large numbers of larvae are potentially ingested by the host and mortalities may occur within a few weeks of ingestion and at times prior to the presence of eggs in faeces (Albers *et al.*, 1989). Merino ewe mortality was investigated during a longitudinal experiment, conducted over two years, on the Northern Tablelands, NSW (Kelly *et al.*, 2010). To determine the effect of GIN on mortality (and other variables), half of the ewes on each farm, were GIN-suppressed (SUP) while remaining ewes were non GIN-suppressed (NSUP). The difference in mortality between the two GIN control groups was a result of the direct effect of GIN. Average mortality due to GIN was 3.2% and is in agreement with mortality rates reported by Lane *et al. (2015)* for summer rainfall regions.

In the high winter rainfall areas of southern Australia, GIN-related mortality predominantly occurs during mid to late winter with *Trichostrongylus vitrinus, T.*

colubriformis and *T. circumcincta* considered the most pathogenic species in this region (Blackburn *et al.*, 2015). Losses of 22% and 56% (low and high stocking rates respectively) have occurred in untreated mobs of Merino lambs in South Australia with high burdens of *Trichostrongylus* spp. and *Teladorsagia* spp. considered responsible for these deaths (Brown *et al.*, 1985). This result is in agreement with another experiment conducted over a five year period where mortality rates for untreated Merino lambs ranged between 30 – 58% (with the exception of one year where there were only 7% mortalities recorded), and in both experiments, planned treatment of lambs reduced mortality to <4% (Beveridge *et al.*, 1985; Brown *et al.*, 1985). The predominant species of parasitic nematodes present were *Trichostrongylus* spp. and *Teladorsagia* spp. It should be noted that these mortality rates described for groups of untreated Merino weaners are considered extreme and not reflective of typical GIN management practices.

The degree of drench resistance can also influence mortality rates. In Western Australia using three groups of Merino weaners were treated with drenches that were 65%, 85% or 100% effective on three occasions during a twelve month period (1996). There was a higher rate of mortality for weaners treated with a drench that was 65% effective than for weaners treated with a drench that was either 85% or 100% effective (7% vs 5% vs 2% respectively).

1.4.8. Ovulation and conception rate

There have been few reported studies investigating the effects of GIN on ovulation rates of ewes, but those that have been conducted have shown that ovulation rates are reduced in ewes infected with GIN (Fernandez-Abella *et al.*, 2006). The mechanism through which infection affects ovulation rate is likely to be mediated through the plane of nutrition and body condition score (Fernandez-Abella *et al.*, 2006) which are considered key indicators of fertility and prolificacy. Fernandez-Abella and colleagues

(2006) examined the effect of a mixed GIN infection (challenged twice weekly for 10weeks with 6,000 L3 consisting of: 87% *H. contortus*, 10% *Trichostrongylus* spp. and 3% *Oesophagostomum* spp.) on ovulation rate and concluded that the detrimental effects of GIN on bodyweight and body condition score led to a significant decrease in ovulation rate of infected ewes.

In a flock of Romney crossbred ewes, ewes were either GIN-suppressed or non GIN-suppressed and the effects of a predominantly *H. contortus* natural infection decreased the number of foetuses by 12.4 per 100 ewes. GIN reduced liveweight of ewes by 2.7 kg at joining and 4.3 kg at ultrasound scanning (West *et al.*, 2009), confirming the importance of ewe bodyweight on conception. While body condition scores (BCS) were not reported in this, ewes should have a BCS $\geq$3.0 at joining to optimise reproductive success (Kenyon *et al.*, 2012; Corner-Thomas *et al.*, 2015) and may have been an influencing factor on differences in conception rates in this experiment.

1.5. Role of immunological responses to gastrointestinal nematodes

The most important defence mechanism available to a host when challenged with GIN is their ability to mount an effective immunological response (Miller & Horohov, 2006). An effective immunological response to GIN decreases establishment rate of infective larvae, the egg laying capabilities of the adult female (Stear *et al.*, 1997) and hastens the expulsion of established adults (McClure *et al.*, 2000). Innate or non-adaptive immunity is the natural ability of the host to resist infection to GIN and is considered the primary barrier to GIN challenge (Kelly & Coutts, 2000). The genetic potential for GIN resistant sheep is not fully expressed early in life and requires exposure to significant levels of larvae overtime to attain an effective immunological response to GIN infection (Albers & Gray, 1986; Eady & Woolaston, 1992). The time taken for the host to develop effective immunity to GIN challenge depends upon age, level of larval exposure, duration of exposure and the nutritional status of the sheep (Barnes & Dobson, 1993; Coop *et al.*, 1995; van Houtert & Sykes, 1996; McClure, 2000). There are occasions where resistance of immune animals to GIN infection may diminish. This is evident when nutrient supply is limiting, during the periparturient relaxation period, severe outbreaks of *H. contortus* larvae or when animals become sick or stressed (van Houtert *et al.*, 1995; Kahn *et al.*, 2000a; Beasley *et al.*, 2012a).

1.5.1. Resistance and resilience

Resistance is defined as 'the ability of a host to initiate and maintain responses to suppress the establishment of parasites and/or eliminate parasite load' (Woolaston & Baker, 1996). The most reliable strategy for improving GIN resistance within a flock is selecting rams with negative Australian Sheep Breeding Values (ASBV) for WEC. The WEC trait has low to moderate heritability (between 0.2 and 0.4) and genetic progress towards increased resistance to GIN within a mob may occur at a slower rate as producers are likely to select rams based on a number of key performance traits rather than GIN resistance alone (Woolaston *et al.*, 1991; Woolaston, 1995; Karlsson & Greeff, 2012). The influence of breeding for GIN resistance was evident on WEC of Merino sheep divergently selected (over four generations) for increased resistance to *H. contortus*. Following natural *H. contortus* challenge, sheep selected for increased resistance to *H. contortus* had significantly lower worm egg counts (140 epg) than sheep selected for decreased resistance to *H. contortus* (8750 epg) and unselected control sheep (3590 epg) (Woolaston, 1990). Interestingly sheep selected for increased resistance to *H. contortus* also had greater resistance to *T. colubriformis.* Likewise breeding for increased GIN resistance may also be unfavourable with associations ranging from zero to negative reported between production traits (growth rate and fleece weights) and GIN resistance and GIN resistance and dag score (described in Section 1.5.2) (Williamson *et al.*, 1995; Bisset & Morris, 1996). It is however impractical for producers to place complete emphasis on one breeding objective and therefore rams selected for increased resistance to GIN infection should also selected on the basis of other production traits.

Resilience is defined as ‘the ability of a host to maintain relatively undepressed production while subjected to a parasite challenge’ (Bisset & Morris, 1996) and is best assessed using a methodology which determines differences in production between periods when uninfected (or GIN-suppressed) and infected (Kelly *et al.*, 2013). This methodology is not commonly practiced at a commercial level; rather selection is more often based on individual performance within a mob in the presence of a managed GIN infection, which Kelly *et al.* (2013) reported was highly correlated with true resilience. A limiting factor for improving resilience within a mob is the low heritability (between 0.10 - 0.19) (Bisset & Morris, 1996; Bisset *et al.*, 2001). There remains some contention on which breeding objective (i.e. resistance or apparent resilience) should be assigned greater importance in a production system, with some considering it more advantageous to focus on low production losses due to GIN infection as opposed to reduction in pasture larval contamination through improved resistance to GIN (Bisset & Morris, 1996; Colditz *et al.*, 1996; Kelly *et al.*, 2013).

1.5.2. Attributes and consequences associated with resistance and resilience

Breeding for resistance rather than resilience may be considered the preferred strategy for reducing the effects of GIN within a mob. Fewer eggs will be deposited on pasture and pasture larval numbers will decline. Conversely, pasture larval contamination will not be reduced when breeding for resilience and consequently susceptible stock within the flock will be continually exposed to large numbers of larvae. Breeding for resistance to one GIN species (e.g. *H. contortus*) can also afford some cross-protection against other GIN species (Windon, 1990; Kahn *et al.*, 2003).

There have been unfavourable reports of negative associations between GIN resistance and production traits (growth rate and fleece weights) and GIN resistance and dag score (Watson & Baker, 1986; Williamson *et al.*, 1995; Bisset & Morris, 1996; Bisset *et al.*, 2001). There is however the potential to manage these consequences as the correlations are well below unity. However, the experiments that have highlighted these unfavourable associations have been based on lines of sheep divergently selected for low and high WEC and have highlighted the cost of an effective immunological response to GIN infection where resources (in particular protein and energy) are diverted from normal physiological and productive processes to mounting an immunological response to GIN challenge (Morris *et al.*, 1995; Bisset *et al.*, 1996).

While performance is not impeded in sheep resilient to GIN, the number of eggs deposited on pasture does not diminish; therefore GIN susceptible sheep are exposed to large numbers of larvae from pasture which in turn reduces productivity within a flock.

In the Australian context, resistance is the preferred trait (used by the national genetic service provider, Sheep Genetics) for managing GIN infection and production traits (such as liveweight or fleece weight) the preferred traits for managing apparent resilience.

1.5.3. Cost of immunity to the host

Selecting and breeding animals with enhanced resistance to GIN is a non-chemical approach for improving GIN control and reducing pasture larval contamination (Morris *et al.*, 1995; Bisset *et al.*, 2001). However, the acquisition and expression of immunity to GIN is costly to the host with nutrients which otherwise would be available for growth and productivity diverted towards acquiring or expressing an immunological response to GIN (Parkins & Holmes, 1989; McClure, 2000; Greer *et al.*, 2005b; Doyle *et al.*, 2014; Dever *et al.*, 2016).

Costs associated with the acquisition and expression of immunity to GIN are influenced by genetic and phenotypic characteristics of both host and GIN and are summarised below (Parkins & Holmes, 1989; Colditz, 2008; Greer, 2008; Doyle *et al.*, 2014):

1) increased metabolic activity due to activation of immune system cells
2) reduced nutrient availability due to a decrease in VFI
3) diversion of nutrients from growth and productivity to non-productive functions associated with acquiring or expressing an immunological response
4) alteration in the size and rate of turnover of pools of immune cells and proteins
5) ineffective or excessive immune activity leading to immunopathology
6) reduced genetic gain in other traits if WEC is included in a selection index

It has been postulated that the process of acquiring immunity to GIN is the causal factor in production losses for naïve lambs as opposed to losses incurred by the direct pathological effects of GIN on the host (Greer *et al.*, 2005b; Greer *et al.*, 2008; Dever *et al.*, 2016). Doyle *et al.* (2014) showed that Merino weaner wethers were able to mount an effective immune response by partitioning protein and nitrogen away from production, such as muscle accretion, towards the immune organs, abomasal nodes and mucosa.

GIN infection often causes a reduction in VFI and anorexia in lambs resulting in depressed performance with fewer nutrients available to the host and an increase in metabolic demands during acquisition of immunity (Colditz, 2008). A number of researchers have investigated the costs associated with acquiring immunity to GIN by abrogating the immunological response of the host to GIN infection using corticosteroids (Greer *et al.*, 2005b; Greer *et al.*, 2008; Blackburn *et al.*, 2015; Dever *et al.*, 2016). Both *T. colubriformis* and *T. circumcincta* have been shown to reduce VFI of lambs by 20 – 30% (Coop *et al.*, 1976; Steel *et al.*, 1980; Greer *et al.*, 2005b), however in lambs infected with GIN and concurrently immunosuppressed, VFI is similar to that of uninfected lambs with little effect on growth and fleece weight (Greer *et al.*, 2005b;

Greer *et al.*, 2008). In addition to evaluating the cost of acquiring host immunity in lambs, Greer *et al.* (2005b) also examined the effect of *T. colubriformis* infection on immunologically competent 17 month-old ewes. WEC for the ewes was low suggesting an effective expression of immunity with liveweight not adversely affected by infection. This provides support that there is a greater cost to production during the acquisition rather than the expression phase of immunity.

1.5.3.1. Use of protein to enhance immune responses

Providing GIN susceptible sheep with increased levels of dietary protein, and more specifically metabolisable protein, enhances the immunological response of the host to GIN infection, hastens acquisition of immunity and reduces production losses associated with the effects of GIN (Wagland *et al.*, 1984; Bown *et al.*, 1991a; Kambara *et al.*, 1993; van Houtert *et al.*, 1995; van Houtert & Sykes, 1996; Datta *et al.*, 1998; Donaldson *et al.*, 1998; Datta *et al.*, 1999; Kahn *et al.*, 2000b). The effects of GIN (Section 1.4) are most pronounced during periods of rapid development in young animals and the periparturient period for the ewe (Coop & Kyriazakis, 1999). The capacity to manipulate or influence host immune response to GIN by increasing protein levels may also have benefit through reducing pasture larval contamination for GIN susceptible stock (Datta *et al.*, 1999; Beasley *et al.*, 2012a).

There have been conflicting reports indicating no apparent advantage or improvement in immunological responses to GIN from increased protein supply (Abbott *et al.*, 1985a; Kambara *et al.*, 1993; Kahn *et al.*, 2000b). It is likely that in those situations, the difference between the levels of protein offered to each group were small or that the base level was already adequate for moderate levels of growth.

Van Houtert *et al.* (1995) investigated the influence of different levels of by-pass protein (Fishmeal: 0, 50 or 100g day^{-1}) on growth of 3 month old Merino wethers either infected (trickle infected with 1,000 *T. colubriformis* larvae three times a week for 20 weeks) or uninfected. There was an interaction between level of by-pass protein offered and *T. colubriformis* infection with growth being increasingly impacted by infection as the level of by-pass protein decreased. These changes were coincident with a significant decline in WEC, total GIN counts, increased eosinophil concentrations and a reduction in the establishment of *T. colubriformis* larvae. Much of the benefit from increased protein on the immune response to infection occurred after day 70. Similar trends have also been observed in the timing of expression of immunity for lambs infected with *T. colubriformis* with a decline in WEC and total GIN burdens observed typically between 8 - 12 weeks following commencement of infection (Abbott *et al.*, 1985a; Bown *et al.*, 1991a; Kahn *et al.*, 2000a). It is likely that the increased levels of dietary protein increase the rate of development of host immunity rather than enhancing innate immunity and is mediated through an upregulation of specific (i.e. lymphocytes and antibodies) and non-specific responses (i.e. effector cells in the gut which release anti-parasitic substances).

1.5.4. Loss of immunity during the periparturient period

Ewes have a temporary relaxation of immunity to GIN during late pregnancy and early lactation, referred to as the periparturient relaxation of immunity (PPRI) and an associated periparturient rise (PPR) in WEC is often observed (Brunsdon, 1967; Courtney *et al.*, 1984; Kahn, 2003; Beasley *et al.*, 2010b, 2012a). The PPRI reduces the host’s capacity to expel established adult GIN, limit larval establishment and reduce fecundity of adult females. Development of arrested L4 larvae may also occur while immunity is suppressed (Donald *et al.*, 1982; Lloyd, 1983; Beasley *et al.*, 2012a). These changes lead to significant increases in WEC which increases pasture larval contamination (Brunsdon, 1967; Donaldson *et al.*, 2001; Beasley *et al.*, 2010b). The increase in number of eggs deposited on pasture during this period is considered the primary source of GIN infection for naïve lambs (Courtney *et al.*, 1984; Sargison *et al.*, 2012). There are differences in the response of the periparturient ewe to different GIN species. Gibbs and Barger (1986) established that the periparturient ewe is more susceptible to challenges of *T. colubriformis* and *T. circumcincta* compared with their dry counterparts while there appears to be little loss of immunity against *H. contortus* L3. However this has been refuted by Macarthur *et al.* (2013a) where there was a typical PPR in WEC for Merino ewes infected with 750 *H. contortus* L3/week.

Beasley *et al. (2010a, 2010b)* described the contributing factors and mechanisms which caused this phenomenon with *T. colubriformis* infection and the temporal association with systemic and local breakdown of immunological responses of the periparturient ewe in late pregnancy. There is an initial decrease in circulating eosinophils and total antibodies followed by an increase in WEC approximately two weeks prior to parturition. The immunological response of lactating ewes to GIN remained negligible following parturition with no increase in circulating total antibody titres and WEC increasing during the six week period after lambing. Similar responses were detected for tissue total antibody titres with little difference in titres between infected and suckled ewes with uninfected ewes following parturition. Reduced numbers of mast cells, globule leukocytes and goblet cells were also evident in infected, lactating ewes six weeks following parturition when compared with dry or early-weaned ewes. Both systemic and local immune responses were rapidly re-established in ewes when lambs were weaned early (two days after parturition), which provides further characterisation of the PPR. There was little evidence that changes in the endocrine system contributed to the PPRI as there was no association with increased levels of progesterone, oestradiol, cortisol, prolactin or leptin.

Other causal factors for initiating PPR in WEC have been postulated and include: inadequate antigenic stimulation, stress of parturition and increased nutrient demands (Dunsmore, 1965; O'Sullivan & Donald, 1970; Donald *et al.*, 1982; Courtney *et al.*, 1984; Jeffcoate *et al.*, 1992; Barger, 1993; Donaldson *et al.*, 1997; Kahn *et al.*, 1999; Walkden-Brown & Kahn, 2002; Houdijk, 2008; Sutherland & Scott, 2010).

The antibody IgA has an important role in the gut as a mediator of immunity to GIN infection and also plays a vital role in providing passive immunity to the neonate. This antibody, which is secreted in the milk, is synthesised in the gut mucosa and transported via serum to the mammary gland, thereby possibly reducing levels of the antibody in the gut during this period (1992). Beasley *et al.* (2010b) confirmed that total antibody titres of IgA in the gut were significantly lower in infected suckled ewes compared with infected dry and early-weaned ewes two weeks post-partum. WEC of the lactating ewes also continued to increase post parturition, confirming the immunological response of ewes remained suppressed during the lactational phase.

There is an abundance of literature showing that the nutritional status of the ewe can regulate the severity of PPRI in the periparturient ewe (Kahn *et al.*, 1999; Houdijk *et al.*, 2000; Walkden-Brown & Kahn, 2002; Houdijk, 2008; Beasley *et al.*, 2010a). Metabolisable protein (MP) and metabolisable energy (ME) requirements of ewes increase significantly during late pregnancy and lactation, suggesting that nutrient requirements for reproductive functions (namely parturition and lactation) have priority over upholding the integrity of immunological responses to GIN during this period. Ewes will mobilise body fat and protein reserves when nutrition is inadequate during this period (Houdijk, 2008; Beasley *et al.*, 2010a) causing decreases in bodyweight, fat score and fat and eye muscle depth (Beasley *et al.*, 2010a). This response is further compounded when ewes are infected with GIN (in particular *T. circumcincta* and *T. colubriformis* infections) since a reduction in VFI is a common effect of GIN infection. Leyva *et al.* (1982) investigated the effects of *T. circumcincta* on pregnant and lactating Poll Dorset ewes. Positive WEC were only observed in 15% of ewe's pre-parturition, indicating that ewes remained largely immune-competent during pregnancy. However during lactation, resistance diminished and a PPR in WEC occurred in all ewes confirming a PPRI postpartum. A 16% reduction in VFI occurred during lactation due to the effects of *T. circumcincta* infection and led to greater bodyweight losses and a more rapid decrease in milk production three weeks after parturition compared with that of uninfected ewes. Prior to parturition no significant differences were observed in VFI between infected and uninfected ewes.

Provision of supplementary feed to increase MP supply and to satisfy nutritional demands has been shown to enhance the immunological status of the ewe and reduce the effects of the PPRI in infected ewes (Donaldson *et al.*, 1997; Kahn *et al.*, 1999; Houdijk, 2008; Doyle *et al.*, 2011). Donaldson *et al.* (1997) investigated the effect of protein on the PPRI of Coopworth ewes. The diets offered to the periparturient ewes were formulated to ensure MP requirements were exceeded, whilst the energy component of the diets were devised such that ewes maintained their current bodyweight or gained 50 g/day. Increasing energy supply in the diet did not reduce the effect of PPRI in ewes as there was no reduction in WEC when energy was supplied at higher levels. In contrast, reductions in WEC occurred in ewes where MP was in excess of calculated requirements for a ewe in the final stages of gestation (Donaldson *et al.*, 1997). These results indicate MP has the capacity to regulate the effects of GIN on the periparturient ewe.

The effect of genotype can also influence the variation in the degree of PPR in WEC exhibited by periparturient ewes. Donald *et al.* (1982) compared GIN burdens of Merino and Border Leicester X Merino (BL x M) periparturient ewes which had been grazing pastures contaminated with *Teladorsagia* spp. Two ewes selected from each genotype on two occasions were humanely euthanised; just prior to lambing and approximately 7 weeks after lambing. On each occasion there were significantly greater numbers of adult *Teladorsagia* spp. in Merino ewes compared with that of BL x M ewes. Although a PPRI was observed in both genotypes, BL x M ewes were more resistant to *Teladorsagia* spp. than Merino ewes during the periparturient period. Similar results have been reported when comparing the PPR in WEC of exotic and domestic breeds (Courtney *et al.*, 1984). Exotic breeds (developed through natural selection) are considered more resistant to GIN infection than domesticated sheep breeds with little or no change in WEC during the periparturient period for exotic bred sheep, while a typical PPR in WEC was detected in domestic ewes.

1.6. Strategies for controlling gastrointestinal nematodes

Previous sections have described the epidemiology of GIN infection in sheep with particular reference to the: (i) major GIN species in the summer rainfall region of the Northern Tablelands of NSW; (ii) regulatory effects of macro-climatic variables on development and survival of infective larvae; and (iii) role and regulation of immunological responses to infection. The following sections review the main components of strategies used in the control of GIN infection.

1.6.1. Chemical treatments

1.6.1.1. Narrow spectrum drenches

Narrow spectrum drenches are classified as having activity against one GIN species. The most common and widely used narrow spectrum drench is closantel from the salicylanilide family. This drench is highly efficacious against all stages of the GIN, *H. contortus* while against the trematode, liver fluke is effective against all stages >6 weeks of age (Sutherland & Scott, 2010). It has sustained activity for up to four weeks against susceptible strains of *H. contortus* with no faecal egg output for approximately seven weeks (Rolfe, 1990). The main benefit for using a narrow-spectrum drench is that it specifically targets one species and no selection pressure is applied to other GIN species. This drench was the integral component of the strategic drenching program, WormKill, in the summer rainfall areas of New South Wales and south-east Queensland (Dash, 1986) for control of *H. contortus*; however there is now widespread closantel resistance in these regions (Playford *et al.*, 2014). Briefly, closantel was administered on three (subsequently reduced to two) occasions each year between October and February to provide protection during the traditionally peak *H. contortus* period. Using this protocol, some producers apparently eradicated *H. contortus* from their properties for some time, whilst haemonchosis was controlled on other farms. Unfortunately after 2 – 3 years of suppressing *H. contortus* burdens using closantel, resistance became evident (Rolfe *et al.*, 1990). This was not solely due to repeated treatments using the same active but through exposing *H. contortus* larvae to sub-optimal levels of closantel as a result of declining closantel plasma concentrations (Rolfe, 1990). There would also be a reproductive advantage for resistant genotypes during the period of protection which increases selection pressure for development of drench resistance as there is; (i) a lag period of four weeks preventing susceptible genotypes from establishing and (ii) a three week pre-patent period before eggs of susceptible genotypes will be deposited on pasture.

Current estimates indicate that >80% of properties in northern New South Wales and south-east Queensland have *H. contortus* which are resistant to closantel (Love, 2011).

1.6.1.2. Mid spectrum drenches

The organophosphate compound, naphthalophos is a short-acting drench with mid spectrum activity against a number of GIN species. This compound is highly efficacious against *H. contortus* but has varying levels of effectiveness (between 70 – 90%) against *Trichostrongylus* spp. and *T. circumcincta* (Kotze *et al.*, 1999). Naphthalophos was regularly used between 1960 and 1980 for control of *H. contortus* and during the 1990s it was combined with other actives (i.e. levamisole (LEV) and benzimidazoles (BZ)) to provide greater control against LEV/BZ resistant strains of GIN. There are confirmed reports of naphthalophos resistant *H. contortus* (Figure 1-8), though it is not widespread (Playford *et al.*, 2014). Combining naphthalophos with other actives provides an effective option for drenching programs against a wide range of GIN species.

1.6.1.3. Broad spectrum drenches

Thiabendazole was the first highly effective active released from the benzimidazole group followed by levamisole from the imidazothiazole group in 1968 (Waller, 2006). These two new classes of actives (with different modes of action) allowed producers to rotate chemical actives within drenching programs with the added advantage that benzimidazoles also provided some control against tapeworm and trematodes (Elsheikha & Khan, 2011). It was twenty years later (1981) that a new group, avermectin (a derivative of the macrocyclic lactone class) was released with ivermectin the first active from this group available commercially (McKellar & Jackson, 2004). It was a valuable active due to its high level of efficacy and activity against a wide range of GIN as well as its effectiveness against a number of external parasites. Other actives developed from avermectin include: abamectin, doramectin and eprinomectin (McKellar & Jackson, 2004; Elsheikha & Khan, 2011), all of which have short-acting broad spectrum activity. The other derivative of the macrocyclic lactone family is milbemycin with moxidectin the active belonging to this family. Moxidectin is extremely lipophilic and persists in tissues longer than other actives from the avermectin group and has persistent activity against *H. contortus* and *Teladorsagia* spp. (Elsheikha & Khan, 2011). Within the ML group, moxidectin has the highest potency against ML resistant GIN, followed by abamectin and then ivermectin (Dobson *et al.*, 2001; Kotze *et al.*, 2014).

Monepantel has a unique mode of action and a very wide safety margin as it attacks a nematode specific receptor (Hco-MPTL-1) (Kaminsky *et al.*, 2008) and derquantel has been formulated in combination with abamectin to provide broad spectrum activity.

1.6.2. Strategic and tactical drench treatments

Drenching remains a key factor in the control of GIN and reducing the effects of GIN on the host. There are two drenching strategies; tactical or strategic. Tactical drenches are administered when WEC exceed treatment thresholds for important GIN species (Maxwell *et al.*, 2012), while the objective of a strategic treatment is to reduce pasture larval contamination, provide low GIN-risk pastures for susceptible stock (not dependent on WEC) and provide protection to GIN susceptible animals when GIN challenge is high (Sutherland & Scott, 2010; Maxwell *et al.*, 2012). Routine WEC monitoring is an important factor to incorporate into drenching programs as it provides guidance for when a tactical drench is required to be administered (Maxwell *et al.*, 2012). A number of strategic drenching programs have been devised to facilitate the reduction in larval numbers on pasture. On the Northern Tablelands, a strategic autumn drench is often administered to sheep which are grazing pastures that will later be used for lambing in September. This drench will prevent autumn contamination of eggs on pasture which otherwise would be a significant source of larvae to the periparturient ewe in late winter and spring (Southcott *et al.*, 1976; Niven *et al.*, 2002). Sheep may remain on this pasture for three weeks and at a higher stocking rate (to increase the number of larvae removed from pasture) when a short-acting drench is administered after which they should be moved to ensure no further eggs are deposited on pastures and also allows suitable time for a significant proportion of remaining larvae to die prior to lambing in spring. Weaning paddocks can be prepared in a similar manner on the Northern Tablelands, NSW with significant reductions in pasture larval numbers likely to occur over three months rather than six due to the faster rate of larval development during warmer temperatures and precipitation. Sheep are drenched in September and placed on weaning paddocks at a higher stocking rate for three weeks. This strategy will remove significant numbers of larvae (Dunn, 1969;

Todd *et al.*, 1976b; Niven *et al.*, 2002), thus providing a low GIN-risk pasture for weaners.

Strategic drenches are often administered to peri-parturient ewes pre-lambing as immunity to GIN diminishes a couple of weeks prior to lambing and continues through lactation (Beasley *et al.*, 2010b).

1.7. Drench resistance

Drench resistance is defined as the 'ability of parasites to survive doses of drugs that would normally kill parasites of the same species and stage' (Besier & Love, 2003) and is present when the percentage reduction in WEC is <95% and the 95% confidence interval is <90% (Coles *et al.*, 1992; Sutherland & Scott, 2010). Drench efficacy is described as: >98% highly effective, 90 – 98% effective, 80 – 89% moderately effective and <80% inadequate protection (Wood *et al.*, 1995).

1.7.1. Implications and production costs

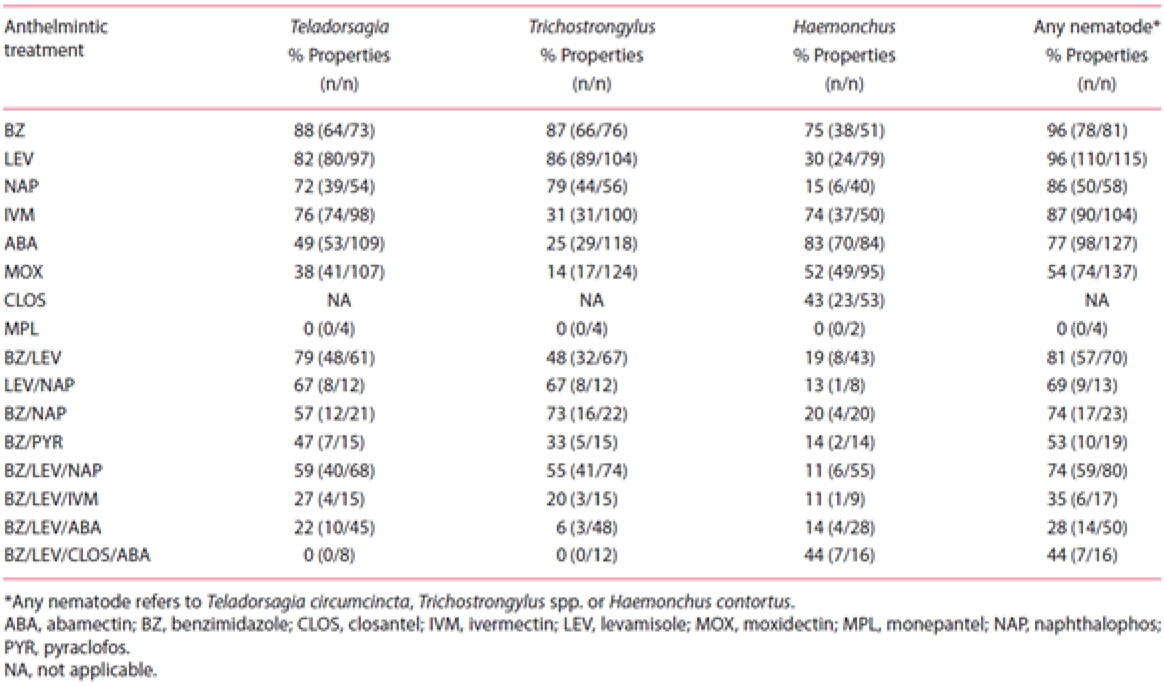
The cost of drench resistance on productivity is difficult to quantify at an industry level as resistance of GIN species to drenches differs between properties, management systems, genotypes, type of GIN infection present and region (Pomroy, 2006; Sutherland *et al.*, 2010; Miller *et al.*, 2012). The significance of quantifying the cost of drench resistance on productivity is necessary to highlight the importance of using drenches that are fully effective as opposed to production losses associated with the administration of drenches with reduced efficacy. Approaches to slow development of drench resistance should be implemented to ensure the longevity of effective drenches and the two main approaches to achieve this are; (i) administering effective combination drenches and (ii) maintaining a proportion of the GIN population in refugia (Barnes *et al.*, 1995; van Wyk, 2001; Dobson *et al.*, 2011; Bartram *et al.*, 2012).

Experiments investigating the effects of drench resistance on host performance have shown significant decreases in bodyweight and wool growth and an increase in scouring and mortality due to the ineffective control of GIN (Besier *et al.*, 1996; Sutherland *et al.*, 2010; Miller *et al.*, 2012). Besier and his colleagues (1996) confirmed that production losses and a decline in sheep value was attributable to the use of ineffective drenches. Three hundred Merinos weaner wethers were treated with drenches that were either; a) 100% effective – moxidectin (MOXI), b) 85% effective – benzimidazole-levamisole combination (BZ/LEV) and c) 65% effective – benzimidazole (BZ). Each treatment group grazed separately. Over a 12 month period three drenches were administered to each group (December, February and August), in accordance with the recommended 'summer drenching' program in Western Australia. The disparity of effectiveness between drench treatments was shown with greater WEC in sheep treated with drenches that were not fully effective (BZ/LEV and BZ). After 12 months, differences in sheep production traits were analysed. Sheep administered the drench which was 65% effective grew 450 g less wool and growth was reduced by 6 kg compared with sheep administered a drench that was 100% effective. Sheep administered the 85% effective drench grew 90 g less wool and grew 1.2 kg less than the 100% treatment group over the year. There was an increase in the prevalence of scouring and mortality within groups treated with drenches of reduced efficacy with the incidence of scouring being 3 and 2.5 times higher and mortality 2.5 and 3.5 times higher in sheep treated with 85% and 65% effective treatments respectively. Although the composition of larval species present was not stated, it may be assumed that in the Mediterranean (winter rainfall) climate (Besier & Love, 2003; Williams *et al.*, 2010a) the most prevalent species present were *Trichostrongylus* spp. and *T. circumcincta.* This would account for the production losses observed given WEC were moderate (not reflective of a typical *H. contortus* infection) and *Trichostrongylus* spp. and *T. circumcincta* typically reduce VFI and feed utilisation (Coop *et al.*, 1976; Bown *et al.*, 1989; van Houtert & Sykes, 1996; Greer *et al.*, 2005b).

Production losses due to drench resistance has also been confirmed in regions of New Zealand where common drenching regimens for controlling GIN is to treat weaners on a monthly basis when pasture larval contamination is high (Sutherland *et al.*, 2010). Often producers are unaware of their drench resistance status as sheep do not show overt clinical signs of parasitism (Miller *et al.*, 2012). An effective (derquantel/abamectin - >99% effective) or ineffective drench (albendazole (BZ) – 48% and 41% efficacious against *Trichostrongylus* spp. and *T. circumcincta* respectively) was administered on a monthly basis to lambs grazing paddocks known to be contaminated with benzimidazole resistant *T. colubriformis*, *T. circumcincta* and *Nematodirus spathiger* (Miller *et al.*, 2012). This drenching frequency is typical for many lamb production systems in New Zealand where pasture larval contamination is very high at weaning (Sutherland *et al.*, 2010). Lambs treated with the ineffective drench had higher WEC and dag scores, reduced growth (9 kg), carcass weight (4.7 kg) and body condition score and there was an overall deficit in carcass value of 10.4% (NZ$11.56) over a five month period. Lambs treated with the effective drench reached the target weight of 38 kg in a significantly shorter period of time (17 days earlier) (Miller *et al.*, 2012). The authors alluded that sheep treated with the ineffective drench appeared healthy which reiterates that difficult to detect, sub-clinical effects of parasitism cause significant production losses (Miller *et al.*, 2012). These results concurred with those obtained earlier by Sutherland *et al.* (2010) when drench resistance (benzimidazole) lead to a 14% reduction in carcass value of lambs. These examples demonstrate the implications of drench resistance on productivity and losses incurred as a result of administering ineffective drenches. The main point for conclusion is that sheep producers need to be aware of the drench resistance status on their farm so as to avoid the use of ineffective drenches which would reduce sub-clinical parasitism.

1.7.2. Prevalence and distribution in Australia

Drench resistance in Australia is widespread and severity continues to worsen (Love, 2011; Playford *et al.*, 2014). Recent reports indicate that the GIN (*H. contortus, Trichostrongylus* spp. and *Teladorsagia circumcincta*) are resistant to one or a number of broad-spectrum drenches (benzimidazole (BZ), levamisole (LEV), ivermectin (IVM) and abamectin (ABA)) on >77% of properties and to moxidectin (MOX) on 54% of properties. There are recent reports of *H. contortus* resistance to monepantel (Van den Brom *et al.*, 2015); however there yet to be any confirmed reports in Australia. Resistance of individual GIN species (*Teladorsagia* spp. *Trichostrongylus* spp. and *H. contortus*) to drench actives is reported in Figure 1-8.



Anthelmintic treatment	*Teladorsagia* % Properties (n/n)	*Trichostrongylus* % Properties (n/n)	*Haemonchus* % Properties (n/n)	Any nematode* % Properties (n/n)
BZ	88 (64/73)	87 (66/76)	75 (38/51)	96 (78/81)
LEV	82 (80/97)	86 (89/104)	30 (24/79)	96 (110/115)
NAP	72 (39/54)	79 (44/56)	15 (6/40)	86 (50/58)
IVM	76 (74/98)	31 (31/100)	74 (37/50)	87 (90/104)
ABA	49 (53/109)	25 (29/118)	83 (70/84)	77 (98/127)
MOX	38 (41/107)	14 (17/124)	52 (49/95)	54 (74/137)
CLOS	NA	NA	43 (23/53)	NA
MPL	0 (0/4)	0 (0/4)	0 (0/2)	0 (0/4)
BZ/LEV	79 (48/61)	48 (32/67)	19 (8/43)	81 (57/70)
LEV/NAP	67 (8/12)	67 (8/12)	13 (1/8)	69 (9/13)
BZ/NAP	57 (12/21)	73 (16/22)	20 (4/20)	74 (17/23)
BZ/PYR	47 (7/15)	33 (5/15)	14 (2/14)	53 (10/19)
BZ/LEV/NAP	59 (40/68)	55 (41/74)	11 (6/55)	74 (59/80)
BZ/LEV/IVM	27 (4/15)	20 (3/15)	11 (1/9)	35 (6/17)
BZ/LEV/ABA	22 (10/45)	6 (3/48)	14 (4/28)	28 (14/50)
BZ/LEV/CLOS/ABA	0 (0/8)	0 (0/12)	44 (7/16)	44 (7/16)

*Any nematode refers to *Teladorsagia circumcincta*, *Trichostrongylus* spp. or *Haemonchus contortus*.
ABA, abamectin; BZ, benzimidazole; CLOS, closantel; IVM, ivermectin; LEV, levamisole; MOX, moxidectin; MPL, monepantel; NAP, naphthalophos; PYR, pyraclofos.
NA, not applicable.

Figure 1-7 National summary of WECRT conducted between 2009 and 2012 indicating the percentage and number of properties where differentiated reduction in WEC was <95% for *T. circumcincta*, *T. colubriformis* and *H. contortus* in sheep. Retrieved from: (Playford *et al.*, 2014)

1.7.3. Causative factors

The combination of frequent drenching, under-dosing, use of single-active and persistent drenches has accelerated the selection pressure for development of drench resistance (Besier & Love, 2003).

1.7.3.1. Use of single actives

Treating animals with a single active offers a reproductive advantage for resistant genotypes (Bartram *et al.*, 2012) with any surviving larvae reproducing and any eggs deposited on pasture will contain resistant alleles and will form the foundation of the next generation of GIN on pasture. This practice is of particular concern particularly when animals are drenched and placed onto a low GIN-risk pasture as selection pressure for development of drench resistance is high. There are challenges (namely; time, environmental influences and larval viability) investigating the rate of development of drench resistance in ‘real-life’ scenarios (Leathwick *et al.*, 2012) and therefore modelling simulations and scenarios have been developed to estimate the increase in frequency of resistant genes within the GIN population over time when both single and combination actives are administered and at different levels of effectiveness. There is little evidence of cross-resistance between actives from different drench groups (Coles & Roush, 1992) and therefore use of combination drenches (actives from different drench groups) which independently target different GIN receptors or have different mechanisms of action on GIN can delay the development of drench resistance (Figure 1-9) (Dobson *et al.*, 2011; Bartram *et al.*, 2012; Leathwick, 2012).

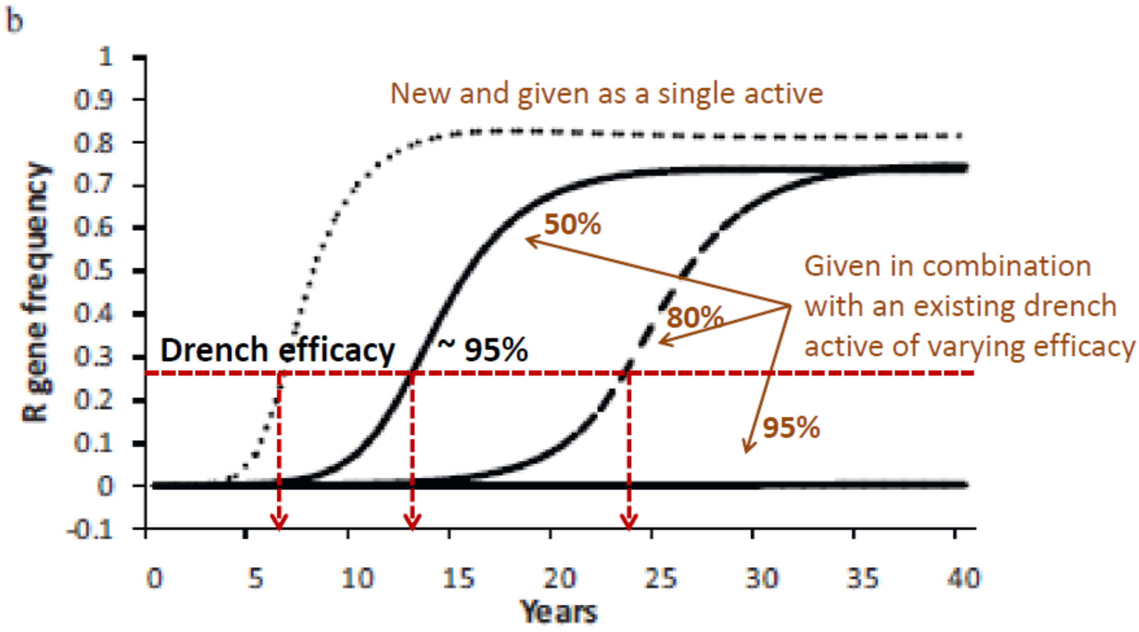


Figure 1-8 Resistance gene frequencies for a new drench active when administered to lambs six times at twenty-eight day intervals starting at weaning when placed into a low GIN-risk paddock. Dotted line is new single active; next 3 lines represent the new active administered in combination with abamectin when abamectin is either 50%, 80% or 95% effective. Retrieved from: (Leathwick, 2012)

1.7.3.2. Drench persistency

Treating sheep with drenches with persistent activity against important GIN species may be considered a strategic management approach to control GIN and reduce pasture larval contamination. Drenches with persistent activity are often administered to; (i) avoid outbreaks when challenge is historically high, (ii) eliminate the peri-parturient rise in WEC of ewes and (iii) prepare low GIN-risk paddocks for lambing or weaning by ensuring no eggs are deposited on pasture during the preparation period. These strategies are designed to reduce the number of drenches administered, pasture larval contamination and production losses.

When treating animals with drenches with persistent activity, particular attention should be given to timing of treatment and the paddock animals will be grazing after treatment as these influences may provide a selection and reproduction advantage for resistant genotypes. Any surviving genotypes will continue to mate and reproduce, and any eggs deposited on pasture will be of resistant genotype, which will increase the proportion of resistant alleles within the population. Depending on drench persistency, there may be a potential lag period of up to 100 days before susceptible L3 have the capacity to establish, develop, reproduce and once the pre-patent period has lapsed deposit viable homozygote susceptible eggs on pasture to resume dilution of the resistant population. It is therefore not recommended to place sheep (recently treated with a drench with persistent activity) onto pastures considered relatively low GIN-risk as any resistant genotypes deposited on the pasture will ultimately be the source of GIN for the next generation within the GIN population.

Further selection advantage occurs for resistant L3 (homozygote and heterozygote) when concentration of an active declines over time (e.g. moxidectin) with resistant L3 establishing (‘tail selection’) earlier than susceptible L3, which provides them with a period of reproductive advantage over susceptible genotypes (Dobson *et al.*, 1996; Sutherland & Scott, 2010). This advantage is shown in a hypothetical situation in Figure 1-10 with resistant genotypes surviving higher concentrations of the active than susceptible genotypes, which provides them with a reproductive advantage.

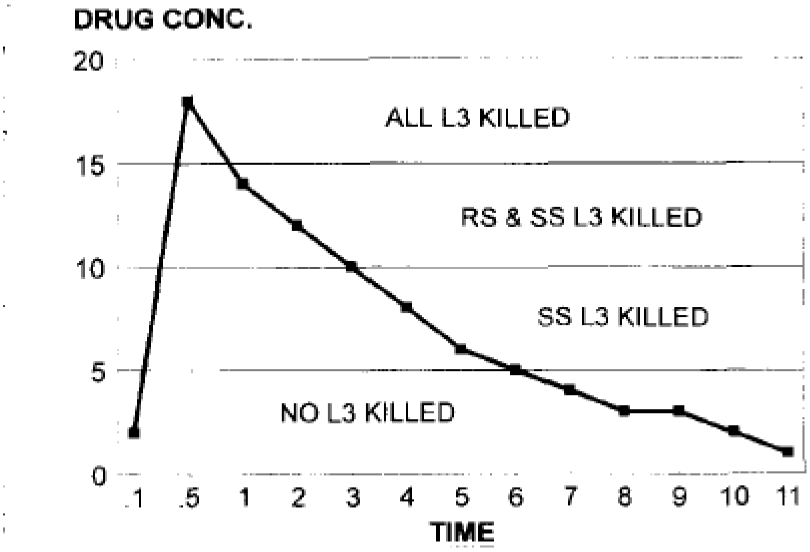


Figure 1-9 Hypothetical illustration of the effect of declining active concentration (in arbitrary units) in the host and the effect on survival of RR (homozygote-resistant L3), RS (heterozygote-resistant L3) and SS (homozygote-susceptible L3) infective larvae at different active concentrations. Source: (Dobson *et al.*, 1996)

1.7.3.3. Frequency of drench administration

The most common approach for controlling GIN or 'resetting the burden to zero' is to administer a drench (Waller, 1994; Besier & Love, 2003; Kahn *et al.*, 2006; Sutherland *et al.*, 2010). However when the modern day broad spectrum drenches were released, little consideration was given towards the concept that frequent use of drenches may hasten the development of drench resistance (Besier & Love, 2003; Waller, 2006). Resistance evolves as the frequency of resistant alleles within the population increases and arises from changes in target receptors, gene mutations and altered metabolism and uptake (Wolstenholme *et al.*, 2004). Frequent treatment with the same active provides resistant alleles a selection advantage allowing them to continue to reproduce and the next generation evolves after susceptible GIN are removed. Overtime there is a dynamic change with an increasing frequency of resistant alleles with the GIN population which occurs at a greater rate when sheep are placed onto low GIN-risk pastures after drenching.

1.8. Refugia

The term refugium is defined as the population of GIN, on pasture or within animals, which has not been exposed to an active/s (van Wyk, 2001). This population of GIN remain more susceptible to that particular active and have the potential to develop, establish and reproduce (with other susceptible GIN) so that more susceptible genotypes contribute to the next generation of eggs deposited on pasture. This will potentially lead to successful dilution of any more resistant genotypes within the population if managed efficiently (Martin *et al.*, 1981; van Wyk, 2001; Sutherland & Scott, 2010; Elsheikha & Khan, 2011; Bartram *et al.*, 2012; Besier, 2012; Dobson *et al.*, 2012; Leathwick *et al.*, 2012). Treating all sheep within a flock and placing them onto prepared low GIN-risk pastures or suppressively treating sheep is not recommended since both provide insufficient opportunity for susceptible GIN genotypes to develop, establish and reproduce (van Wyk, 2001). In these instances there is an increased selective advantage for resistant GIN genotypes (van Wyk, 2001; Sutherland & Scott, 2010) combined with an increase in the rate of development of drench resistance (Leathwick *et al.*, 2012). Maintaining suitable levels of susceptible GIN in refugia is a strategic management technique to reduce the rate of development of drench resistance (Martin *et al.*, 1981; Besier, 2012; Knox *et al.*, 2012; Leathwick *et al.*, 2012).

Targeted selective treatment (TST) is a strategy (established on phenotypic effects of GIN infection on the host) aimed at reducing the rate of development of drench resistance and maintaining a level of genotypes that are more susceptible to the active in refugia (Besier, 2012). It has been established that when up to 20% of the mob remain untreated a suitable reservoir of susceptible GIN will be preserved on pasture (Barnes *et al.*, 1995; Leathwick *et al.*, 2012). The actual proportion of animals that should remain untreated to attain a certain level of dilution is dependent upon the effectiveness of the drenches administered. Leathwick *et al.* (2009) reported that in order to achieve a 10-fold dilution rate using a 99.9% effective drench, one per cent of the flock would be required to remain untreated, however when drench efficacy was reduced to 95%, the number of animals required to remain untreated increases significantly to 34% to achieve the same level of dilution. Due to the high incidence of drench resistance to broad spectrum drenches many parasitologists and advisors advocate the use of combination drenches to improve efficacy and decrease the number of eggs of resistant genotype deposited on pasture. Leathwick *et al.* (2012) conducted a study over a 3 year period to establish whether the use of a combination drench and leaving a proportion of the group untreated would slow the development of resistance to ivermectin. Lambs were either treated with a single active (IVM) or with a combination of actives (IVM + LEV) and either the entire (100%) mob was treated or 90%, with the heaviest 10% of lambs selected to remain untreated (TST). New lambs were purchased each year for three years and remained at the research farm for approximately 6 months over which time they were treated on a monthly basis within their respective groups. At the conclusion of the experiment it was shown that development of resistance to ivermectin was reduced when a combination drench (IVM + LEV) was administered and when 10% of the lambs remained untreated. The lambs which remained untreated increased the refugia pool of unselected GIN genotypes on the paddocks (Leathwick *et al.*, 2012). A number of computer modelling studies (Barnes *et al.*, 1995; Leathwick *et al.*, 1995; Dobson *et al.*, 2012; Learmount *et al.*, 2012) which investigated the development of drench resistance supported the outcomes of Leathwick *et al.* (2012) and showed that resistance is delayed when a proportion of the flock is left untreated and also when combination drenches are administered, and supports results observed in field studies.

Strategic treatment regimens are highly effective for decreasing pasture larval contamination, however if drenches are administered at times when minimal larvae are on pasture (e.g. administering a long acting drench to ewes pre-lambing) or when sheep are treated and then moved to a pasture with minimal larval contamination there will be a selection advantage for resistant GIN genotypes and a rapid change in the dynamics of the susceptible GIN population in refugia (Leathwick *et al.*, 2009)

Despite the advantages for maintaining a population of unselected GIN genotypes in refugia, TST has not been rapidly adopted by producers (Leathwick *et al.*, 2009; Besier, 2012) due to an increased risk of parasitism and production loss. The objective is to maintain a suitable level of susceptible GIN in refugia while not compromising productivity (Leathwick *et al.*, 2009). However, if little emphasis is placed on refugia based strategies and there is a continued reliance on drenches, then the sustainability of a production system is likely to decline at a greater rate due to an increased rate of development of drench resistance.

1.9. Non-chemical approaches to gastrointestinal nematode control

While the prevalence of drench resistance continues to worsen, non-chemical strategies for controlling GIN need to be adopted to mitigate production losses associated with ineffective drenches and reduce dependency on chemical control. Focus on implementing integrated parasite management strategies (IPM) which include grazing management and breeding for worm resistance have been publicised for some time.

1.9.1. Grazing management

One approach to reduce reliance on drenches is to prepare paddocks with low levels of larvae for susceptible stock. This strategy relies on a comprehensive knowledge of the epidemiology of the most important GIN species present, familiarity of the region's macroclimate and an awareness of the influence of pasture conditions and aspects of the microclimate on GIN development and survival (Anderson, 1983; Barger, 1999a). A significant decline in larval numbers on pasture can take between 3 – 9 months (Barger *et al.*, 1972; Barger, 1999a) and is dependent on climatic conditions and pasture coverage with a faster rate of decline occurring during the summer months (Figure 1-11). On the Northern Tablelands, NSW lambing paddocks are often prepared by removing stock from paddocks for six months from March with the key being the prevention of autumn contamination of eggs on pasture as this would otherwise be a significant source of larvae in late winter and spring for ewes and lambs (Southcott *et al.*, 1976; Barger, 1999a). While preparation of low GIN-risk paddocks for susceptible stock is an effective approach for good GIN control, there is a potential threat which may increase the severity of drench resistance. Any larvae that survived a drench treatment prior to sheep being placed on the pasture will have a reproductive advantage and the proportion of resistant genotypes on pasture will increase.

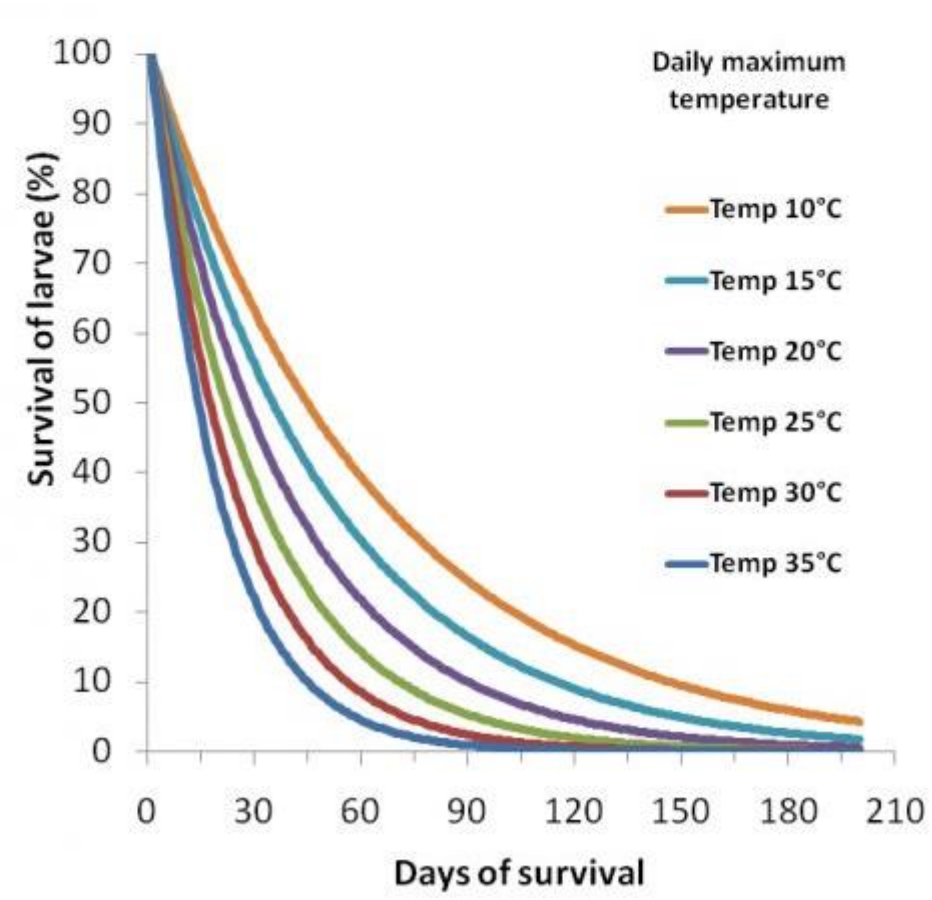


Figure 1-10 Survival of *Haemonchus contortus* infective larvae on pasture at various daily maximum temperatures and 60% relative humidity. Source: Developed from death rate of the L3 population in 'Simulation of pasture larval populations of *Haemonchus contortus*' (Barger *et al*., 1972).
Obtained from: http://www.wormboss.com.au/programs/tablelands-slopes/appendices/roundworm-life-cycle-and-larval-survival.php (WormBoss).

Alternating grazing with mature cattle is another approach to reduce larval numbers on pasture. Cattle are used to prepare paddocks as sheep GIN have negligible larval establishment rates in mature cattle. Cattle can significantly reduce *H. contortus* and *T. colubriformis* larval populations in as little as six weeks and *T. circumcincta* by twelve weeks (Southcott & Barger, 1975). Only small numbers of *T. circumcincta* were found at six and twelve weeks but this may have been favoured by the experiment design as it commenced in the summer months which is not conducive to *T. circumcincta* development (Southcott *et al*., 1976).

Three different methodologies for preparing spring lambing paddocks with low levels of larvae on pasture on the Northern Tablelands, NSW were investigated by Bailey *et al.* (2009b). Paddocks were either; a) grazed intensively by recently drenched wethers for twenty-one days in late January/February and again in late March at a high stocking rate (SSR), b) continuously grazed by adult sheep (CS) or c) continuously grazed by cattle (CC). These management strategies may be considered best practice (SSR and CC) or typical regional standard practice (CS) for preparation of lambing paddocks. As expected WEC of ewes and lambs were significantly lower when pastures were prepared using SSR and CC strategies. Neither ewes nor lambs required drenching at marking or weaning, while on CS prepared pastures ewes were drenched at both marking and weaning and lambs at weaning. There were production benefits from the grazing strategies with ewes and lambs grazing SSR and CC prepared pastures being significantly heavier than those grazing CS prepared pastures despite remaining untreated.

Rotational grazing requires paddocks to be subdivided with each paddock grazed for a short period of time (to avoid autoinfection) and rested for an extended period so that a significant proportion of infective L3 die prior to the paddock being re-grazed. This strategy is an effective system for controlling levels of GIN whilst reducing the effects of GIN on the host and fewer drenches are administered. Timing of the grazing and resting periods is dependent upon the GIN species present, region and seasonal conditions, as larval development rate increases as temperature and moisture increases (Krecek *et al.*, 1992; Rossanigo & Gruner, 1995; Khadijah *et al.*, 2013a). Rotational grazing is particularly successful in tropical regions as translation from unembryonated egg to infective larvae is rapid due to high temperatures and rainfall (Barger, 1999a) while L3 survival is reduced (Waller, 1997). Conversely, there is greater complexity with rotational grazing in temperate regions as climatic conditions are more favourable for L3 survival which can remain on pasture for longer periods

(Colvin *et al.*, 2012). Ideally in tropical regions sheep should be rotated between pastures every 3-4 days as this is minimum time for eggs to develop to the infective larval stage (Hsu & Levine, 1977). Larval concentrations on pasture will be highest approximately one week following deposition and within 4-6 weeks there will be few larvae surviving on pasture (Barger, 1994). The period of grazing in the temperate summer rainfall regions on the Northern Tablelands, may be extended over the winter period since larval development rate is reduced at cooler temperatures and with insignificant rainfall.

On the Northern Tablelands, the Cicerone Project investigated the effects of different management systems on the incidence and severity of GIN using three different classes of sheep; ewes, hoggets and lambs (Colvin *et al.*, 2008). The three management systems included intensive rotational grazing (mean grazing period: 5 days, mean rest period 103 days), high input (long graze periods, high stocking rate, improved pastures) and typical standard management for the Northern Tablelands, NSW (i.e. long graze periods). WEC were monitored monthly and were lower for sheep managed under the intensive rotational grazing system than the high input and typical systems. These sheep also required fewer drenches with the interval between treatments significantly greater under intensive rotational grazing. The proportion of *H. contortus* was lower in faecal cultures from sheep under intensive rotational grazing highlighting the importance of understanding the epidemiology of the important GIN species.

1.10. Conclusion

Gastrointestinal nematodes continue to place significant economic constraints on the Australian sheep industry and cost Australian sheep producers an estimated $436 million/year of which 78% is attributed to production losses (Lane *et al.*, 2015).

Although parasitism is ranked the second highest endemic sheep disease in Australia, the effects of GIN are not only confined to this disease but also contribute significantly to the disease costs associated with flystrike and post-weaning mortality.

The most common strategy for controlling GIN is to administer a drench, however the increasing prevalence of drench resistance (Playford *et al.*, 2014) together with the infrequent release of new compounds (two in the last 30 years) indicates that alternative and integrated strategies for controlling GIN need to be adopted by producers. There are extensive reports in the literature highlighting the influence of chemical and non-chemical approaches to GIN control, including; genetics, grazing management, nutrition, GIN monitoring and drenching. Implementation of IPM strategies has been shown to reduce the effects of GIN and reliance on drenches for Merino sheep (Scrivener *et al.*, 2006; Kelly *et al.*, 2010; Kahn & Woodgate, 2012).

Research into the effects of GIN has previously focused on Merinos (particularly in Australia), with few reports on the effects of GIN on meat-breed lambs. Meat-breed lamb production systems are not considered impervious to the effects of GIN and are estimated to have a higher cost from GIN than Merino operations (Sackett *et al.*, 2006). In the high winter rainfall regions of southern Australia where *Trichostrongylus* spp. and *Teladorsagia* spp. predominate, reduced lamb growth rate is the highest cost associated with GIN infection for meat-breed lamb production (Carmichael, 2009).

Production systems in southern Australia differ markedly to that in the high summer rainfall region on the Northern Tablelands NSW, where lambs typically graze pastures consisting of improved and native grasses as opposed to annual crops, legume dominant pastures and the use of irrigation. GIN species also differ between regions with *Haemonchus contortus* the predominant species on the Northern Tablelands, NSW and *Trichostrongylus* spp. and *Teladorsagia* spp. of seasonal importance.

The experiments reported in this thesis were designed to define the effect of ewe and lamb GIN control on meat-breed lamb and ewe performance and identify implications for drench resistance and host immunity in the summer rainfall regions in Australia.

Chapter 2 Persistent challenge with *Trichostrongylus colubriformis* and *Haemonchus contortus* larvae does not affect growth of meat-breed lambs suppressively treated with anthelmintics when grazing

M.L. Dever, L.P. Kahn, E.K. Doyle

Accepted 7 February 2015, Veterinary Parasitology 209: 76-83

Dever, M. L., Kahn, L. P. and Doyle, E. K. (2015). Persistent challenge with *Trichostrongylus colubriformis* and *Haemonchus contortus* larvae does not affect growth of meat-breed lambs suppressively treated with anthelmintics when grazing. *Veterinary Parasitology*, *209*(1-2), 76-83.

http://dx.doi.org/10.1016/j.vetpar.2015.02.009

Chapter 3 Immune-mediated responses account for the majority of production loss for grazing meat-breed lambs during *Trichostrongylus colubriformis* infection

M.L. Dever, L.P. Kahn, E.K. Doyle, S.W. Walkden-Brown

Accepted 28 November 2015, Veterinary Parasitology 216: 23-32

Dever, M. L., Kahn, L. P., Doyle, E. K., & Walkden-Brown, S. W. (2016). Immunemediated responses account for the majority of production loss for grazing meatbreed lambs during *Trichostrongylus colubriformis* infection. *Veterinary Parasitology*, *216*, 23-32.

http://dx.doi.org/10.1016/j.vetpar.2015.11.017

Chapter 4 Integrated parasite management improves control of gastrointestinal nematodes in lamb production systems in a high summer rainfall region, on the Northern Tablelands, NSW.

M.L. Dever, L.P. Kahn, E.K. Doyle

Accepted to Animal Production Science

Dever, M. L., Kahn, L. P. & Doyle, E. K. (2017). Integrated parasite management improves control of gastrointestinal nematodes in lamb production systems in a high summer rainfall region, on the Northern Tablelands, New South Wales. *Animal Production Science*, *57*(5), 958-968.

http://dx.doi.org/10.1071/AN15805

Chapter 5 Growth is impeded by gastrointestinal nematodes in weaned rather than suckling meat-breed lambs in a high summer rainfall region, on the Northern Tablelands, New South Wales.

M.L. Dever, L.P. Kahn, E.K. Doyle

Accepted to Animal Production Science

Dever, M. L., Kahn, L. P. & Doyle, E. K. (2017). Growth is impeded by gastrointestinal nematodes in weaned rather than suckling meat-breed lambs in a high summer rainfall region, on the Northern Tablelands, New South Wales. *Animal Production Science*, *57*(5), 969-974.

http://dx.doi.org/10.1071/AN15806

Chapter 6 Decline in faecal worm egg counts in lambs suckling ewes treated with lipophilic anthelmintics: Implications for hastening development of anthelmintic resistance.

M.L. Dever, L.P. Kahn

Accepted 15 February 2015, Veterinary Parasitology 209: 229-234

Dever, M. L. & Kahn, L. P. (2015). Decline in faecal worm egg counts in lambs suckling ewes treated with lipophilic anthelmintics: Implications for hastening development of anthelmintic resistance. *Veterinary Parasitology*, *209*(3-4), 229-324

http://dx.doi.org/10.1016/j.vetpar.2015.02.018

Chapter 7 Removal of tapeworm (*Moniezia* spp.) did not increase growth rates of meat-breed lambs in the Northern Tablelands of NSW

M.L. Dever, L.P. Kahn, E.K. Doyle

Accepted 19 January 2015, Veterinary Parasitology 208: 190-194

Dever, M. L., Kahn, L. P., & Doyle, E. K. (2015). Removal of tapeworm (*Moniezia* spp.) did not increase growth rates of meat-breed lambs in the Northern Tablelands of NSW. *Veterinary Parasitology*, *208*(3-4), 190-194

http://dx.doi.org/10.1016/j.vetpar.2015.01.016

Chapter 8 General Discussion

8.1. Introduction

Parasitism from gastrointestinal nematodes (GIN) remains one of the most costly endemic sheep diseases in Australia (Lane *et al.*, 2015). Traditionally the most common method for controlling GIN is to administer an anthelmintic (referred to as drench here and thereafter). However the increasing prevalence and severity of drench resistance (Playford *et al.*, 2014), has highlighted that alternative approaches to GIN control should be adopted by producers as continual and routine drenching of sheep is no longer sustainable. To reduce GIN-related production losses and to ensure the longevity of effective anthelmintic actives, producers are being encouraged to adopt regional WormBoss integrated parasite management (IPM) programs, which comprise of both chemical and non-chemical approaches to GIN control (Scrivener *et al.*, 2006; Kelly *et al.*, 2010; Kahn & Woodgate, 2012).

Production costs, due to the direct effects of GIN, have recently been quantified for Merino sheep in a summer-dominant, rainfall region. This cost was greatly diminished on farms using IPM programs to control GIN (Kelly *et al.*, 2010), due largely to a lower rate of mortality due to haemonchosis.

Research into the effects of GIN on sheep production in Australia has primarily focused on the Merino breed. Reports investigating the effects of GIN (predominantly *Trichostrongylus* spp. and *Teladorsagia* spp.) on meat-breed lamb production are limited to the high winter rainfall regions of southern Australia with the highest associated cost being reduced lamb growth (Carmichael, 2009). The lack of literature in this area, relevant to Australian conditions in general, and to summer-dominant rainfall regions in particular, highlights the need to better define the effect of ewe and lamb GIN control on meat-breed lamb and ewe performance. There is a need to develop GIN control programs appropriate to these breed types and production systems and to identify implications for drench resistance and host immunity in a summer-dominant rainfall region.

8.2. Methodology

Defining the effect of GIN on ewe and lamb performance that remains after implementation of a GIN control program required groups of animals to remain GIN-free. Experiments conducted under grazing conditions encounter difficulties maintaining GIN-free groups because of the presence of anthelmintic resistance and also because sheep are continually challenged with infective larvae (L3). One methodology for maintaining sheep as GIN-free is to serially treat sheep with a combination of effective short and long-acting anthelmintics to provide continual GIN-suppression (Kelly *et al.*, 2010). While this approach overcomes the problem of anthelmintic resistance, a residual concern is the uncertainty of production loss associated with the host's immunological response to larval challenge. In an animal house experiment, Kelly et al. (2012) reported no loss of production for Merino wethers challenged with susceptible *T. colubriformis*, *T. circumcincta* and *H. contortus* L3, while concurrently treated with effective short and long-acting drenches, despite the L3 challenge stimulating an immunogenic response. To validate this finding under grazing conditions and with meat-breed lambs, animals received a trickle challenge with anthelmintic susceptible *H. contortus* and *T. colubriformis* L3 and were suppressively treated (or not) with effective anthelmintics (see Chapter 2). Even though there was an immunogenic response to GIN challenge, there was no negative effect of persistent larval challenge on growth of the lambs (Dever *et al.*, 2015). The conclusion formed from these studies, is that the method of serially treating sheep, with a combination of effective short and long-acting anthelmintics, is a valid way of providing GIN-free groups of sheep from which the residual effects of GIN infection can be determined. Further research may be warranted to determine if similar outcomes are obtained for sheep with increased resistance to GIN, given the immunological response to GIN challenge may be greater. It is appropriate to mention that this methodology is not considered a commercially-relevant or sustainable treatment regime for controlling GIN and was solely used as an experimental method.

8.3. Defining the effect of gastrointestinal nematode control for meat-breed lamb and ewe performance

One of the key objectives for meat-breed lamb production systems is to optimise lamb growth (Carmichael, 2009). In Chapter 4 it was reported that GIN depressed ewe liveweight change by 1.1 kg (up to weaning) with the effects of GIN most apparent between enrolment and pre-lambing on IPM farms. While GIN depressed liveweight changes in ewes, there was little effect of ewe GIN control on growth of their meat-breed lambs up to weaning, and no effect on lamb marking rates. Nutritional demands of the ewe are amplified during late pregnancy and lactation (Adams & Liu, 2003; Beasley *et al.*, 2012b; Macarthur *et al.*, 2013b), however the small effect of ewe GIN control on lamb growth indicates that ewes were able to mobilise fat and muscle tissue to support lactation (Gibb & Treacher, 1980; Adams & Liu, 2003). This highlights the ability of the Border Leicester X Merino ewe to tolerate the effects of GIN, with only a small adverse effect of GIN on their reproductive efficiency.

Similarly, GIN infection in the lamb did not affect lamb growth up to weaning. Lamb WEC were negligible one month after lamb marking but by weaning had increased markedly and had reached treatment threshold levels (Maxwell *et al.*, 2012). This supports the notion that suckling meat-breed lambs are also resilient to GIN infection (Bisset & Morris, 1996) and on most occasions, lambs will not require treatment prior to weaning. This would in turn reduce the number of unnecessary treatments and potentially slow the development of drench resistance by providing greater refugia on pasture (Besier *et al.*, 2010).

Weaning is considered a stressful period for lambs (Watson & Gill, 1991) and weaners are known for their increased susceptibility to GIN infection. GIN reduced growth of lambs by 0.5 kg in the two months after weaning, confirming the susceptibility of weaners to GIN (Watson & Gill, 1991; Shaw *et al.*, 1995; Dever *et al.*, 2016). WEC remained below the WormBoss regional treatment threshold value for *H. contortus* dominant (>60% from coproculture) infections (Maxwell *et al.*, 2012). Production loss in lambs following weaning, suggests these thresholds may need revision if they seek to completely protect against production loss. However, lowering the WEC threshold is not likely to achieve this aim for lambs as during the acquisition phase of immunity, the majority of production losses are associated with the host’s immune-mediated response to GIN infection (Dever *et al.*, 2016) rather than the direct pathological effects arising from infection.

Ewe and lamb mortality rates were unaffected by GIN and provides further support of the increased resilience of this sheep type to GIN infection in a productive system. To gain a better understanding of the resilience of meat-breed lambs to *H. contortus* infection (prior to weaning), blood and faecal samples were collected from twenty GIN-infected suckling lambs and eleven GIN-infected lactating ewes from one property (the naturally acquired infection was 100% *H. contortus*). The relationship between WEC and packed cell volume for Border Leicester x Merino ewes and meat-breed lambs (Figure 8-1) showed regression slopes (decline in packed cell volume with increasing WEC) were similar for both but the starting PCV value for lambs was much higher. Meat-breed lambs had the highest starting PCV values, indicating that within their production-based systems, they have a greater capacity to maintain packed cell volume and tolerate *H. contortus* infection. While ewes were resilient to the effects of GIN infection, the lower PCV values of lactating ewes (Figure 8-1) indicates greater susceptibility, than suckling lambs, to the blood-feeding effects of *H. contortus* infection as reported by van Wyk and Bath (2002).

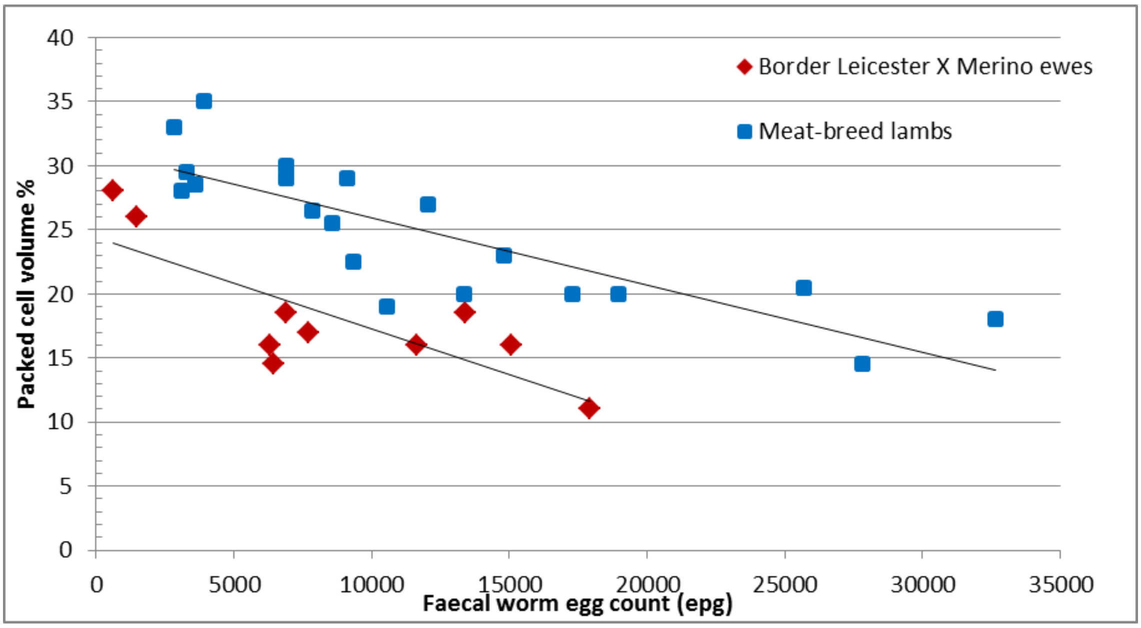


Figure 8-1 Relationship comparisons between faecal worm egg count and packed cell volume for Border Leicester X Merino ewes (y = -0.0007x + 24.4; r2 = 0.62) and meat-breed lambs (y = -0.0005x + 31.2; r2 =0.69). Samples were collected from the experiment reported in Chapter 6 of this thesis.

8.4. Implementation of integrated parasite management programs for control of gastrointestinal nematodes

The increasing prevalence and severity of drench resistance (Playford *et al.*, 2014), highlights the importance for adopting alternative approaches to GIN control such as regional WormBoss integrated parasite management (IPM) programs (Walkden-Brown *et al.*, 2004; Kelly *et al.*, 2010; Kahn & Woodgate, 2012). In Chapter 4, the effect of ewe and lamb GIN control on performance was contrasted between IPM and TYP GIN management. Fully implementing the grazing component of regional IPM programs, to prepare lambing and weaning paddocks for controlling GIN, was hampered as a result of very low rainfall and poor pasture growth.

WEC of ewes on IPM farms was lower than on TYP farms with much of the difference occurring during Year 2. This was unlikely due to environmental influences as a similar trend was not observed for WEC of ewes on TYP farms. A strategic drench was administered to ewes in Year 2 at enrolment, as the period between enrolment and pre-lambing in Year 1 was where the greatest effect of GIN on liveweight occurred, despite being the period with the lowest WEC. The magnitude of the periparturient rise in WEC for ewes on IPM farms was greatly lower in Year 2 (Year 1, 1407 epg vs Year 2, 359 epg) and subsequently reduced what is considered a main source of pasture larval contamination for ewes and lambs during the post-partum period.

While WEC were lower for ewes on IPM farms, the overall negative effect of GIN was greater on IPM farms for ewe live weight (1 kg), clean fleece weight (0.1 kg) and lamb weaning weight (0.9 kg). The annual rate of apparent ewe mortality (6.5%) did not differ between IPM and TYP. This was an unexpected finding and is not accounted for by differences in the proportion of GIN species present on IPM and TYP farms. It is possible that the smaller effect of GIN with TYP might be associated with lower stocking rates (IPM 10.6 DSE/ha vs TYP 8.9 DSE/ha) and the supplementary feeding of ewes on one TYP farm during late pregnancy and lactation. Despite these differences, a local Animal Health Advisory Group, composed of animal health advisors and producers, suggested that from a commercial context, the residual effect of GIN was small for both IPM and TYP management confirming the resilience of these sheep types within a meat production system.

8.5. Factors hastening the development of drench resistance

8.5.1. Treating lactating ewes with lipophilic drenches

In some regions of Australia, ewes are often treated with a drench with persistent activity prior to lambing to prevent a periparturient rise in WEC. In the experiment described in Chapter 6, a decrease in effectiveness of GIN-suppressive treatments was observed during the lactational period on farms with known moxidectin drench resistance. This was unexpected and was most likely associated with the lipophilic nature of moxidectin (1 mg/kg, Cydectin LA® - Virbac Animal Health) and monepantel (Alvinerie *et al.*, 1998; Imperiale *et al.*, 2004; European Medicines Agency, 2013). Potentially a portion of each dose administered to ewes is partitioned towards the mammary gland and subsequently eliminated in milk. The apparent consequences of these losses are a more rapid decline in the concentration of the active in the ewe and the transfer of a sub-therapeutic dose of the active to the suckling lamb via milk. This assumption was supported by the work reported in Chapter 6 which investigated the effect of ewe GIN treatment on WEC and haematocrit levels of their suckling lambs. Seven days after ewes were treated there was evidence of the transfer of actives via milk to the suckling lamb, with WEC of their suckling lambs reduced by 51% and packed cell volumes significantly higher than lambs suckling untreated ewes. While a reduction in lamb WEC may be considered advantageous and beneficial for production, sub-therapeutic doses will increase selection pressure for development of drench resistance (Smith *et al.*, 1999; Sangster & Dobson, 2002). The process of milk transfer at sub-therapeutic levels to a lamb susceptible to infection from pasture, establishes the potential for a double screening for drench resistance (Leathwick *et al.*, 2015). Lactating ewes treated with moxidectin (as part of the SUP regimen, see Chapter 4) continued to shed eggs from resistant GIN adults onto pasture where the subsequent L3 stages were likely to establish at high rates in lambs (Bailey *et al.*, 2009b). This shift towards resistance may be amplified in lambs passively receiving sub-therapeutic doses of active, thereby accelerating the process leading towards drench resistance. Whether selection for anthelmintic resistance occurs for the entire duration of active ingestion via milk is uncertain as there are no reports that specify the existence of a truncation point, where selection for resistant genotypes within the GIN population will not occur.

8.5.2. Removal of tapeworm infection with a product containing a single active against GIN

Clinical signs of diarrhoea and ill thrift are often associated with tapeworm infection due to the visual presence of proglottids in faeces of lambs. There is however little evidence to support the view that these cestodes are pathogenic (Brunsdon, 1964; Elliott, 1984) but this remains a contentious subject (Southworth *et al.*, 1996; Strobel *et al.*, 2013). Results from a national survey of Australian sheep producers have shown that 5.4% of all drenches administered in 2012 contained the active praziquantel (Reeve & Walkden-Brown, 2014). Commercially, praziquantel is only available in Australia as a mixture with one other active ingredient to remove GIN burdens and use of this drench as a single entity will increase development of drench resistance (Dobson *et al.*, 2011). Given that weaning weights of lambs were not improved by suppressive GIN control (see Chapter 5), the use of praziquantel-containing products appeared to provide a high-risk and low-value proposition for sheep producers. The experiments described in Chapter 7 were designed to determine the effects of tapeworm infection on meat-breed lamb production. These showed that tapeworm infection did not impede lamb growth and confirmed that (at least within the Northern Tablelands, NSW) treatment for tapeworm is unwarranted.

8.6. Economic cost of gastrointestinal nematodes for meat-breed lamb production on the Northern Tablelands, New South Wales

In the most recent report on the cost of endemic diseases for the Australian red meat industry, the cost of GIN for Merino’s in a summer-dominant rainfall region (described as a high GIN risk region) can be calculated to be $28.29/head and $8.49/head for meat-breed lambs (Lane *et al.*, 2015). This estimate is considerably higher than that previously reported ($5.93/head) for sheep in this region (Sackett *et al.*, 2006) and more recently for Merino ewes ($11.09/ewe/year) (Kelly *et al.*, 2010) suggesting that the cost of GIN have increased over time.

Chapter 4 investigated the effects of GIN control on meat-breed lamb and ewe performance in a summer-dominant rainfall region and reported production losses due to GIN for two different farm management systems; IPM and TYP. A gross margin analysis was used to calculate the cost of GIN for the two GIN management systems.

8.6.1. Gross Margin Analysis

The economic cost of GIN for meat-breed lamb production on farms managed using IPM and TYP programs was calculated using a gross margin analysis for a self-replacing Border Leicester X Merino flock. As described in Chapter 4, there were two levels of GIN control on each farm; GIN-suppressed (SUP) and GIN-non suppressed (NSUP) which permitted calculation of the cost of GIN for each management system. The analysis accounted for assumptions that 1,000 first cross ewes (Border Leicester X Merino) would be joined to rams (kept for 3 years) at a rate of 1 ram per 50 ewes, ewes of 7 years of age would be cast for age, application of maintenance rates of fertiliser to pastures and standard fly control would form part of management strategies. Replacement ewes were purchased each year. Ewes lambed in September and lambs were sold at weaning in January. On IPM farms, GIN monitoring was assumed to be conducted on an average of 1.3 mobs (based on 4 mobs each with 250 ewes), seven times per year, and a WECRT conducted once every 2.5 years. On TYP farms, GIN monitoring was assumed to be conducted on 1.3 mobs twice each year with no WECRT conducted. Values for pregnancy rate, weaning rate, clean fleece weight (ewe), pre-mating liveweight, lamb liveweight at weaning and ewe mortality rates were obtained from results reported in Chapter 4. Prices for wool and stock sales and purchases were obtained from: Wool Cheque (http://www.woolcheque.awex.com.au), Auctions Plus (www.auctionsplus.com.au) and Meat and Livestock Australia (www.mla.com.au). The gross margin analysis model is summarised in Table 8-1.

The values used for revenue and costs were:

- Cast for age ewes ($2.00/kg liveweight)
- Replacement ewes ($198/head)
- Rams ($900/head)
- Weaners ($3.40/kg liveweight)
- Drenches at $0.55/head for short and sustained activity and $1.65/head for long-acting products
- Labour at $200/day to muster and drench 1000 sheep
- Worm test at $70/sample
- Drench test at $1000

The gross margin for TYP farms was heavily influenced by the reduced number of lambs sold as weaners that were reared by SUP ewes (Part A in Table 8-1). There is no biological reason for weaning rates to be reduced by the SUP treatment on TYP farms and therefore this result may not provide a true indication of the comparison with IPM. Therefore, two gross margins have been presented (with and without the effect of ewe SUP treatment on the number of weaners) to allow a more balanced comparison of the management systems. The adjustment involved the setting of identical weaning rates for NSUP and SUP treatments within management system (i.e. LTL and TYP = 156%) and the use of the NSUP weaning weights relevant for each management system (i.e. LTL = 31.5 kg, TYP = 32.1kg). The effect of a change in number of weaners was also accounted for with enterprise costs (Part B in Table 8-1).

Using the values in part B of the gross margin analyses, the annual cost of GIN averaged across IPM and TYP management was $5.92 per ewe. This is less than the annual figure calculated from Lane et al. (Lane *et al.*, 2015) and for Merino ewes (Kelly *et al.*, 2010) based on 2010 values, providing further evidence of the resilience of these sheep types and production systems to GIN infection. GIN was more costly for ewes on IPM than on TYP farms ($1.11/ewe per year) because (i) NSUP ewes had lighter fleece weights than SUP ewes but only on IPM farms (accounting for 81% of difference in the cost of GIN); and (ii) there was a larger difference between NSUP and SUP ewes in the weight of cast for age ewes on IPM farms (accounting for 17% of the difference). The financial benefit from fewer drenches with reduced costs of labour with IPM was almost perfectly matched by the increased cost of monitoring and WECRT. The gross margin of twin-bearing NSUP ewes on IPM and TYP farms was $120.56/ewe and $120.14/ewe respectively, indicating that with a higher stocking rate (+1.7 DSE/ha), the gross margin per hectare is likely to be greater with IPM.

Despite the higher cost of GIN on IPM farms, reducing the number of drench treatments within a common environment, will inevitably slow development of drench resistance over the long term (Laurenson *et al.*, 2013) provided refugia is considered when drenches are administered. Overtime the cost of GIN on IPM farms is likely to decline, as the compounded benefits arising from the adoption of IPM components will continue to reduce pasture larval challenge. Conversely, the cost of GIN is expected to increase on TYP farms, due to increased production losses associated with declining efficacy of drench actives. The cost of treatment is also likely to increase, as farms with few drenching options (due to a high incidence of drench resistance) will have greater reliance on the two recently released drench actives (monepantel and derquantel (+ abamectin)), which are also the most costly short-acting drenches commercially available (Maxwell, 2015).

Table 8-1 Gross margin analysis from using integrated parasite management (IPM) and regionally typical (TYP) programs in the control of gastrointestinal nematodes for meat-breed lamb production systems on the Northern Tablelands, NSW.

	IPM		TYP		
Enterprise					
Ewes	1000		1000		
Rams	20		20		
Stocking rate (DSE/ha)	10.6		8.9		
Ewe GIN control	**NSUP**	**SUP**	**NSUP**	**SUP**	
Pregnancy rate (foetuses/ewe)	1.67	1.74	1.70	1.70	
Weaning rate (lambs/ewe)	1.56	1.50	1.56	1.45	
Clean fleece weight (kg/ewe)	3.2	3.3	3.0	3.0	
Wool price (c/kg)	10.24	10.24	11.38	11.38	
Pre-mating liveweight (kg)	61.2	63.2	60.1	61.2	
Lamb liveweight (kg): weaning	31.5	32.7	32.1	31.9	
Ewe mortality rate (% p.a.)	6.9	6.6	6.5	6.2	
Enterprise revenue ($)					
Shear and crutch	35,722	36,746	37,185	37,185	
Cast for age ewes and rams	14,583	15,194	14,519	14,924	
Weaners	166,913	166,594	169,855	157,551	
Enterprise costs ($)					
Replacements (ewes and rams)	40,737	40,435	40,315	40,021	
Shearing and crutching	8,139	8,139	8,139	8,139	
Cartage	3,965	3,850	3,950	3,742	
Taxes and commission	10,865	10,929	10,978	10,383	
Drenches	2,695	23,720	3,410	23,720	
Labour, fertiliser and additional animal health practices	28,325	28,325	28,325	28,325	
Supplementary feeding	-	-	$5,000	$5,000	
Gross Margin (per ewe) – part A					**IPM - TYP**
NSUP-SUP income	-$1.32		$11.90		-$13.22
NSUP-SUP costs	$0.35		$1.10		-$0.74
drench	$3.60		$4.51		-$0.91
monitor and WECRT*	$1.04		$0.18		$0.86
Total	**-$6.30**		**$6.11**		**-$12.41**
Gross Margin (per ewe) – part B (removed differences in weaner sale numbers)					
NSUP-SUP income	-$1.63		-$0.41		-$1.23
NSUP-SUP costs	$0.22		$0.28		-$0.06
Drench	$3.60		$4.51		-$0.91
Monitor and WECRT	$1.04		$0.18		$0.86
Total	**-$6.48**		**-$5.37**		**-$1.11**

*WECRT: worm egg count reduction test

8.7. Improvements in experimental design and concepts for future research

In Chapters 4 and 5, the key approach for defining the effect of GIN for meat-breed lamb production was suppression of GIN burdens in ewes and lambs using a combination of short and long-acting drenches. While this strategy was effective, there were occasions where GIN-suppressed ewes and lambs had positive WEC. Positive WEC for GIN-suppressed ewes were observed during the lactation period and at weaning and this was most likely attributable to the lipophilic nature of moxidectin. With mobilization of fat to support lactation, a proportion of the dose administered to ewes may have been partitioned to the mammary gland and subsequently eliminated in milk. This would have shortened the period of protection against re-infection on farms with known moxidectin resistance. To improve the methodology for GIN-suppression of ewes, in the absence of other suitable long-acting drench treatments, treatment with a drench containing closantel in December may have provided increased protection during the later stages of the lactational period, after which ewes were re-treated at weaning in January according to the existing methodology. It is cautionary to note that because resistance of *H. contortus* to closantel exists on 43% of properties in NSW (Playford *et al.*, 2014), and it is likely that resistance has a greater prevalence in the Northern Tablelands of NSW, it would be necessary to confirm the efficacy and persistency of closantel prior to adopting the proposed improvement.

Positive WEC for GIN-suppressed lambs were observed in March after GIN-suppressive treatments were administered in November and a short-acting drench given in February. The protection period was as expected from the product choice but it became increasingly difficult with time to maintain very low WEC of SUP lambs. The choice of the short-acting drench was made to ensure further restrictions were not placed on withholding periods (WHP) or export slaughter intervals (ESI). Due to the imminent sale of lambs (now aged 6 months), the only other option to have maintained suppression of GIN burdens would have been to continue to re-treat lambs with short-acting drenches at an interval of 2–3 weeks; which was not possible with project resources.

One of the objectives in Chapter 3 was to re-define treatment thresholds for meat-breed lambs, infected with *T. colubriformis*, so as to reduce the effects of GIN. A previous report showed that lamb growth is reduced when lambs are infected with between 950 – 3,000 *T. colubriformis* L3/week (Steel *et al.*, 1980). In the experiment described in Chapter 3, two levels of GIN infection (2,000 and 4,000 *T. colubriformis* L3/week) were chosen to identify more specifically when production is impeded, due to the effects of *T. colubriformis*. However, in this experiment WEC and GIN burdens did not differ with infection level. In addition, there was an absence of a strong negative relationship between WEC and growth and therefore WEC treatment thresholds were unable to be redefined. While these results indicate that a binomial approach (all or none) to infection is displayed by meat-breed lambs, inclusion of an additional group at a higher level of infection (i.e. 6,000-8,000 *T. colubriformis* L3/week) would have provided supplementary data to be more certain of the response. This may have either assisted in redefining WEC treatment thresholds or query the use of WEC thresholds to detect sub-clinical production loss associated with *T. colubriformis* infection in meat-breed lambs.

8.8. Conclusion

The experiments reported in this thesis have shown that the effects of GIN on meat-breed lamb and ewe performance are small, indicating considerable resilience of these breed types to GIN infection within a productive system. IPM programs led to lower WEC achieved with fewer drenches which should slow development of drench resistance and improve sustainability of GIN control. Paradoxically, there were no direct production benefits of IPM and, although the gross margin per ewe was similar for IPM and TYP farms, there was a greater cost of GIN on farms using IPM programs. Despite these differences, the cost of GIN infection of twin-bearing ewes and their lambs was small with both IPM and TYP. The experiments have also highlighted the risks for increasing drench resistance in these production systems from the unnecessary use of products to remove tapeworm and lipophilic long-acting products during lactation. The work described in Chapter 6 on the danger from using long-acting moxidectin during lactation for drench resistance was the first report to highlight this risk. This thesis has also provided greater awareness of the importance of the production costs associated with the immune-mediated responses of the lamb to *T. colubriformis* during the early stages of the acquisition phase of immunity. The implications of this highlight the need to balance selection for reduced worm egg count with better production so as to select animals capable of mounting an effective immune response while also meeting production targets. Collectively these outcomes have provided a solid platform to develop GIN control programs appropriate to these sheep types and production systems in a summer-dominant rainfall region of NSW.

References

ABARES. (2014). Agricultural commodity statistics 2014 (Department of Agriculture: ABARES, Trans.).

Abbott, E. M., Parkins, J. J., & Holmes, P. H., 1985a. Influence of dietary protein on parasite establishment and pathogensis in Finn Dorset and Scottish Blackface lambs given a single moderate infection of *Haemonchus contortus*. *Res. Vet. Sci.* 38, 6-13.

Abbott, E. M., Parkins, J. J., & Holmes, P. H., 1985b. Influence of dietary protein on the pathophysiology of ovine haemonchosis in Finn Dorset and Scottish Blackface lambs given a single moderate infection. *Res. Vet. Sci.* 38, 54-60.

Abbott, E. M., Parkins, J. J., & Holmes, P. H., 1986a. The effect of dietary protein on the pathogenesis of acute ovine haemonchosis. *Vet. Parasitol.* Vol: 20, 275-289.

Abbott, E. M., Parkins, J. J., & Holmes, P. H., 1986b. The effect of dietary protein on the pathophysiology of acute ovine haemonchosis. *Vet. Parasitol.* Vol. 20, 291-306.

Abbott, E. M., Parkins, J. J., & Holmes, P. H., 1988. Influence of dietary protein on the pathophysiology of haemonchosis in lambs given continuous infections. *Res. Vet. Sci.* Vol. 45, 41-49.

Abbott, K. A., Cobb, R. M., & Holm Glass, M., 1995. Duration of the persistent activity of moxidectin against *Haemonchus contortus* in sheep. *Aust. Vet. J.* 72, 408-410.

Adams, C. 1976. Adam's Micro-Hematocrit II Centrifuge - Operators Manual. Division of Becton, Dickinson and Company. Canada

Adams, D. B., 1983. Observations on the self-cure reaction and other forms of immunological responsiveness against *Haemonchus contortus* in sheep. *Int. J. Parasitol.* 13, 571-578.

Adams, N. R., & Liu, S. M., 2003. Principles of nutrient partitioning for wool, growth and reproduction: implications for nematode parasitism. *Aust. J. Exp. Agric.* 43, 1399-1407.

Afolayan, R. A., Fogarty, N. M., Ingham, V. M., Gilmour, A. R., Gaunt, G. M., Cummins, L. J., & Pollard, T., 2007. Genetic evaluation of crossbred lamb production. 3. Growth and carcass performance of second-cross lambs. *Aust J Agr Res*. 58, 457-466.

Albers, G. A., & Gray, G. D., 1986. Breeding for worm resistance: a perspective. *Int. J. Parasitol.* 17, 559-566.

Albers, G. A. A., Gray, G. D., Le Jambre, L. F., Barger, I. A., & Barker, J. S. F., 1990. The effect of *Haemonchus contortus* infection on haematological parameters in young Merino sheep and its significance for productivity. *Anim Prod.* 50, 99-109.

Albers, G. A. A., Gray, G. D., Le Jambre, L. F., Piper, L. R., Barger, I. A., & Barker, J. S. F., 1989. The effects of *Haemonchus contortus* on liveweight gain and wool growth in young Merino sheep. *Aust J Agr Res*. 40, 419-432.

Albers, G. A. A., Gray, G. D., Piper, L. R., Barker, J. S. F., Le Jambre, L. F., & Barger, I. A., 1987. The genetics of resistance and resilience to *Haemonchus contortus* infection in young Merino sheep. *Int. J. Parasitol.* 17, 1355-1363.

Alford, A., Griffith, G., & Davies, L. (2003). Livestock farming systems in the Northern Tablelands of NSW: An economic analysis *Economic Research Report No. 12*.

Alvinerie, M., Escudero, E., Sutra, J. F., Eeckhoutte, C., & Galtier, P., 1998. The pharmacokinetics of moxidectin after oral and subcutaneous administration to sheep. *Vet. Res.* 29, 113-118.

Alvinerie, M., Sutra, J. F., Lanusse, C., & Galtier, P., 1996. Plasma profile study of moxidectin in a cow and its suckling calf. *Vet. Res.* 27, 545-549.

Amaradasa, B. S., Lane, R. A., & Manage, A., 2010. Vertical migration of *Haemonchus contortus* infective larvae on *Cynodon dactylon* and *Paspalum notatum* pastures in response to climatic conditions. *Vet. Parasitol.* 170, 78-87.

Amarante, A. F., Bricarello, P. A., Rocha, R. A., & Gennari, S. M., 2004. Resistance of Santa Ines, Suffolk and Ile de France sheep to naturally acquired gastrointestinal nematode infections. *Vet. Parasitol.* 120, 91-106.

Andersen, F. L., Wang, G. T., & Levine, N. D., 1966. Effect of temperature on survival of the free-living stages of *Trichostrongylus colubriformis*. *J. Parasitol.* 52, 712-721.

Anderson, N., 1983. The availability of trichostrongylid larvae to grazing sheep after seasonal contamination of pastures. *Aust J Agr Res*. 34, 583-592.

Armour, J., Jarrett, W. F. H., & Jennings, F. W., 1966. Experimental *Ostertagia circumcincta* infections in sheep: development and pathogenesis of a single infection. *Am. J. Vet. Res.* 27, 1267-1278.

AUS-MEAT Limited. 2005. Handbook of Australian Meat (7th ed.). AUS-MEAT Limited. Tingalpa, Queensland

AWI and MLA. (2007). Visual sheep scores. Sydney, Australia.

Ayres, J. F., McPhee, M. J., Turner, A. D., & Curll, M. L., 2000. The grazing value of tall fescue (*Festuca arundinacea*) and phalaris (*Phalaris aquatica*) for sheep production in the northern tablelands of New South Wales. *Aust J Agr Res*. 51, 57-68.

Bailey, J. N. (2008). *The integration of grazing management and anthelmintic treatment to provide clean lambing paddocks in the northern tablelands region of NSW, Australia.* (Doctor of Philosophy), University of New England.

Bailey, J. N., Kahn, L. P., & Walkden-Brown, S. W., 2009a. The relative contributions of *T. colubriformis*, *T. vitrinus*, *T. axei* and *T. rugatus* to sheep infected with *Trichostrongylus* spp. on the northern tablelands of New South Wales. *Vet. Parasitol.* 165, 88-95.

Bailey, J. N., Playford, M., Smith, A., Love, S., Besier, R. B., & Kluver, P. (2013). *NAH Drench resistance survey.* International Sheep Veterinarians Conference (ISVC) Rotorua, New Zealand.

Bailey, J. N., Walkden-Brown, S. W., & Kahn, L. P., 2009b. Comparison of strategies to provide lambing paddocks of low gastro-intestinal nematode infectivity in a summer rainfall region of Australia. *Vet. Parasitol.* 161, 218-231.

Balic, A., Bowles, V. M., & Meeusen, E. N. T., 2000. The immunobiology of gastrointestinal nematode infections in ruminants. *Adv. Parasitol.* 45, 181-241.

Barger, I. A., 1993. Influence of sex and reproductive status on susceptibility of ruminants to nematode parasitism. *Int. J. Parasitol.* 23, 463-469.

Barger, I. A., 1994. Rotational grazing for control of gastrointestinal nematodes of goats in a wet tropical environment. *Vet. Parasitol.* 53, 109-116.

Barger, I. A., 1999a. The role of epidemiological knowledge and grazing management for helminth control in small ruminants. *Int. J. Parasitol.* 29, 41-47.

Barger, I. A., 1999b. The role of epidemiological knowledge and grazing management for helminth control in small ruminants. *Int. J. Parasitol.* 29, 41-47.

Barger, I. A., Beynon, P. R., & Southcott, W. H. (1972). *Simulation of pasture larval populations of Haemonchus contortus.* Proceedings of the Australian Society of Animal Production.

Barger, I. A., & Cox, H. W., 1984. Wool production of sheep chronically infected with *Haemonchus contortus*. *Vet. Parasitol.* 15, 169-175.

Barger, I. A., Le Jambre, L. F., Georgi, J. R., & Davies, H. I., 1985. Regulation of *Haemonchus contortus* populations in sheep exposed to continuous infection. *Int. J. Parasitol.* 15, 529-533.

Barnes, E. H., & Dobson, R. J., 1993. Persistence of acquired immunity to *Trichostrongylus colubriformis* in sheep after termination of infection. *Int. J. Parasitol.* 23, 1019-1026.

Barnes, E. H., Dobson, R. J., & Barger, I. A., 1995. Worm control and anthhelmintic resistance: Adventures with a model. *Parasitology Today*. 11, 56-63.

Bartram, D. J., Leathwick, D. M., Taylor, M. A., Geurden, T., & Maeder, S. J., 2012. The role of combination anthelmintic formulations in the sustainable control of sheep nematodes. *Vet. Parasitol.* 186, 151-158.

Beasley, A. M., Kahn, L. P., & Windon, R. G., 2010a. The periparturient relaxation of immunity in Merino ewes infected with *Trichostrongylus colubriformis*: endocrine and body compositional responses. *Vet. Parasitol.* 168, 51-59.

Beasley, A. M., Kahn, L. P., & Windon, R. G., 2010b. The periparturient relaxation of immunity in Merino ewes infected with *Trichostrongylus colubriformis*: parasitological and immunological responses. *Vet. Parasitol.* 168, 60-70.

Beasley, A. M., Kahn, L. P., & Windon, R. G., 2012a. The influence of reproductive physiology and nutrient supply on the periparturient relaxation of immunity to the gastrointestinal nematode *Trichostrongylus colubriformis* in Merino ewes. *Vet. Parasitol.* 188, 306-324.

Beasley, A. M., Kahn, L. P., & Windon, R. G., 2012b. The influence of reproductive physiology and nutrient supply on the periparturient relaxation of immunity to the gastrointestinal nematode *Trichostrongylus colubriformis* in Merino ewes. *Vet. Parasitol.* 188, 306-324.

Beck, T., Moir, B., & Meppem, T., 1985. The cost of parasites to the Australian sheep industry. *Quarterly Review of the Rural Economy*. 7, 336-343.

Bell, A. (2007). Measuring herbage mass – the median quadrat technique. Primefacts Second edition. from www.dpi.nsw.gov.au

Bendixsen, T., Windon, R. G., Huntley, J. F., Mackellar, A., Davey, R. J., McClure, S. J., & Emery, D. L., 2004. Development of a new monoclonal antibody to ovine chimeric IgE and its detection of systemic and local IgE antibody responses to the intestinal nematode *Trichostrongylus colubriformis*. *Vet. Immunol. Immunopathol.* 97, 11-24.

Besier, B., Lyon, J., & McQuade, N., 1996. Drench resistance - a large economic cost. *W. A. Journal of Agriculture*. 37.

Besier, R. B., 2012. Refugia-based strategies for sustainable worm control: Factors affecting the acceptability to sheep and goat owners. *Vet. Parasitol.* 186, 2-9.

Besier, R. B., & Dunsmore, J. D., 1993. The ecology of *Haemonchus contortus* in a winter rainfall region in Australia: the development of eggs to infective larvae. *Vet. Parasitol.* 45, 275-292.

Besier, R. B., Love, L. A., Lyon, J., & van Burge, L. A., 2010. A targeted selective treatment approach for effective and sustainable sheep worm management: investigations in Western Australia. *Anim. Prod. Sci*. 50, 1034-1042.

Besier, R. B., & Love, S. C. J., 2003. Anthelmintic resistance in sheep nematodes in Australia: the need for new approaches. *Aust. J. Exp. Agric.* 43, 1383-1391.

Beveridge, I., Brown, T. H., Fitzsimons, S. M., Ford, G. E., Judson, G. J., Martin, R. R., & Miller, D. W., 1985. Mortality in weaner sheep in South Australia under different regimes of anthelmintic treatment. *Aust J Agr Res*. 36, 857-865.

Beveridge, I., Pullman, A. L., Phillips, P. H., Martin, R. R., Barelds, A., & Grimson, R., 1989. Comparison of the effects of infection with *Trichostrongylus colubriformis*, *T. vitrinus* and *T. rugatus* in Merino lambs. *Vet. Parasitol.* 32, 229-245.

Bisset, S. A., & Morris, C. A., 1996. Feasibility and implications of breeding sheep for resilience to nematode challenge. *Int. J. Parasitol.* 26, 857-868.

Bisset, S. A., Morris, C. A., McEwan, J. C., & Vlassoff, A., 2001. Breeding sheep in New Zealand that are less reliant on anthelmintics to maintain health and productivity. *N. Z. Vet. J.* 49, 236-246.

Bisset, S. A., Morris, C. A., Squire, D. R., Hickey, S. M., & Wheeler, M., 1994. Genetics of resilience to nematode parasites in Romney sheep. *New Zeal. J. Agr. Res.* 37, 521-534.

Bisset, S. A., Vlassoff, A., Douch, P. G. C., Jonas, W. E., West, C. J., & Green, R. S., 1996. Nematode burdens and immunological responses following natural challenge in Romney lambs selectively bred for low or high faecal worm egg count. *Vet. Parasitol.* 61, 249-263.

Bisset, S. A., Vlassoff, A., Morris, C.A., Southey, B.R., Baker, R.L. & Parker, A.G.H., 1992. Heritability of and genetic correlations among faecal egg counts and productivity traits in Romney sheep. *New Zeal. J. Agr. Res.* 35, 51-58.

Blackburn, P. J., Carmichael, I. H., & Walkden-Brown, S. W., 2015. Effects of chronic infection with *Trichostrongylus vitrinus* and immune suppression with corticosteroid on parasitological, immune and performance variables in crossbred meat lambs. *Res. Vet. Sci.* 100, 138-147.

Boughton, I. B., & Hardy, W. T. (1935). Stomach worms (*Haemonchus contortus*) of sheep and goats *48th Annual Report of the Texas Agricultural Experimental Station* (Vol. 48, pp. 236-236).

Bown, M. D., Poppi, D. P., & Sykes, A. R., 1989. The effects of a concurrent infection of *Trichostrongylus colubriformis* and *Ostertagia circumcincta* on calicum, phosphorus and magnesium transactions along the digestive tract of lambs. *J. Comp. Pathol.* 101, 11-20.

Bown, M. D., Poppi, D. P., & Sykes, A. R., 1991a. The effect of post-ruminal infusion of protein or energy on the pathophysiology of *Trichostrongylus colubriformis* infection and body composition in lambs. *Aust J Agr Res*. 42, 253-267.

Bown, M. D., Poppi, D. P., & Sykes, A. R., 1991b. Nitrogen transactions along the digestive tract of lambs concurrently infected with *Trichostrongylus colubriformis* and *Ostertagia circumcincta*. *Br. J. Nutr.* 66, 237-249.

Brien, F., Hebart, M. L., Jaensch, K. S., Smith, D. H., & Grimson, R. J. (2009). *Genetics of lamb survival: A study of merino resource flocks in South Australia*. Paper presented at the Association for the Advancement of Animal Breeding and Genetics.

Broughan, J. M., & Wall, R., 2007. Faecal soiling and gastrointestinal helminth infection in lambs. *Int. J. Parasitol.* 37, 1255-1268.

Brown, T. H., Ford, G. E., Miller, D. W., & Beveridge, I., 1985. Effect of anthelmintic dosing and stocking rate on the productivity of weaner sheep in a Mediterranean climate environment. *Aust J Agr Res*. 36, 845–855.

Brunsdon, R., 1964. The effect of infestation by nematodes of the family trichostrongylidae and the tapeworm, *Moniezia expansa*, upon the liveweight gain and wool production of young sheep. *N. Z. Vet. J.* 12, 129-134.

Brunsdon, R. V., 1967. The spring-rise phenomenon: the relationship between the time of lambing and the commencement of the rise in faecal worm-egg counts. *N. Z. Vet. J.* 15, 35-40.

Bureau of Meterology (BOM). (2015). Monthly rainfall: Site number 56037. http://www.bom.gov.au/climate/data/weather-data

Burke, J., Kaplan, R., Miller, J., Terrill, T., Getz, W., Mobini, S., Valencia, E., Williams, M., Williamson, L., & Vatta, A., 2007. Accuracy of the FAMACHA system for on-farm use by sheep and goat producers in the southeastern United States. *Vet. Parasitol.* 147, 89-95.

Burris, M. J., & Baugus, C. A., 1955. Milk consumption and growth of suckling lambs. *J. Anim. Sci.* 14, 186-199.

Butler, L. (2004). *Identifying lambs to their mothers*. Western Australia: Department of Agriculture.

Callinan, A. P. L., 1978. The ecology of the free-living stages of *Ostertagia circumcincta. Int. J. Parasitol.* 8, 233-237.

Carceles, C. M., Diaz, M. S., Vicente, M. S., Sutra, J. F., Alvinerie, M., & Escudero, E., 2001. Milk kinetics of moxidectin and doramectin in goats. *Res. Vet. Sci.* 70, 227-231.

Carmichael, I. (2009). Parasite control in southern prime lamb production systems (pp. 114). North Sydney NSW 2059: Meat & Livestock Australia Limited.

Clark, C. H., Kisel, G. K., & Goby, C. H., 1962. Measurements of blood loss caused by *Haemonchus contortus* infection in sheep. *Am. J. Vet. Res.* 23.

Cobon, D. H., & O'Sullivan, B. M., 1992. Effect of *Haemonchus contortus* on productivity of ewes, lambs and weaners in a semi-arid environment. *J. Agri. Sci.* 118, 245-248.

Cohen, R. D. H., Eastoe, R. D., Hotson, I. K., & Smeal, M. G., 1972. Sheep production on the north coast of New South Wales 1. Effect of anthelmintics and grazing management on production and helminthosis of Merino wethers. *Aust. J. Exp. Agr. Anim. Husb.* 12, 247-251.

Colditz, I. G., 2008. Six costs of immunity to gastrointestinal nematode infections. *Parasite Immunol.* 30, 63-70.

Colditz, I. G., Watson, D. L., Gray, G. D., & Eady, S. J., 1996. Some relationships between age, immune responsiveness and resistance to parasites in ruminants. *Int. J. Parasitol.* 26, 869-877.

Coles, G., Jackson, F., Pomroy, W., Prichard, R., von Samson-Himmelstjerna, G., Silvestre, A., Taylor, M., & Vercruysse, J., 2006. The detection of anthelmintic resistance in nematodes of veterinary importance. *Vet. Parasitol.* 136, 167-185.

Coles, G. C., Bauer, C., Borgsteede, F. H. M., Geerts, S., Klei, T. R., Taylor, M. A., & Waller, P. J., 1992. World Association for the Advancement of Veterinary Parasitology (W.A.A.V.P.) methods for the detection of anthelmintic resistance in nematodes of veterinary importance. *Vet. Parasitol.* 44, 35-44.

Coles, G. C., & Roush, R. T., 1992. Slowing the spread of anthelmintic resistant nematodes of sheep and goats in the United Kingdom. *Vet. Rec.* 130, 505-510.

Colvin, A., Walkdenbrown, S., Knox, M., & Scott, J., 2008. Intensive rotational grazing assists control of gastrointestinal nematodosis of sheep in a cool temperate environment with summer-dominant rainfall. *Vet. Parasitol.* 153, 108-120.

Colvin, A. F., Walkden-Brown, S. W., & Knox, M. R., 2012. Role of host and environment in mediating reduced gastrointestinal nematode infections in sheep due to intensive rotational grazing. *Vet. Parasitol.* 184, 180-192.

Coop, R. L., Huntley, J. F., & Smith, W. D., 1995. Effect of dietary protein supplementation on the development of immunity to *Ostertagia circumcincta* in growing lambs. *Res. Vet. Sci.* 59, 24-29.

Coop, R. L., & Kyriazakis, I., 1999. Nutrition-parasite interaction. *Vet. Parasitol.* 84, 187-204.

Coop, R. L., Sykes, A. R., & Angus, K. W., 1976. Subclinical trichostrongylosis in growing lambs produced by continuous larval dosing. The effect on performance and certain plasma constituents. *Res. Vet. Sci.* 21, 253-258.

Coop, R. L., Sykes, A. R., & Angus, K. W., 1982. The effect of three levels of intake on *Ostertagia circumcincta* larvae on growth rate, food intake and body composition of growing lambs. *J. Agri. Sci.* 98, 247-255.

Corbett, J. L., 1968. Variation in the yield and composition of milk of grazing merino ewes. *Aust J Agr Res*. 19, 283-294.

Corner-Thomas, R. A., Ridler, A. L., Morris, S. T., & Kenyon, P. R., 2015. Ewe lamb live weight and body condition scores affect reproductive rates in commercial flocks. *New Zeal. J. Agr. Res.* 58, 26-34.

Courtney, C. H., Parker, C. F., McClure, K. E., & Herd, R. P., 1984. A comparison of the periparturient rise in faecal egg counts of exotic and domestic ewes. *Int. J. Parasitol.* 14, 377-381.

Coyne, M. J., & Smith, G., 1992. The development and mortality of the free-living stages of *Haemonchus contortus* in laboratory culture. *Int. J. Parasitol.* 22.

Coyne, M. J., Smith, G., & Johnstone, C., 1991. Fecundity of gastro-intestinal trichostongyloid nematodes of sheep in the field. *Am. J. Vet. Res.* 52, 1182-1188.

Crofton, H. D., 1965. Ecology and biological plasticity of sheep nematodes. 1. The effect of temperature on the hatching of eggs of some nematode parasites of sheep. *Cornell Vet.* 55, 242-250.

Crowther, J. R. (1995). ELISA: Theory and Practice. In Walker, J. M. (Ed.), Methods Mol. Biol. (Vol. 42). Totowa, New Jersey: Humana Press Inc.

Dargie, J. D., & Allonby, E. W., 1975. Pathophysiology of single and challenge infections of *Haemonchus contortus* in Merino sheep: studies on red cell kinetics and the 'self cure' phenomenon. *Int. J. Parasitol.* Vol: 5, 147-157.

Dash, K. M., 1986. Control of helminthosis in lambs by strategic treatment with closantel and broad-spectrum anthelmintics. *Aust. Vet. J.* 63, 4-8.

Datta, F. U., Nolan, J. V., Rowe, J. B., & Gray, G. D., 1998. Protein supplementation improves the performance of parasitised sheep fed a straw-based diet. *Int. J. Parasitol.* 28, 1269-1278.

Datta, F. U., Nolan, J. V., Rowe, J. B., Gray, G. D., & Crook, B. J., 1999. Long-term effects of short-term provision of protein-enriched diets on resistance to nematode infection, and liveweight gain and wool growth in sheep. *Int. J. Parasitol.* 29, 479-488.

De Liguoro, M., Longo, F., Brambilla, G., Cinquina, A., Bocca, A., & Lucisano, A., 1996. Distribution of the anthelmintic drug albendazole and its major metabolites in ovine milk and milk products after a single oral dose. *J. Dairy Res.* 63, 533-542.

Dever, M. L., Kahn, L. P., & Doyle, E. K., 2015. Persistent challenge with *Trichostrongylus colubriformis* and *Haemonchus contortus* larvae does not affect growth of meat-breed lambs suppressively treated with anthelmintics when grazing. *Vet. Parasitol.* 209, 76-83.

Dever, M. L., Kahn, L. P., & Doyle, E. K., 2015 accepted for publication-a. Growth is impeded by gastrointestinal nematodes in weaned rather than suckling meat-breed lambs in a high summer rainfall region, on the Northern Tablelands, NSW. . *Anim. Prod. Sci*.

Dever, M. L., Kahn, L. P., & Doyle, E. K., 2015 accepted for publication-b. Integrated parasite management improves control of gastrointestinal nematodes in lamb production systems in a high summer rainfall region, on the Northern Tablelands, NSW. *Anim. Prod. Sci*.

Dever, M. L., Kahn, L. P., Doyle, E. K., & Walkden-Brown, S. W., 2016. Immune-mediated responses account for the majority of production loss for grazing meat-breed lambs during Trichostrongylus colubriformis infection. *Vet. Parasitol.* 216, 23-32.

Dobson, R. J., Barnes, E. H., & Windon, R. G., 1992. Population dynamics of *Trichostrongylus colubriformis* and *Ostertagia circumcincta* in single and concurrent infections. *Int. J. Parasitol.* 22, 997-1004.

Dobson, R. J., Besier, R. B., Barnes, E. H., Love, S. C. J., Vizard, A., Bell, K., & Jambre, L. F., 2001. Principles for the use of macrocyclic lactones to minimise selection for resistance. *Aust. Vet. J.* 79.

Dobson, R. J., Hosking, B. C., Besier, R. B., Love, S., Larsen, J. W., Rolfe, P. F., & Bailey, J. N., 2011. Minimising the development of anthelmintic resistance, and optimising the use of the novel anthelmintic monepantel, for the sustainable control of nematode parasites in Australian sheep grazing systems. *Aust Vet J*. 89, 160-166.

Dobson, R. J., Hosking, B. C., Jacobson, C. L., Cotter, J. L., Besier, R. B., Stein, P. A., & Reid, S. A., 2012. Preserving new anthelmintics: A simple method for estimating faecal egg count reduction test (FECRT) confidence limits when efficacy and/or nematode aggregation is high. *Vet. Parasitol.* 186, 79-92.

Dobson, R. J., Le Jambre, L. F., & Gill, J. H., 1996. Management of anthelmintic resistance: Inheritance of resistance and selection with persistent drugs. *Int. J. Parasitol.* 26, 993-1000.

Dobson, R. J., Waller, P. J., & Donald, A. D., 1990. Population dynamics of *Trichostrongylus colubriformis* in sheep: the effect of infection rate on the establishment of infective larvae and parasite fecundity. *Int. J. Parasitol.* 20, 347-352.

Donald, A. D., 1968. Ecology of free-living stages of nematode parasites of sheep. *Aust. Vet. J.* 44, 139-144.

Donald, A. D., Morley, F. H. W., Waller, P. J., Axelsen, A., Dobson, R. J., & Donnelly, J. R., 1982. Effects of reproduction, genotype and anthelmintic treatment of ewes on *Ostertagia* spp. populations. *Int. J. Parasitol.* 12, 403-411.

Donald, A. D., Southcott, W. H., & Dineen, J. K. (Eds.). (1978). *The epidemiology and control of gastrointestinal parasites of sheep in Australia*. Melbourne: CSIRO.

Donaldson, J., Houtert, M. F. J. v., & Sykes, A. R., 1997. The effect of protein supply on the periparturient parasite status of the mature ewe. *Proceedings of the New Zealand Society of Animal Production*. 57, 186-189.

Donaldson, J., van Hourtert, M. F. J., & Sykes, A. R., 2001. The effect of dietary fish-meal supplementation on parasite burdens of periparturient sheep. *Anim. Sci.* 72, 149-158.

Donaldson, J., van Houtert, M. F. J., & Sykes, A. R., 1998. The effect of nutrition on the periparturient parasite status of mature ewes. *Anim. Sci.* 67, 523-533.

Douch, P. G. C., Green, R.S., Morris, C.A., Bisset, S.A., Vlassoff, A., Baker, R.L., Watson, T.G., Hurford, A.P., Wheeler, M., 1995. Genetic and phenotypic relationships among anti-*Trichostrongylus colubriformis* antibody level, faecal egg count and body weight traits in grazing Romney sheep. *Livest. Prod. Sci.* Vol: 41, 121-132.

Doyle, E. K., Kahn, L. P., & McClure, S. J., 2014. Nutrient partitioning of Merino sheep divergently selected for genetic difference in resistance to *Haemonchus contortus*. *Vet. Parasitol.* 205, 175-185.

Doyle, E. K., Kahn, L. P., McClure, S. J., & Lea, J. M., 2011. Voluntary feed intake and diet selection of Merino sheep divergently selected for genetic difference in resistance to *Haemonchus contortus*. *Vet. Parasitol.* 177, 316-323.

Dunn, A. M. 1969. Veterinary Helminthology (2nd ed.). William Heinemann. London

Dunsmore, J. D., 1965. *Ostertagia* spp. in lambs and pregnant ewes. *J. Helminthol.* 39, 159-184.

Dupuy, J., Sutra, J. F., Alvinerie, M., Rinaldi, L., Veneziano, V., Mezzino, L., Pennacchio, S., & Cringoli, G., 2008. Plasma and milk kinetic of eprinomectin and moxidectin in lactating water buffaloes (Bubalus bubalis). *Vet. Parasitol.* 157, 284-290.

Dynes, R. A., Ankersmit, A. E. L., Poppi, D. P., Barrell, G. K., & Sykes, A. R. (1990). *Studies on the physiological basis of appetite depression in nematode infection in sheep.* Proceedings of the New Zealand Society of Animal Production.

Eady, S. J., Dobson, R. J., & Barnes, E. H. (1997). *Impact of improved host resistance on worm control in Merino's - a computer simulation study.* Fourth International Congress For Sheep Veterinarians, UNE, Armidale.

Eady, S. J., & Woolaston, R. R. (1992). *A guide to selection of Merino sheep for worm resistance*.

Elliott, D. C., 1984. Tapeworm (*Moniezia expansa*) in sheep: Anthelmintic treatment studies to assess possible pathogenic effects and production loss in young infected animals in the field. *N. Z. Vet. J.* 32, 185-188.

Elliott, D. C., 1986. Tapeworm (*Moniezia expansa*) and its effect on sheep production: The evidence reviewed. *N. Z. Vet. J.* 34, 61-65.

Elsheikha, H. M., & Khan, N. A. (Eds.). (2011). *Essentials of Veterinary Parasitology*. Norfolk, UK: Caister Academic Press.

Emery, D. L., McClure, S. J., Wagland, B. M., & Jones, W. O., 1992. Studies of stage-specific immunity against *Trichostrongylus colubriformis* in sheep: immunization with adult parasites. *Int. J. Parasitol.* 22, 221-225.

European Medicines Agency. (2013). European public MRL assessment report (EPMAR): Monepantel (caprine and ovine milk). *EMA/CVMP/741250/2011*. Retrieved from http://www.ema.europa.eu/docs/en_GB/document_library/Maximum_Residue_Limits_-_Report/2013/05/WC500143639.pdf

Eysker, M., 1997. Some aspects of inhibited development of trichostrongylids in ruminants. *Vet. Parasitol.* 72, 265-283.

Fagbemi, B. O., & Dipeolu, O. O., 1983. *Moniezia* infection in the dwarf breeds of small ruminants in Southern Nigeria. *Vet. Q.* 5, 75-80.

Fernandez-Abella, D., Hernandez, Z., & Villegas, N., 2006. Effect of gastrointestinal nematodes on ovulation rate of Merino Booroola heterozygote ewes (Fec B Fec). *Anim. Res.* 55, 545-550.

Fowler, D. G. (2007). Lamb marking performance for ultrasound scanned ewes in Australian sheep flocks *Final report AHW.131* (pp. 17). Sydney: Meat & Livestock Australia.

Freer, M., Moore, A. D., & Donnelly, J. R., 1997. GRAZPLAN: Decision support systems for Australian grazing enterprises – II. The animal biology model for feed intake, production and reproduction and the GrazFeed DSS. *Agr. Syst.* 54, 77-126.

Geenty, K. G., 1979. Lactation performance, growth, and carcass composition of sheep 1. Milk production, milk composition, and live weights of Romney, Corriedale, Dorset, Romney X Dorset, and Dorset X Romney ewes in relation to the growth of their lambs. *New Zealand Journal of Agricultural Research*. 22, 241-250.

Georgi, J. R. 1985. Parasitology for Veterinarians (4th ed.). W.B. Saunders Company. Philadelphia, PA

Gibb, M. J., & Treacher, T. T., 1980. The effect of ewe condition at lambing on the performance of ewes and their lambs at pasture. *J. Agri. Sci.* 95, 631-640.

Gibbs, H. C., & Barger, I. A., 1986. *Haemonchus contortus* and other trichostrongylid infections in parturient, lactating and dry ewes. *Vet. Parasitol.* 22, 57-66.

Goldberg, A., 1970. Development, migration and survival on pasture of gastrointestinal nematodes of cattle: summer contamination. *Proceedings of the Helminthological Society of Washington*. 37, 166-169.

Gordon, H., 1967. The diagnosis of helminthosis in sheep. *Vet. Med. Rev.* 67, 140-168.

Gordon, H. M., 1948. The epidemiology of parasitic diseases, with special reference to studies with nematode parasites of sheep. *Aust. Vet. J.* 24, 17-45.

Gordon, H. M., 1950. Some aspects of parasitic gastro-enteritis of sheep. *Aust. Vet. J.* 26, 14-27 (pages 19-21 missing from photocopy before scanning).

Greer, A. W., 2008. Trade-offs and benefits: Implications of promoting a strong immunity to gastrointestinal parasites in sheep. *Parasite Immunol.* 30, 61-32.

Greer, A. W., Huntley, J. F., Mackellar, A., McAnulty, R. W., Jay, N. P., Green, R. S., Stankiewicz, M., & Sykes, A. R., 2008. The effect of corticosteroid treatment on local immune responses, intake and performance in lambs infected with *Teladorsagia circumcincta*. *Int. J. Parasitol.* 38, 1717-1728.

Greer, A. W., McAnulty, R. W., Stankiewicz, M., & Sykes, A. R., 2005a. Corticosteroid treatment prevents the reduction in food intake and growth in lambs infected with the abomasal parasite *Teladorsagia circumcincta*. *Proceedings of the New Zealand Society of Animal Production*. 65, 9-12.

Greer, A. W., Sedcole, R. J., Jay, N. P., McAnulty, R. W., Green, R. S., Stankiewicz, M., & Sykes, A. R., 2009. Protein supply influences the nutritional penalty associated with the development of immunity in lambs infected with *Trichostrongylus colubriformis*. *Animal*. 3, 437-445.

Greer, A. W., Stankiewicz, M., Jay, N. P., McAnulty, R. W., & Sykes, A. R., 2005b. The effect of concurrent corticosteroid induced immuno-suppression and infection with the intestinal parasite *Trichostrongylus colubriformis* on food intake and utilization in both immunologically naïve and competent sheep. *Anim. Sci.* 80, 89-99.

Hansen, J., & Perry, B. 1994. The epidemiology, diagnosis and control of helminth parasites of ruminents: A handbook. International Laboratory for Research on Animal Diseases. Nairobi

Hansen, M. F., Kelley, G. W., & Todd, A. C., 1950. Observations on the effects of a pure infection of *Moniezia expansa* on lambs. *Trans. Am. Microsc. Soc.* 69, 148-155.

Hawkins, P. A., 1946. Studies of Sheep Parasites. VII. *Moniezia expansa* Infections. *The Journal of Parasitology*. 32, 14.

Haynes, F. E. M., Greenwood, P. L., Siddell, J. P., McDonagh, M. B., & Oddy, V. H. (2010). *Computer tomography software program 'OsiriX' aids prediction of sheep body composition.* Australian Society of Animal Production 28th Biennial Conference - Livestock Production in a Changing Environment, Armidale, NSW, Australia.

Hocking Edwards, J. E., Copping, K. J., & Thompson, A. N., 2011. Managing the nutrition of twin-bearing ewes during pregnancy using Lifetimewool recommendations increases production of twin lambs. *Anim. Prod. Sci*. 51, 813-820.

Holasová, E., Pavlásek, I., & Kotrlá, B., 1989. Migration of infective larvae of sheep gastrointestinal nematodes. *Acta Veterinaria Brno*. 58, 369-378.

Holmes, P. H., 1986. Pathophysiology of nematode infections. *Proceedings of the Sixth International Congress of Parasitology*, 443-451.

Holmes, P. H., 1987. Pathophysiology of nematode infections. *Int. J. Parasitol.* 17, 443-451.

Houdijk, J. G. M., 2008. Influence of periparturient nutritional demand on resistance to parasites in livestock. *Parasite Immunol.* 30, 113-121.

Houdijk, J. G. M., Kyriazakis, I., Jackson, F., Huntley, J. F., & Coop, R. L., 2000. Can an increased intake of metabolizable protein affect the periparturient relaxation in immunity against *Teladorsagia circumcincta* in sheep? *Vet. Parasitol.* 91, 43-62.

Hsu, C. K., & Levine, N. D., 1977. Degree-day concept in development of infective larvae of *Haemonchus contortus* and *Trichostrongylus colubriformis* and constant and cyclic conditions. *Am. J. Vet. Res.* 38, 1115-1119.

Imperiale, F., Lifschitz, A., Sallovitz, J., Virkel, G., & Lanusse, C., 2004. Comparative depletion of ivermectin and moxidectin milk residues in dairy sheep after oral and subcutaneous administration. *J. Dairy Res.* 71, 427-433.

INNERVISION™. (2011). AutoCAT (Version 2.0.5526.20427) [Semi automated CT image analysis program]: INNERVISION™ and AgResearch Landcorp Farming Ltd.

Iposu, S. O., Greer, A. W., McAnulty, R. W., Stankiewicz, M., & Sykes, A. R., 2010. Does milk supply have long-term benefits for resistance and resilience to nematode parasites in sheep? *Small Ruminant Research*. 94, 142-149.

Iposu, S. O., McAnulty, R. W., Greer, A. W., Xie, H. L., Green, R. S., Stankiewicz, M., & Sykes, A. R., 2008. Does suckling offer protection to the lamb against *Teladorsagia circumcincta* infection? *Vet. Parasitol.* 153, 294-301.

Jacobson, C., 2006. Scouring and dag in sheep in Western Australia. The role of parasitic nematodes and nutritional factors in diarrhoea in sheep of post weaning age. *PhD thesis*.

Jacobson, C. L., Bell, A., & Besier, R. B., 2009. Nematode parasites and faecal soiling of sheep in lairage: Evidence of widespread potential production losses for the sheep industry. *Anim. Prod. Sci*. 49, 326–332.

Jasmer, D. P., Wescott, R. B., & Crane, J. W., 1986. Influence of cold temperatures upon development and survival of eggs of Washington isolates of *Haemonchus contortus* and *Ostertagia circumcincta*. *Proceedings of the Helminthological Society of Washington*. 53, 244-247.

Jeffcoate, I. A., Wedrychowicz, H., Fishwick, G., Dunlop, E. M., Duncan, J. L., & Holmes, P. H., 1992. Pathophysiology of the periparturient egg rise in sheep: a possible role for IgA. *Res. Vet. Sci.* 53, 212-218.

Kahn, L. P., 2003. Regulation of the resistance and resilience of periparturient ewes to infection with gastrointestinal nematode parasites by dietary supplementation. *Aust. J. Exp. Agric.* 43, 1477-1485.

Kahn, L. P., Knox, M. R., & Gray, G. D., 1999. Enhancing immunity to nematode parasites in pregnant and lactating sheep through nutrition and genetic selection. *Recent Advances in Animal Nutrition in Australia*. 12, 15-22.

Kahn, L. P., Knox, M. R., Walkden-Brown, S. W., & Lea, J. M., 2003. Regulation of the resistance to nematode parasites of single- and twin-bearing Merino ewes through nutrition and genetic selection. *Vet. Parasitol.* 114, 15-31.

Kahn, L. P., Kyriazakis, I., Jackson, F., & Coop, R. L., 2000a. Temporal effects of protein nutrition on the growth and immunity of lambs infected with *Trichostrongylus colubriformis*. *Int. J. Parasitol.* 30, 193-205.

Kahn, L. P., Walkden-Brown, S. W., & Lea, J. M., 2000b. Dietary enhancement of resistance to *Trichostrongylus colubriformis* in Merino weaners. *Asian Australas. J. Anim. Sci.* 13, 68-71.

Kahn, L. P., Walkden-Brown, S. W., Scrivener, C. J., & Crampton, A. (2006). *A structured, evidence-based approach as an aid when deciding the need for anthelmintic treatment of sheep.* Proceedings of the Australian Sheep Veterinarians Annual Conference, Wagga.

Kahn, L. P., & Woodgate, R. G., 2012. Integrated parasite management: Products for adoption by the Australian sheep industry. *Vet. Parasitol.* 186, 58-64.

Kambara, T., McFarlane, R. G., Abell, T. J., McAnulty, R. W., & Sykes, A. R., 1993. The effect of age and dietary protein on immunity and resistance in lambs vaccinated with *Trichostrongylus colubriformis*. *Int. J. Parasitol.* 23, 471-476.

Kaminsky, R., Ducray, P., Jung, M., Clover, R., Rufener, L., Bouvier, J., Weber, S. S., Wenger, A., Wieland-Berghausen, S., Goebel, T., Gauvry, N., Pautrat, F., Skripsky, T., Froelich, O., Komoin-Oka, C., Westlund, B., Sluder, A., & Mäser, P., 2008. A new class of anthelmintics effective against drug-resistant nematodes. *Nature*. 452, 176-180.

Karlsson, L. J., & Greeff, J. C., 2012. Genetic aspects of sheep parasitic diseases. *Vet. Parasitol.*

Kates, K. C., & Goldberg, A., 1951. The pathogenicity of the common sheep tapeworm, *Moniezia expansa*. *Proceedings of the Helminthological Society of Washington*. 18, 87-101.

Kelly, D., & Coutts, A. G. P., 2000. Development of digestive and immunological function in neonates: role of early nutrition. *Livest. Prod. Sci.* 66, 161-167.

Kelly, G. A. (2011). *Investigating the effect of gastrointestinal nematodiasis in Merino sheep on the Northern Tablelands of New South Wales and implications for*

Integrated Parasite Management. (Doctor of Philosophy), University of New England, Armidale, New South Wales.

Kelly, G. A., Kahn, L. P., & Walkden-Brown, S. W., 2010. Integrated parasite management for sheep reduces the effects of gastrointestinal nematodes on the Northern Tablelands of New South Wales. *Anim. Prod. Sci*. 50, 1043-1052.

Kelly, G. A., Kahn, L. P., & Walkden-Brown, S. W., 2013. Measurement of phenotypic resilience to gastro-intestinal nematodes in Merino sheep and association with resistance and production variables. *Vet. Parasitol.* 193, 111-117.

Kelly, G. A., Walkden-Brown, S. W., & Kahn, L. P., 2012. No loss of production due to larval challenge in sheep given continuous anthelmintic treatment via a controlled release capsule. *Vet. Parasitol.* 183, 274-283.

Kenyon, P. R., Hickson, R. E., Hutton, P. G., Morris, S. T., Stafford, K. J., & West, D. M., 2012. Effect of twin-bearing ewe body condition score and late pregnancy nutrition on lamb performance. *Anim. Prod. Sci*.

Khadijah, S., Kahn, L. P., Walkden-Brown, S. W., Bailey, J. N., & Bowers, S. F., 2013a. Effect of simulated rainfall timing on faecal moisture and development of *Haemonchus contortus* and *Trichostrongylus colubriformis* eggs to infective larvae. *Vet. Parasitol.* 192, 199-210.

Khadijah, S., Kahn, L. P., Walkden-Brown, S. W., Bailey, J. N., & Bowers, S. F., 2013b. Soil moisture influences the development of *Haemonchus contortus* and *Trichostrongylus colubriformis* to third stage larvae. *Vet. Parasitol.* 196, 161-171.

Khadijah, S., Kahn, L. P., Walkden-Brown, S. W., Bailey, J. N., & Bowers, S. F., 2013c. Soil moisture modulates the effects of the timing and amount of rainfall on faecal moisture and development of *Haemonchus contortus* and *Trichostrongylus colubriformis* to infective third stage larvae. *Vet. Parasitol.* 196, 347-357.

Khadijah, S., Kahn, L. P., Walkden-Brown, S. W., Bailey, J. N., & Bowers, S. F., 2013d. Translation of *H. contortus* and *T. colubriformis* from egg to establishment in grazing sheep is unaffected by rainfall timing, rainfall amount and herbage height under conditions of high soil moisture in the Northern Tablelands of NSW. *Vet. Parasitol.* 197, 204-211.

Khan, F. A., Sahoo, A., Sonawane, G. G., Karim, S. A., Dhakad, S., Pareek, A. K., & Tripathi, B. N., 2012. Effect of dietary protein on responses of lambs to repeated *Haemonchus contortus* infection. *Livestock Science*. 150, 143-151.

Killeen, I. D., 1967. The effects of body weight and level of nutrition before, during and after joining on ewe fertility. *Aust. J. Exp. Agr. Anim. Husb.* 7 126 -135.

Kimambo, A. E., MacRae, J. C., & Dewey, P. L., 1988a. The effect of daily challenge with *Trichostrongylus colubriformis* larvae on the nutrition and performance of immunologically resistant sheep. *Vet. Parasitol.* 28, 205-212.

Kimambo, A. E., MacRae, J. C., Walker, A., Watt, C. F., & L., C. R., 1988b. Effect of prolonged subclinical infection with *Trichostrongylus colubriformis* on the performance and nitrogen metabolism of growing lambs. *Vet. Parasitol.* 28, 191-203.

Knight, T. W., Atkinson, D. S., Haack, N. A., Palmer, C. R., & Rowland, K. H., 1993. Effects of suckling regime on lamb growth rates and milk yields of Dorset ewes. *New Zeal. J. Agr. Res.* 36, 215-222.

Knox, M. R., Besier, R. B., Le Jambre, L. F., Kaplan, R. M., Torres-Acosta, J. F., Miller, J., & Sutherland, I., 2012. Novel approaches for the control of helminth parasites of livestock VI: Summary of discussions and conclusions. *Vet. Parasitol.* 186, 143-149.

Knox, M. R., & Steel, J. W., 1999. The effects of urea supplementation on production and parasitological responses of sheep infected with *Haemonchus contortus* and *Trichostrongylus colubriformis*. *Vet. Parasitol.* 83, 123-135.

Kotze, A. C., Ruffell, A. P., Knox, M. R., & Kelly, G. A., 2014. Relative potency of macrocyclic lactones in in vitro assays with larvae of susceptible and drug-resistant Australian isolates of *Haemonchus contortus* and *H. placei*. *Vet. Parasitol.* 203, 294-302.

Kotze, A. C., Stein, P. A., & Dobson, R. J., 1999. Investigation of intestinal nematode responses to naphthalophos and pyrantel using a larval development assay. *Int. J. Parasitol.* 29, 1093-1099.

Krecek, R. C., Groeneveld, H. T., & Maritz, J. I., 1992. A preliminary study of the effect of microclimate on third-stage larvae of *Haemonchus contortus* and *Haemonchus placei* on irrigated pasture. *Int. J. Parasitol.* 22, 747-752.

Kyriazakis, I., Anderson, D. H., Coop, R. L., & Jackson, F., 1996a. The pathophysiology and development of immunity during long-term subclinical infection with *Trichostrongylus colubriformis* of sheep receiving different nutritional treatments. *Vet. Parasitol.* 65, 41-54.

Kyriazakis, I., Anderson, D. H., Oldham, J. D., Coop, R. L., & Jackson, F., 1996b. Long-term subclinical infection with *Trichostrongylus colubriformis*: effects on food intake, diet selection and performance of growing lambs. *Vet. Parasitol.* 61, 297-313.

Lane, J., Jubb, T., Shephard, R., Webb-Ware, J., & Fordyce, G. (2015). Priority list of endemic diseases for the red meat industries (pp. 282). Sydney: Meat & Livestock Australia Limited.

Larsen, J. W. A., Anderson, N., & Vizard, A. L., 1999. The pathogenesis and control of diarrhoea and breech soiling in adult Merino sheep. *Int. J. Parasitol.* 29, 893-902.

Larsen, J. W. A., Anderson, N., Vizard, A. L., Anderson, G. A., & Hoste, H., 1994. Diarrhoea in Merino ewes during winter: association with trichostrongylid larvae. *Aust. Vet. J.* 71, 365-372.

Laurenson, Y. C. S. M., Bishop, S. C., Forbes, A. B., & Kyriazakis, I., 2013. Modelling the short- and long-term impacts of drenching frequency and targeted selective treatment on the performance of grazing lambs and the emergence of anthelmintic resistance. *Parasitology*. 140, 780-791.

Le Jambre, L. F., 1995. Relationship of blood loss to worm numbers, biomass and egg production in *Haemonchus* infected sheep. *Int. J. Parasitol.* 25, 269-273.

Le Jambre, L. F., Dominik, S., Eady, S. J., Henshall, J. M., & Colditz, I. G., 2007. Adjusting worm egg counts for faecal moisture in sheep. *Vet. Parasitol.* 145, 108-115.

Le Jambre, L. F., Windon, R. G., & Smith, W. D., 2008. Vaccination against *Haemonchus contortus*: Performance of native parasite gut membrane glycoproteins in Merino lambs grazing contaminated pasture. *Vet. Parasitol.* 153, 302-312.

Learmount, J., Taylor, M. A., & Bartram, D. J., 2012. A computer simulation study to evaluate resistance development with a derquantel-abamectin combination on UK sheep farms. *Vet. Parasitol.* 187, 244-253.

Leathwick, D. M., 2012. Modelling the benefits of a new class of anthelmintic in combination. *Vet. Parasitol.* 186, 93-100.

Leathwick, D. M., Barlow, N. D., & Vlassoff, A., 1995. A model for nematodiasis in New Zealand lambs: The effect of drenching regime and grazing management on the development of anthelmintic resistance. *Int. J. Parasitol.* 25, 1479-1490.

Leathwick, D. M., Godfrey, P. L., Miller, C. M., & Vlassoff, A., 1999. Temperature, resistance status and host effects on the development of nematode eggs. *New Zealand Journal of Zoology*. 26, 76.

Leathwick, D. M., Hosking, B. C., Bisset, S. A., & McKay, C. H., 2009. Managing anthelmintic resistance: Is it feasible in New Zealand to delay the emergence of resistance to a new anthelmintic class? *N. Z. Vet. J.* 57, 181-192.

Leathwick, D. M., Miller, C. M., & Fraser, K., 2015. Selection for anthelmintic resistant Teladorsagia circumcincta in pre-weaned lambs by treating their dams with long-acting moxidectin injection. *International Journal for Parasitology: Drugs and Drug Resistance*. 5, 209-214.

Leathwick, D. M., Waghorn, T. S., Miller, C. M., Candy, P. M., & Oliver, A. M., 2012. Managing anthelmintic resistance - Use of a combination anthelmintic and leaving some lambs untreated to slow the development of resistance to ivermectin. *Vet. Parasitol.* 187, 285-294.

Levine, N. D., & Andersen, F. L., 1973. Development and survival of *Trichostrongylus colubriformis* on pasture. *The Journal of Parasitology*. 59, 147-165.

Leyva, V., Henderson, A. E., & Sykes, A. R., 1982. Effect of daily infection with *Ostertagia circumcincta* larvae on food intake, milk production and wool growth in sheep. *J. Agri. Sci.* 99, 249-259.

Lloyd, S., 1983. Effect of pregnancy and lactation upon infection. *Vet. Immunol. Immunopathol.* 4, 153-176.

Love, S. C. J. (2011, February, 2011). Drench resistance and sheep worm control. Primefacts 2nd. Retrieved February, 2011, 2011, from http://www.dpi.nsw.gov.au/__data/assets/pdf_file/0009/111060/Drench-resistance-and-sheep-worm-control.pdf

Macarthur, F. A., Kahn, L. P., & Windon, R. G., 2013a. Immune response of twin-bearing Merino ewes when infected with *Haemonchus contortus*: Effects of fat score and prepartum supplementation. *Livestock Science*. 157, 568-576.

Macarthur, F. A., Kahn, L. P., & Windon, R. G., 2013b. Regulating maternal production of twin-bearing Merino ewes through fat score and prepartum supplementation when infected with *Haemonchus contortus*. *Livestock Science*. 157, 442-451.

Macarthur, F. A., Kahn, L. P., & Windon, R. G., 2014. The influence of dietary manipulations and gastrointestinal nematodes on twin-bearing merino ewes and determinants of lamb survival. *Livestock Science*. 167, 342-352.

Malan, F. S., van Wyk, J. A., & Wessels, C. D., 2001. Clinical evaluation of anaemia in sheep: early trials *Oonderstepoort J. Vet.* 68, 165-174.

Martin, P. J., Le Jambre, L. F., & Claxton, J. H., 1981. The impact of refugia on the development of thiabendazole resistance in *Haemonchus contortus*. *International Journal for Parasitology,*. 11, 35-41.

Maxwell, D. (2015). Barbervax® - a vaccine to protect against barber's pole worm. Retrieved from http://www.wormboss.com.au/news/articles/nonchemical-management/barbervaxa-vaccine-to-protect-against-barbers-pole-worm.php

Maxwell, D., Kahn, L. P., Love, S., Lyndal-Murphy, M., & Walkden-Brown, S. W. (2012). WormBoss worm control program - Summer rainfall/tablelands and slopes. Retrieved from http://www.wormboss.com.au/files/pages/programs/tablelands-slopes/liver-fluke-control/worm-control-program/WB_Program_TABLELANDS__SLOPES_30_June_2012_JH.pdf

McClure, S. (2000). Sheep immunity to gastrointestinal nematode parasites - review 2000 (pp. 1-14): CSIRO.

McClure, S. J., Emery, D. L., & Steel, J. W. (2000). Host resistance to gastrointestinal parasites of sheep. In Cronje, P. B. (Ed.), Ruminant Physiology: Digestion, Metabolism, Growth and Reproduction (pp. 425-436). Oxon, UK: CABI Publishing.

McKellar, Q. A., & Jackson, F., 2004. Veterinary anthelmintics: old and new. *Trends Parasitology*. 20, 456-461.

McLeod, R. S., 1995. Costs of major parasites to the Australian livestock industries. *Int. J. Parasitol.* 25, 1363-1367.

McNeilly, T. N., Devaney, E., & Matthews, J. B., 2009. *Teladorsagia circumcincta* in the sheep abomasum: defining the role of dendritic cells in T cell regulation and protective immunity. *Parasite Immunol.* 31, 347-356.

Meat and Livestock Australia. (2009). Building the Australian prime lamb industry. North Sydney, New South Wales: Meat and Livestock Australia (MLA).

Meeusen, E. N. T., 1999. Immunology of helminth infections, with special reference to immunopathology. *Vet. Parasitol.* 84, 259-273.

Meeusen, E. N. T., & Balic, A., 2000. Do eosinophils have a role in the killing of helminth parasites? *Parasitology Today*. 16, 95-101.

Miller, C. M., Waghorn, T. S., Leathwick, D. M., Candy, P. M., Oliver, A. M. B., & Watson, T. G., 2012. The production cost of anthelmintic resistance in lambs. *Vet. Parasitol.* 186, 376-381.

Miller, J. E., & Horohov, D. W., 2006. Immunological aspects of nematode parasite control in sheep. *J. Anim. Sci.* 84, E124-E132.

Morley, N. (2006). *Effect of immunosuppression on host-parasite interaction in sheep infected with Haemonchus contortus.* (B.Rur.Sc. (Hons).), University of New England, Armidale.

Morris, C. A., Bisset, S. A., Vlassoff, A., Mackay, A., Betteridge, K., Alderton, M. J., West, C. J., & Devantier, B. P. (2001). *Genetic studies of resilience of Romney sheep to nematode challenge in New Zealand.* Proceedings of the New Zealand Society of Animal Production.

Morris, C. A., Watson, T. G., Bisset, S. A., Vlassoff, A., & Douch, P. G. C. (1995). Breeding sheep in New Zealand for resistance or resilience to nematode parasites. In Gray, G. D., Woolaston, R. R. & Eaton, B. T. (Eds.), Breeding for resistance to infectious disease in small ruminants (pp. 77-98). Canberra: Australian Centre for International Agricultural Research (ACIAR).

Nagasinha, C. (2000). *Effects of Trichostrongylus colubriformis on protein and phoshorus metabolism in sheep.* (Doctor of Philosophy), Lincoln University.

Nieuwoudt, S. W., Theron, H. E., & Krüger, L. P., 2002. Genetic parameters for resistance to *Haemonchus contortus* in Merino sheep in South Africa. *J. S. Afr. Vet. Assoc.* 73, 4-7.

Niven, P. G., Anderson, N., & Vizard, A. L., 2002. The integration of grazing management and summer treatments for the control of trichostrongylid infections in Merino weaners. *Aust. Vet. J.* 80, 559-566.

O'Connor, L., Walkden-Brown, S., & Kahn, L., 2006. Ecology of the free-living stages of major trichostrongylid parasites of sheep. *Vet. Parasitol.* 142, 1-15.

O'Connor, L. J., Kahn, L. P., & Walkden-Brown, S. W., 2007. Moisture requirements for the free-living development of *Haemonchus contortus*: quantitative and temporal effects under conditions of low evaporation. *Vet. Parasitol.* 150, 128-138.

O'Connor, L. J., Kahn, L. P., & Walkden-Brown, S. W., 2008. Interaction between the effects of evaporation rate and amount of simulated rainfall on development of the free-living stages of *Haemonchus contortus*. *Vet. Parasitol.* 155, 223-234.

O'Sullivan, B. M., & Donald, A. D., 1970. A field study of nematode parasite populations in the lactating ewe. *Parasitology*. 61, 301-315.

Ørskov, E. R., Benzie, D., & Kay, R. N. B., 1970. The effects of feeding procedure on closure of the oesophageal groove in young sheep. *Br. J. Nutr.* 24, 785-795.

Parkins, J. J., & Holmes, P. H., 1989. Effects of gastrointestinal helminth parasites on ruminant nutrition. *Nutrition Research Reviews*. 2, 227-246.

Pethick, D. W., Banks, R. G., Hales, J., & Ross, I. R. (2006). *Australian prime lamb—a vision for 2020.* Australian Sheep Industry CRC Conference.

Pfizer. (2011). Single shot scab and worm treatment with persistency.. It's the only one! : Pfizer Animal Health.

Playford, M., Smith, A., Love, S., Besier, R., Kluver, P., & Bailey, J., 2014. Prevalence and severity of anthelmintic resistance in ovine gastrointestinal nematodes in Australia (2009-2012). *Aust Vet J*. 92, 464-471.

Pomroy, W. E., 2006. Anthelmintic resistance in New Zealand: A perspective on recent findings and options for the future. *N. Z. Vet. J.* 54, 265-270.

Poppi, D. P., MacRae, J. C., Brewer, A., & L., C. R., 1986. Nitrogen transactions in the digestive tract of lambs exposed to the intestinal parasite, *Trichostrongylus colubriformis*. *Br. J. Nutr.* 55, 593-602.

Pradhan, S. L., & Johnstone, I. L., 1972a. *Haemonchus contortus* - haematological changes in lambs during prolonged exposure to daily and weekly doses of infective larvae. *Parasitology*. 64, 153-160.

Pradhan, S. L., & Johnstone, I. L., 1972b. *Haemonchus contortus* - the effect on lambs of prolonged exposure to daily and weekly doses of infective larvae. *Parasitology*. 64, 143-152.

Prichard, R. K., Hall, C. A., Kelly, J. D., Martin, I. C. A., & Donald, A. D., 1980. The problem of anthelmintic resistance in nematodes. *Aust. Vet. J.* 56, 239-250.

Ratib, O., Rosset, A., & Heuberger, J. 2009. OsiriX: The Pocket Guide (Second ed.). The OsiriX Foundation. Geneva, Switzerland

Reeve, I., & Walkden-Brown, S. (2014). Benchmarking Australian sheep parasite control: Cross-sectional survey report: Institute For Rural Futures and Animal Science, University of New England.

Reveron, A. E., Topps, J. H., & Gelman, A. L., 1974a. Mineral metabolism and skeletal development of lambs affected by *Trichostrongylus colubriformis*. *Res. Vet. Sci.* 16, 310-319.

Reveron, A. E., Topps, J. H., MacDonald, D. C., & Pratt, G., 1974b. The intake, digestion and uitlization of food and growth rates of lambs affected by *Trichostrongylus colubriformis*. *Res. Vet. Sci.* 16, 299-309.

Roberts, J. L., & Swan, R. A., 1981. Quantitative studies of ovine haemonchosis. 1. Relationship between faecal egg counts and total worm counts. *Vet. Parasitol.* 8, 165-171.

Roberts, J. L., & Swan, R. A., 1982. Quantitative studies of ovine haemonchosis. 2. Relationship between total worm counts of *Haemonchus contortus*, haemoglobin values and bodyweight. *Vet. Parasitol.* 9, 201-209.

Roeber, F., Jex, A. R., & Gasser, R. B., 2013. Impact of gastrointestinal parasitic nematodes of sheep, and the role of advanced molecular tools for exploring epidemiology and drug resistance - an Australian perspective. *Parasit Vectors*. 6, 153.

Roeber, F., & Kahn, L., 2014. The specific diagnosis of gastrointestinal nematode infections in livestock: Larval culture technique, its limitations and alternative DNA-based approaches. *Vet. Parasitol.* 205, 619-628.

Rolfe, P. F. (1990). *Chemical resistance in livestock - an overview.* Weeds and worms: Combat Resistance - Proceedings of the Riverina Outlook conference, Wagga Wagga.

Rolfe, P. F., Boray, J. C., Fitzgibbon, C., Parsons, G., Kemsley, P., & Sangster, N., 1990. Closantel resistance in *Haemonchus contortus* from sheep. *Aust. Vet. J.* 67, 29-31.

Rossanigo, C. E., & Gruner, L., 1995. Moisture and temperature requirements in faeces for the development of free-living stages of gastrointestinal nematodes of sheep, cattle and deer. *J. Helminthol.* 69, 357-362.

Rowe, J. B., Nolan, J. V., de Chaneet, G., & Teleni, E., 1988. The effect of haemonchosis and blood loss into the abomasum on digestion in sheep. *Br. J. Nutr.* 59, 125-139.

Sackett, D., Holmes, P., Abbott, K., Jephcott, S., & Barber, M. (2006). Assessing the economic cost of endemic disease on the profitability of Australian beef cattle and sheep producers (pp. 119). Sydney: Meat and Livestock Australia.

Sangster, N. C., & Dobson, R. J. (2002). Anthelmintic resistance. In Lee, D. L. (Ed.), The biology of nematodes (pp. 531-567). London: Taylor and Francis.

Sargison, N. D., Bartram, D. J., & Wilson, D. J., 2012. Use of a long acting injectable formulation of moxidectin to control the periparturient rise in faecal *Teladorsagia circumcincta* egg output of ewes. *Vet. Parasitol.*

Scott, I., Hodgkinson, S. M., Khalaf, S., Lawton, D. E. B., Collett, M. G., Reynolds, G. W., Pomroy, W. E., & Simpson, H. V., 1998. Infection of sheep with adult and larval *Ostertagia circumcincta*: abomasal morphology. *Int. J. Parasitol.* 28, 1383-1392.

Scott, I., Khalaf, S., Simcock, D. C., Knight, C. G., Reynolds, G. W., Pomroy, W. E., & Simpson, H. V., 2000. A sequential study of the pathology associated with the infection of sheep with adult and larval *Ostertagia circumcincta*. *Vet. Parasitol.* 89, 79-94.

Scrivener, C. J., Kahn, L. P., & Walkden-Brown, S. W. (2006). *No loss of sheep production with IPM-sheep control programs.* Proceedings of the Australian Sheep Veterinarians Annual Conference, Wagga.

Seddon, H. R., 1932. The development in sheep of immunity to *Moniezia expansa*. *Aust. Vet. J.* 8, 112.

Shaw, K. L., Nolan, J. V., Lynch, J. J., Coverdale, O. R., & Gill, H. S., 1995. Effects of weaning, supplementation and gender on acquired immunity to *Haemonchus contortus* in lambs. *Int. J. Parasitol.* 25, 381-387.

Shaw, R. J., Morris, C. A., Green, R. S., Wheeler, M., Bisset, S. A., Vlassoff, A., & Douch, P. G. C., 1999. Genetic and phenotypic relationships among *Trichostrongylus colubriformis*-specific immunoglobulin E, anti-*Trichostrongylus colubriformis* antibody, immunoglobulin G1, faecal egg count and body weight traits in grazing Romney lambs. *Livest. Prod. Sci.* 58, 25-32.

Sheriff, D., & Habel, J. D. 1976. Sheep haematology in diagnosis (Vol. 16). The University of Sydney, Post Graduate Foundation in Veterinary Science.

Silangwa, S. M., & Todd, A. C., 1964. Vertical migration of trichostrongylid larvae on grasses. *J. Parasitol.* 50, 278-285.

Silva, B. F., Amarante, M. R. V., Kadri, S. M., Carrijo-Mauad, J. R., & Amarante, A. F. T., 2008. Vertical migration of *Haemonchus contortus* third stage larvae on *Brachiaria decumbens* grass. *Vet. Parasitol.* 158, 85-92.

Silvestre, A., Cabaret, J., & Humbert, J. F., 2001. Effect of benzimidazole under-dosing on the resistant allele frequency in *Teladorsagia circumcincta* (Nematoda). *Parasitology*. 123, 103-111.

Smith, G., Grenfell, B. T., Isham, V., & Cornell, S., 1999. Anthelmintic resistance revisited: under-dosing, chemoprophylactic strategies and mating probabilities. *Int. J. Parasitol.* 29, 77-91.

Southcott, W. H., & Barger, I. A., 1975. Control of nematode parasites by grazing management—II. Decontamination of sheep and cattle pastures by varying periods of grazing with the alternate host. *Int. J. Parasitol.* 5, 45-48.

Southcott, W. H., Major, G. W., & Barger, I. A., 1976. Seasonal pasture contamination and availability of nematodes for grazing sheep. *Aust J Agr Res*. 27, 277-286.

Southworth, J., Harvey, C., & Larson, S., 1996. Use of praziquantel for the control of *Moniezia expansa* in lambs. *N. Z. Vet. J.* 44, 112-115.

Spedding, C. R. W., Brown, T. H., & Large, R. V. (1963). *The effect of milk intake on nematode infestation of the lamb.* Nutrition and the host-parasite relationship.

Stear, M. J., Bairden, K., Duncan, J. L., Holmes, P. H., McKellar, Q. A., Park, M., Strain, S., Murray, M., Bishop, S. C., & Gettinby, G., 1997. How hosts control worms. *Nature*. 389, 27.

Stear, M. J., Bishop, S. C., Doligalska, M., Duncan, J. L., Holmes, P. H., Irvine, J., McCririe, L., McKellar, Q. A., Sinski, E., & Murray, M., 1995. Regulation of egg production, worm burden, worm length and worm fecundity by host responses in sheep infected with *Ostertagia circumcincta*. *Parasite Immunol.* 17, 643-652.

Steel, J. W., 1972. Effects of the intestinal nematode *Trichostrongylus colubriformis* on ruminal acetate metabolism in young sheep. *Proceedings of the Australian Society for Animal Production*. Vol: 9, 402-407.

Steel, J. W., Jones, W. O., & Symons, L. E. A., 1982. Effects of a concurrent infection of *Trichostrongylus colubriformis* on the productivity and physiological and metabolic responses of lambs infected with *Ostertagia circumcincta*. *Aust J Agr Res*. 33, 131-140.

Steel, J. W., Symons, L. E. A., & Jones, W. O., 1980. Effects of level of larval intake on the productivity and physiological and metabolic responses of lambs infected with *Trichostrongylus colubriformis*. *Aust J Agr Res*. 31, 821-838.

Stewart, D. F., 1953. Studies on resistance of sheep to infestation with *Haemonchus contortus* and *Trichostrongylus spp.* and on the immunological reactions of sheep exposed to infestation. V. The nature of the "self-cure" phenomenon. *Aust J Agr Res*. 4, 100-117.

Stoll, N. R., 1936. Tapeworm Studies. III. Sheep parasitized with one *Moniezia expansa* each. *The Journal of Parasitology*. 22, 161-179.

Strobel, H., de Ponte, M., Knoppe, T. N., & Bhushan, C., 2013. Comparison of three different treatment schedules for praziquantel (Cestocur(R), Bayer) in the treatment of tapeworm infections (*Moniezia* spp.) and their impact on body weight gains in a German sheep flock. *Parasitol. Res.* 112 Suppl 1, 139-147.

Sutherland, I., & Scott, I. 2010. Gastrointestinal nematodes of sheep and cattle: Biology and control. Wiley-Blackwell. United Kingdom

Sutherland, I. A., Leathwick, D. M., Green, R. S., Miller, C. M., & Brown, A. E., 1998. The effect of continuous drug exposure on the immune response of lambs challenged with drug-susceptible or drug-resistant nematode larvae. *Vet. Res. Commun.* 22, 305-314.

Sutherland, I. A., Shaw, J., & Shaw, R. J., 2010. The production costs of anthelmintic resistance in sheep managed within a monthly preventive drench program. *Vet. Parasitol.* 171, 300-304.

Sykes, A. R., 1994. Parasitism and production in farm animals. *Anim Prod.* 59, 155-172 (The pages 166-172 were not available to scan).

Sykes, A. R., 2000. Environmental effects on animal production: The nutritional demands of nematode parasite exposure in sheep. *Asian Australian Journal of Animal Sciences*. 13, 343-350.

Sykes, A. R., 2010. Host immune responses to nematodes: benefit or cost? Implications for future development of sustainable methods of control. *R. Bras. Zootec.* 39, 376-382.

Sykes, A. R., & Coop, R. L., 1976. Intake and utilization of food by growing lambs with parasitic damage to the small intestine caused by daily dosing with *Trichostrongylus colubriformis* larvae. *J. Agri. Sci.* 86, 507-515.

Sykes, A. R., & Coop, R. L., 1977. Intake and utilisation of food by growing sheep with abomasal damage caused by daily dosing with *Ostertagia circumcincta* larvae. *J. Agri. Sci.* 88, 671-677.

Symons, L. E. A., & Jones, W. O., 1975. Skeletal muscle, liver and wool protein synthesis by sheep infected by the nematode *Trichostrongylus colubriformis*. *Aust J Agr Res*. 26, 1063-1072.

Symons, L. E. A., Steel, J.W. & Jones, W.O., 1981. Effects of level of larval intake on the productivity and physiological and metabolic responses of lambs infected with *Ostertagia circumcincta*. *Aust J Agr Res*. 32, 139-148.

Thomas, P. L., Downey, N. E., & Dreadon, R. S., 1956. Mortality in lambs due to enterotoxaemia associated with heavy infestations of *Moniezia expansa*. *N. Z. Vet. J.* 4, 161-165.

Thomas, R. J., & Ali, D. A., 1983. The effect of *Haemonchus contortus* infection on the pregnant and lactating ewe. *Int. J. Parasitol.* 13, 393-398.

Thompson, J., & Meyer, H. (1994). Body condtion scoring of sheep. Oregon State University: Oregon State University Extension Service.

Thrusfield, M. 1995. Veterinary Epidemiology (2 ed.). Blakewell Science.

Todd, K. S., Jr, Levine, N. D., & Boatman, P. A., 1976a. Effect of desication on the survival of infective *Haemonchus contortus* larvae under laboratory conditions. *J. Parasitol.* 62, 247-249.

Todd, K. S., Jr, Levine, N. D., & Boatman, P. A., 1976b. Effect of temperature on survival of free-living stages of *Haemonchus contortus*. *Am. J. Vet. Res.* 37, 991-992.

Urquhart, G. M. 1996. Veterinary Parasitology (2nd ed.). Blackwell Science.

Van den Brom, R., Moll, L., Kappert, C., & Vellema, P., 2015. *Haemonchus contortus* resistance to monepantel in sheep. *Vet. Parasitol.*

van Houtert, M. F., J,, Barger, I. A., Steel, J. W., Windon, R. G., & Emery, D. L., 1995. Effects of dietary protein intake on responses of young sheep to infection with *Trichostrongylus colubriformis*. *Vet. Parasitol.* 56, 163-180.

van Houtert, M. F., J,, & Sykes, A. R., 1996. Implications of nutrition for the ability of ruminants to withstand gastrointestinal nematode infections. *Int. J. Parasitol.* 26, 1151-1167.

van Wyk, J. A., 2001. Refugia - overlooked as perhaps the most potent factor concerning the development of anthelmintic resistance. *Onderstepoort J. Vet. Res.* 68, 55-67 (pages 64-67 missing from photocopy).

van Wyk, J. A., & Bath, G. F., 2002. The FAMACHA system for managing haemonchosis in sheep and goats by clinically identifying individual animals for treatment. *Vet. Res.* 33, 509-529.

van Wyk, J. A., Cabaret, J., & Michael, L. M., 2004. Morphological identification of nematode larvae of small ruminants and cattle simplified. *Vet. Parasitol.* 119, 277-306.

Vaughan, A. L., Greer, A. W., McAnulty, R. W., & Sykes, A. R. 2006. Plasma protein loss in lambs during a mixed infection of *Trichostrongylus colubriformis* and *Teladorsagia circumcincta* - a consequence of the immune response? (Vol. 66). New Zealand Society of Animal Production.

Vlassoff, A., Leathwick, D. M., & Heath, A. C. G., 2001. The epidemiology of nematode infections of sheep. *N. Z. Vet. J.* 49, 213-221.

Wagland, B. M., Steel, J. W., Windon, R. G., & Dineen, J. K., 1984. The response of lambs to vaccination and challenge with *Trichostrongylus colubriformis*: effect of plane of nutrition on, and the inter-relationship between, immunological responsiveness and resistance. *Int. J. Parasitol.* 14, 39-44.

Walkden-Brown, S. W., & Kahn, L. P., 2002. Nutritional modulation of resistance and resilience to gastro-intestinal nematode infection - A Review. *Asian-Australian Journal of Animal Science*. 15, 912-924.

Walkden-Brown, S. W., Kahn, L. P., Larsen, J. W., Woodgate, R. G., Knights, G. I., de Fegely, C. R., & Williams, S. H. (2004). *Integrated parasite management in sheep (IPMs) - A national AWI project.* Proceedings of the Australian Sheep Veterinary Society, Canberra.

Wallace, D. S., Bairden, K., Duncan, J. L., Eckersall, P. D., Fishwick, G., Gill, M., Holmes, P. H., McKellar, Q. A., Murray, M., Parkins, J. J., & Stear, M. J., 1998. The influence of dietary supplementation with urea on resilience and resistance to infection with *Haemonchus contortus*. *Parasitology*. 116, 67-72.

Wallace, D. S., Bairden, K., Duncan, J. L., & Fishwick, G., 1996. Influence of soyabean meal supplementation on the resistance of Scottish blackface lambs to haemonchosis. *Res. Vet. Sci.* 60, 138-143.

Wallace, D. S., Bairden, K., Duncan, J.L., Fishwick, G., Holmes, P.H., McKellar, Q.A., Murray, M., Parkins, J.J., Stear, M.J., 1995. Influence of supplementation with dietary soyabean meal on resistance to haemonchosis in Hampshire down lambs. *Res. Vet. Sci.* Vol: 58, 232-237.

Wallace, L. R., 1948. Growth of lambs before and after birth in relation to the level of nutrition. *J. Agri. Sci.* 38, 93-153.

Waller, P. J., 1994. The development of anthelmintic resistance in ruminant livestock. *Acta Trop.* 56, 233-243.

Waller, P. J., 1997. Sustainable helminth control of ruminants in developing countries. *Vet. Parasitol.* 71, 195-207.

Waller, P. J., 1999. International approaches to the concept of integrated control to nematode parasites of livestock. *Int. J. Parasitol.* 29, 155-164.

Waller, P. J., 2006. From discovery to development: current industry perspectives for the development of novel methods of helminth control in livestock. *Vet. Parasitol.* 139, 1-14.

Waller, P. J., Rudby-Martin, L., Ljungstrˆm, B. L., & Rydzik, A., 2004. The epidemiology of abomasal nematodes of sheep in Sweden, with particular reference to over-winter survival strategies. *Vet. Parasitol.* 122, 207-220.

Watson, D. L., & Gill, H. S., 1991. Effect of weaning on antibody responses and nematode parasitism in merino lambs. *Res. Vet. Sci.* 51, 128-132.

Watson, T. G., & Baker, R. L., 1986. Genetic variation in resistance or tolerance to internal nematode parasites in strains of sheep at Rotomahana. *Proceedings of the New Zealand Society of Animal Production*. 46, 23-26.

West, D. M., Pomroy, W. E., Kenyon, P. R., Morris, S. T., Smith, S. L., & Burnham, D. L., 2009. Estimating the cost of subclinical parasitism in grazing ewes. *Small Ruminant Research*. 86, 84-86.

Whitlock, H. V., 1948. Some modifications of the McMaster helminth egg-counting technique and apparatus. *J Sci Ind Res India*. 21, 177-180.

Williams, A. R., Karlsson, L. J. E., Palmer, D. G., Vercoe, P. E., Williams, I. H., Greeff, J. C., & Emery, D. L., 2010a. Relationships between faecal dry matter, worm burdens and inflammatory mediators and cells in parasite-resistant Merino rams. *Vet. Parasitol.* 171, 263-272.

Williams, A. R., Palmer, D. G., Williams, I. H., Vercoe, P. E., & Karlsson, L. J. E., 2010b. Faecal dry matter, inflammatory cells and antibodies in parasite-resistant sheep challenged with either *Trichostrongylus colubriformis* or *Teladorsagia circumcincta*. *Vet. Parasitol.* 170, 230-237.

Williamson, J. F., Blair, H. T., Garrick, D. J., Pomroy, W. E., Douch, P. G. C., Green, R. S., & Simpson, H. V., 1995. Parasitism and production in fleece-weight-selected and control sheep. *New Zeal. J. Agr. Res.* 38, 381-388.

Windon, R. G. (1985). *Genetic aspects of resistance against infection of Trichostrongylus colubriformis in sheep.* (PhD), University of New South Wales, Sydney.

Windon, R. G., 1990. Selective breeding for the control of nematodiasis in sheep. *Revue Scientifique et Téchnique Office International des Epizooties*. 9, 555-576.

Windon, R. G., Chaplin, P. J., McWaters, P., Tavarnesi, M., Tzatzaris, M., Kimpton, W. G., Cahill, R. N. P., Beezum, L., Coulter, A., Drane, D., Sjolander, A., Pearse, M., Scheerlink, J.-P. Y., & Tennent, J. M., 2002. Local immune responses to influenza antigen are synergistically enhanced by the adjuvant ISCOMATRIX^R. *Vaccine*. 20, 490-497.

Wolstenholme, A. J., Fairweather, I., Prichard, R., von Samson-Himmelstjerna, G., & Sangster, N. C., 2004. Drug resistance in veterinary helminths. *Trends Parasitol*. 20, 469-476.

Wood, I. B., Amaral, N. K., Bairden, K., Duncan, J. L., Kassai, T., Malone, J. B., Pankavich, J. A., Reinecke, R. K., Slocombe, O., Taylor, S. M., & Vercruysse, J., 1995. World Association for the Advancement of Veterinary Parasitology (W.A.A.V.P.) second edition of guidelines for evaluating the efficacy of anthelmintics in ruminants (bovine, ovine, caprine). *Vet. Parasitol.* 58, 181-213.

Woolaston, R. R., & Baker, R. L., 1996. Prospects of breeding small ruminants for resistance to internal parasites. *Int. J. Parasitol.* 26, 845-855.

Woolaston, R. R., Barger, I.A. & Piper, L.R., 1990. Response to helminth infection of sheep selected for resistance to *Haemonchus contortus*. *Int. J. Parasitol.* 20, 1015-1018.

Woolaston, R. R., Windon, R. G., & Gray, G. D. (1991). Genetic variation in resistance to internal parasites in Armidale experimental flocks. In Gray, G. D. & Woolaston, R. R. (Eds.), Breeding for disease resistance in sheep (pp. 1-9). Melbourne: Wool Research & Development Corporation.

Woolaston, R. R. E., S.J., 1995. Australian research on genetic resistance to nematode parasites. *In: Breeding for resistance to infectious diseases in small ruminants ACAIR, Canberra, Australia. Ed. Gray, G.D., Woolaston, R.R. & Eaton, B.T.*, 53-75.

Yacob, H., Mistre, C., Adem, A., & Basu, A., 2009. Parasitological and clinical responses of lambs experimentally infected with *Haemonchus contortus* (L3) with and without ivermectin treatment. *Vet. Parasitol.*

Yu, F., Bruce, L. A., Calder, A. G., Milne, E., Coop, R. L., Jackson, F., Horgan, G. W., & MacRae, J. C., 2000. Subclinical infection with the nematode *Trichostrongylus colubriformis* increases gastrointestinal tract leucine metabolism and reduces availability of leucine for other tissues. *J. Anim. Sci.* 78, 380-390.

Zajac, A. M., Krakowka, S., Herd, R,P. & McClure, K.E., 1990. Experimental *Haemonchus contortus* infection in three breeds of sheep. *Vet. Parasitol.* 36, 221-235.

Zeng, S., Brown, S., Przemeck, S. M. C., & Simpson, H. V., 2003. Milk and milk components reduce the motility of *Ostertagia circumcincta* larvae in vitro. *N. Z. Vet. J.* 51, 174-178.

Zeng, S., Lawton, D. E. B., Przemeck, S. M. C., Simcock, D. C., & Simpson, H. V., 2001. Reduced *Ostertagia circumcincta* burdens in milk-fed lambs. *N. Z. Vet. J.* 9, 2-7.