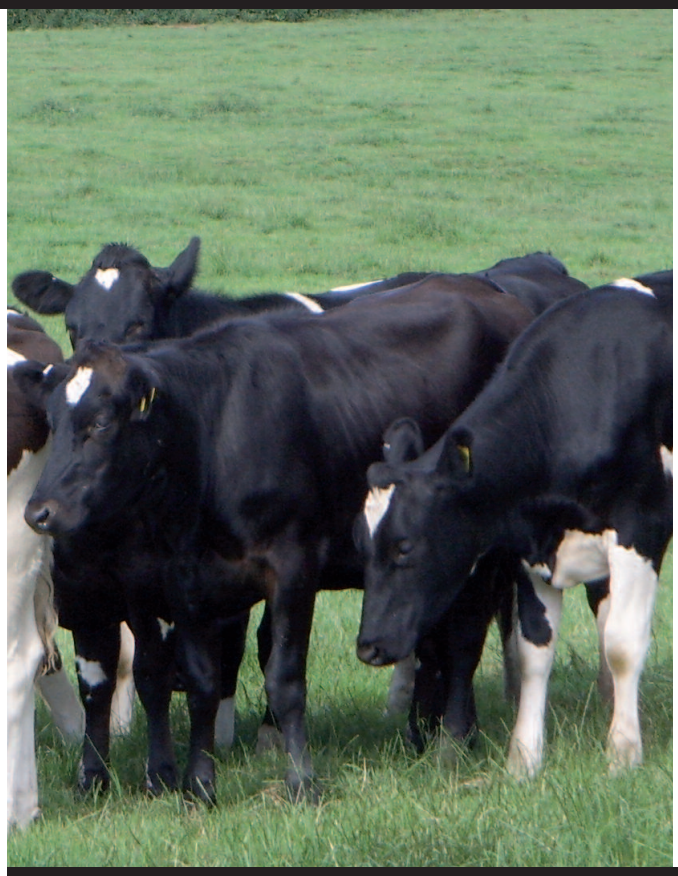
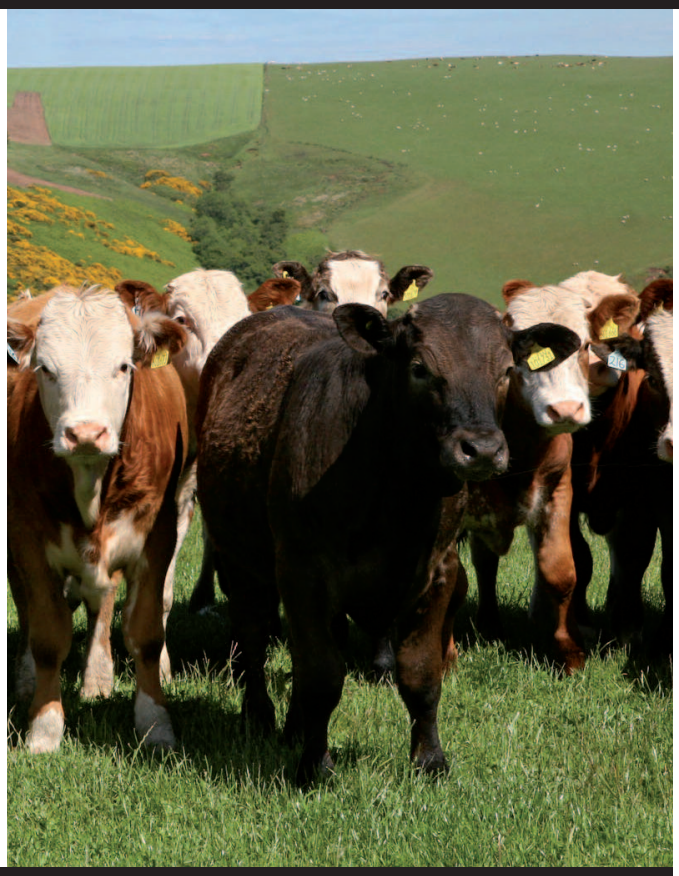
COWS

Control Of Worms Sustainably





SUSTAINABLE WORM CONTROL STRATEGIES FOR CATTLE

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A Technical Manual for Veterinary Surgeons and Advisors

EBLEX

DairyCo

Supporting organisations

Foreword

It has been perceived wisdom that helminth infections can be quite easily treated and controlled by the use of one of the many anthelmintics that are available. However, over-use or inappropriate wormer usage in other species, especially sheep and horses, has resulted in increasing levels of anthelmintic resistance in their endoparasites. Whilst there is some evidence of emerging resistance in roundworms of cattle, it appears to still be at a very low level. However the potential presence of such anthelmintic resistance in helminths is a timely warning. If it is not heeded it will result in some worms becoming very resistant to certain wormers, and with movements of animals onto other farms these can then become widespread amongst the helminth populations of cattle. This in turn will result in real problems with keeping cattle and allowing them to be economically reared. At a time of reducing resources it is important that all food animals are reared to their maximum potential in an economic and sustainable way.

It is thus opportune that EBLEX and DairyCo, both members of RUMA, have joined with it to help with the production of this manual. The acronym COWS (Control Of Worms Sustainably) has been devised to allow an easy way of identifying cattle worming programmes that will help to ensure more effective and efficient use of anthelmintics. While there is no need to panic, complacency cannot be an option.

Using this manual to make specific decisions between farmers and advisers on an individual farm basis will ensure that wormers are used effectively and responsibly. All anthelmintics should be integrated with grassland management systems, along with other management tools, to allow effective use and ensure they are cost effective. Using wormers just because animals at grass are "not doing well" or are "loose" are not options. Faecal samples should be taken to assist in determining anthelmintic usage. Each dose of anthelmintic must be justified and targeted for its known benefit to the cattle. There is no rocket science in what needs to be done. Just a little application, common sense and responsible action are all that is required.

Using just a little thought and converting this into action will ensure that we will be able to use anthelmintics with confidence for many years to come.

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List of Abbreviations

Abbreviation	
AR	Anthelmintic Resistance
ATP	Adenosine Triphosphate
BZ	Benzimidazole
EL4	Early Fourth Stage Larva
ELISA	Enzyme Linked Immunosorbant Assay
EU	European Union
FEC	Faecal Egg Count
FECRT	Faecal Egg Count Reduction Test
FERA	Food and Environment Research Agency
GB	Great Britain
GI	Gastro-intestine or gastrointestinal
L3	Third Stage Larva
L4	Fourth Stage Larva
LDT	Larval Development Test
LV	Levamisole
ML	Macrocyclic Lactone
NADH	Nicotinamide Adenine Dinucleotide Hydride
NADPH	Nicotinamide Adenine Dinucleotide Phosphate Hydride
OD	Optical Density
PB	Parasitic Bronchitis
PGE	Parasitic Gastroenteritis
PP	Patent Period
PPP	PrePatent Period
PRB	Pulse Release Bolus
SCOPS	Sustained Control of Parasites in Sheep
SRB	Sustained Release Bolus
TCB	Triclabendazole
TST	Targeted Selective Treatment
VLA	Veterinary Laboratories Agency
WT	Wormer Test
USA	United States of America
UK	United Kingdom

Sustainable worm control strategies for cattle

1. Introduction

Anthelmintics are widely used both in the treatment and prevention of parasitic helminth infections of cattle. For cattle there exists a range of application methods that include pour-ons and boluses, as well as more conventional injections and oral drenches. These products can be used in a number of highly successful control and treatment strategies. All of these strategies have proved successful over the last three decades, particularly since the launch of the macrocyclic lactones (ML) class of anthelmintics which now dominate the cattle 'wormer' market. Individual product activity and persistence against re-infection varies with the different compounds, and also with the formulation and method of application. Given this wide range of treatments and application methods there is always the potential for incorrect usage resulting in control failure, which may be perceived as anthelmintic resistance (AR). Reports of resistance to anthelmintics in cattle nematodes are relatively uncommon in comparison to reports of nematode resistance in sheep and goats worldwide. Similarly, whilst resistance to all three anthelmintic groups has been reported in sheep and goats in the UK, the situation in cattle appears less problematic. This may be a reflection of the relative frequencies of treatment or of the differences in parasite population dynamics between the different host species. Furthermore, prolonged survivability of susceptible worms in the larger bovine faecal pats may reduce anthelmintic selection pressure by maintaining a large '*in-refugia*' population.

Where AR has been suspected or reported, this has often involved an avermectin and the dose-limiting species *Cooperia oncophora*. In light of sporadic reports of AR in cattle nematodes, and in keeping with "The Need for Change" highlighted in the SCOPS Technical Manual for sheep, it seems appropriate to produce a similar technical manual for sustainable worm control strategies in cattle, based around the same basic principles that are applicable to all grazing livestock.

1.1. The cattle industry

The GB cattle population is the third largest in the EU and the most recent statistics from June 2008 indicate that the national herd comprised 8.87 million animals on 77,774 premises (Cattle Book 2008, Defra).

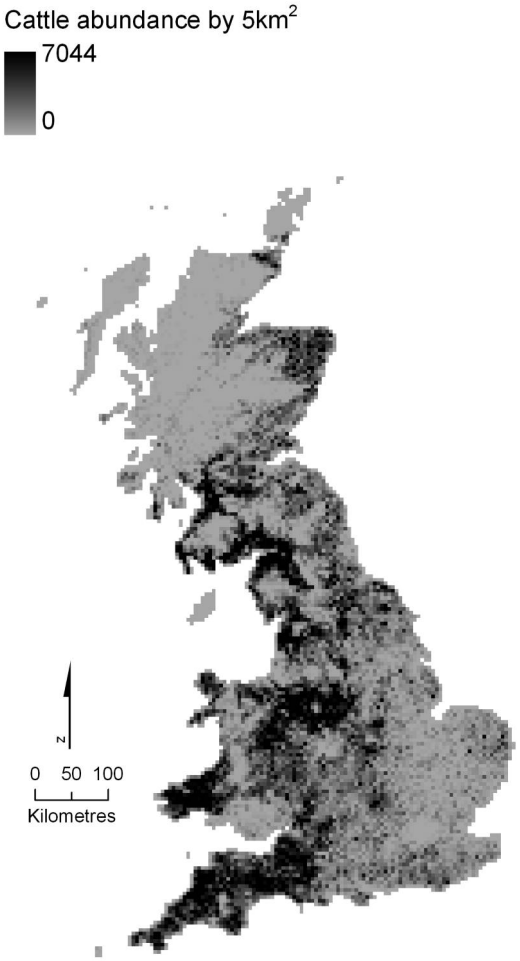
Dairy herds are concentrated in Central and SW England and SW Wales, with approximately 1.6 million adult cows, 762,500 followers (1st and 2nd year heifers) and 396,000 female calves.

Beef herds are mainly in SW England, East and West Wales and NE Scotland, with around 1.40 million cows, 1.25 million 1st and 2nd year heifers and 882,000 female calves. The numbers of male cattle primarily for beef production were 2.44 million.

The highest numbers of cattle were on specialist lowland dairy holdings (35%) and lowland grazing livestock holdings (23%). The majority of female dairy cattle were on specialist dairy holdings in the lowlands (73%) and uplands (14%).

Female beef cattle were more evenly spread among the farm types, with the most predominant numbers (36%) being on lowland grazing livestock holdings.

There has been a downward trend in both cattle numbers and cattle premises with a drop of 6% in cattle, and 11% in cattle premises during the 5 year period 2003-2008.



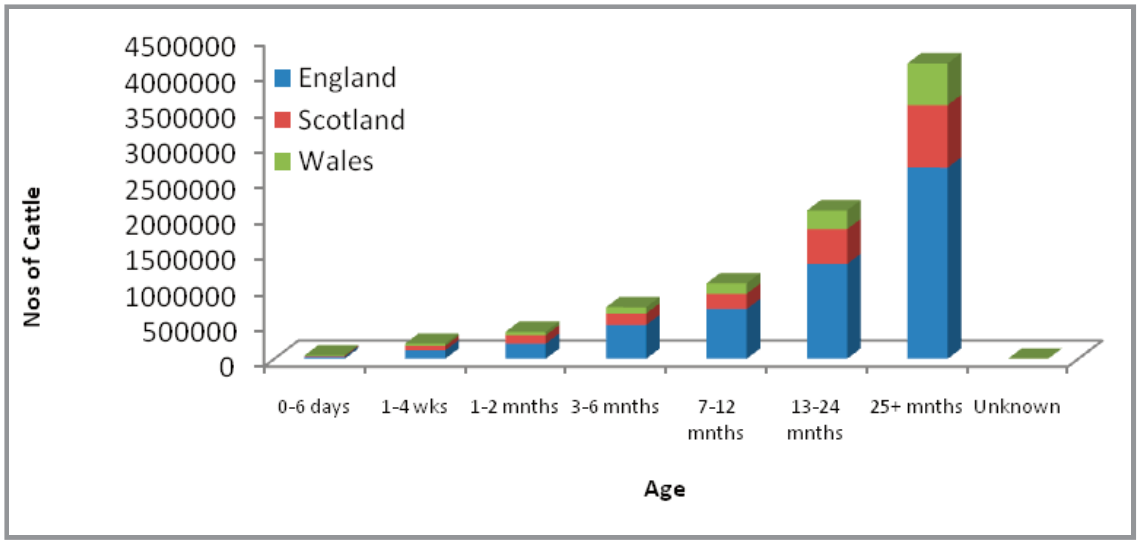


Figure 1.2. Numbers of Cattle by Age Group (2008)

For most age categories there were at least as twice as many beef cattle as dairy cattle. There were, however, similar numbers of adult beef and dairy cattle (25 months and over).

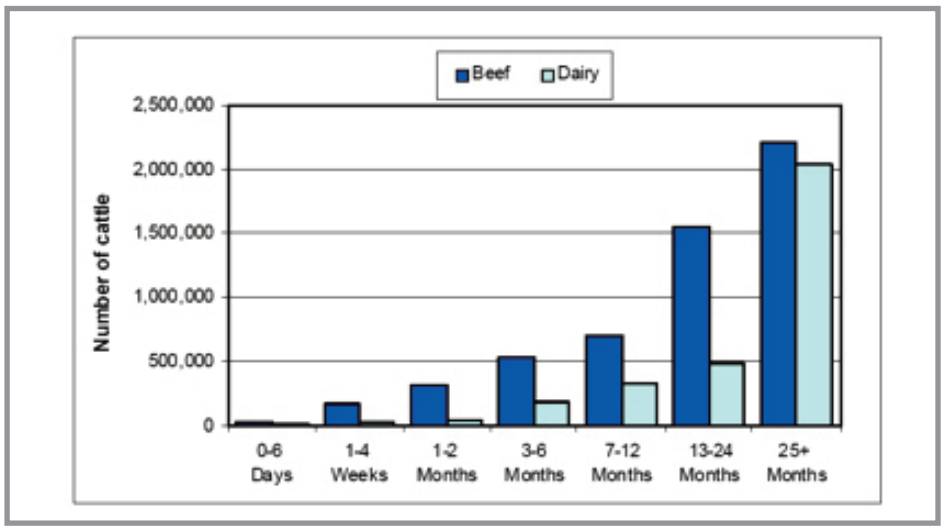
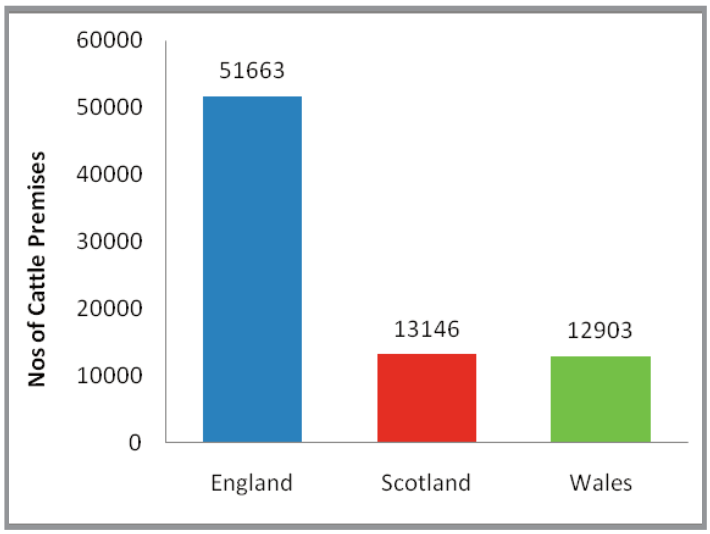


Figure 1.3. Numbers of Beef and Dairy Cattle by Age Group (2008)



The areas of greatest density of premises were in the west and SW England and Wales, with a small high-density area in NE Scotland. These broadly coincide with the areas of greatest cattle density

Figure 1.4. Numbers of GB Cattle Premises (2008)

About 48% of farms in GB have less than 50 cattle, with 3% of farms over 500 cattle. England has the largest number of cattle premises (66%), with Scotland (17%) and Wales (17%) having roughly the same numbers.

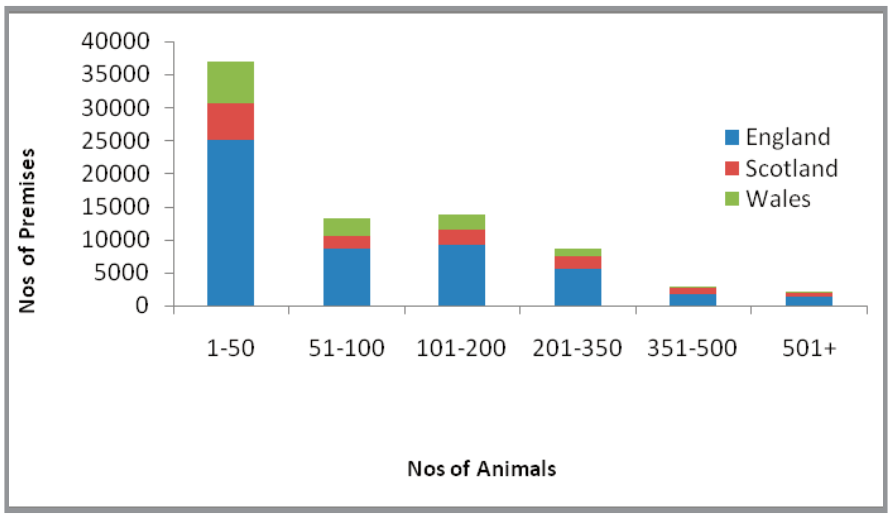


Figure 1.5. Numbers of GB Cattle Premises by Herd Size (2008)

Of the 8.7 million cattle in GB in 2008 there were a total of 4.0 million pure bred cattle and 4.7 million cross-bred cattle. Black & White cattle (Friesian, Holstein Friesian, British Friesian and Holstein breeds) and Limousin cattle accounted for over half of all cattle.

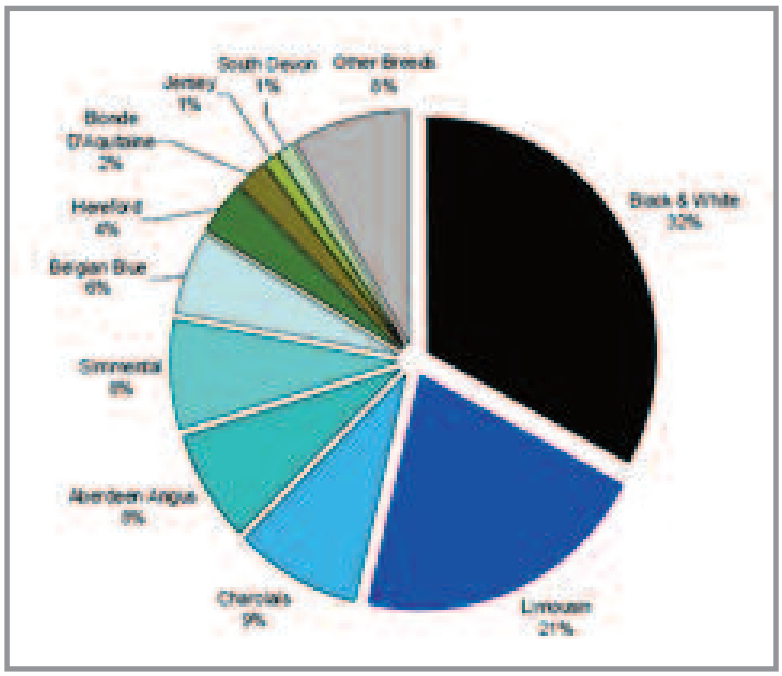


Figure 1.6. British Cattle Breeds

Beef births were higher in the period June 2007 to June 2008 compared with dairy births, reflecting a greater number of breeding beef cows and in-calf heifers, and peaked in spring (March to May) 2008. There was less seasonal variation in the births of dairy calves, though the number of births in late summer / early autumn was higher than in the rest of the year. This year-round calving pattern helps maintain milk production at a steadier rate than if all cows calved in spring.

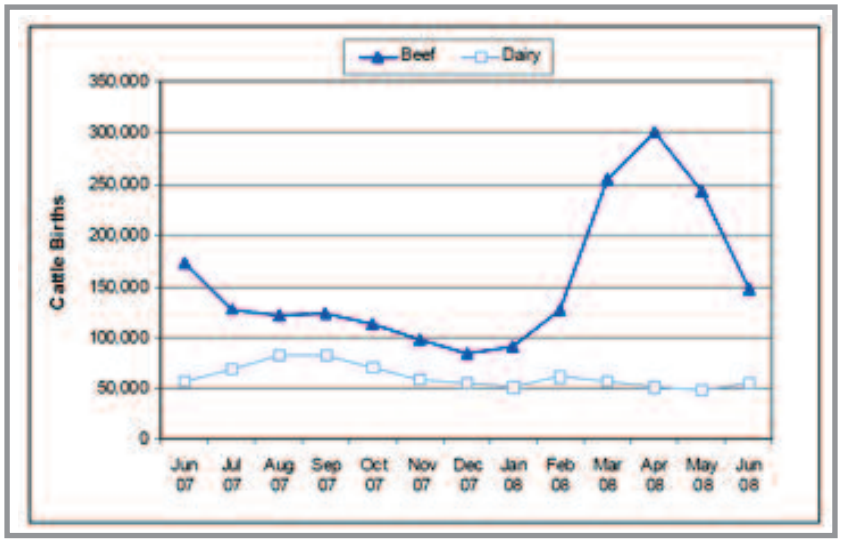


Figure 1.7. Cattle Births June 2007 to June 2008 (Cattle Book 2008)

1.2. The parasites

Unlike the situation with sheep, there have been few studies on the epidemiology of cattle endoparasites in recent years. Surveillance data from various sources indicates *Ostertagia ostertagi* to be the main parasite associated with disease. However, *Cooperia spp.* are very common in young cattle in their first grazing season and are the main contributor to faecal worm egg counts, particularly where treatment failures associated with macrocylic lactones are suspected. The lungworm, *Dictyocaulus viviparus*, has been increasingly reported in first-year grazing animals in summer or early autumn and, over the past few years, in older animals including adult cattle. Other parasites such as *Nematodirus helvetianus* and *Haemonchus contortus* are reported sporadically.

1.3. The anthelmintics

Strategies for the control of parasitic nematode infections of cattle have generally been targeted at first year grazing calves, although increasingly control measures are applied to both cattle in their second grazing season and adult cattle. This is especially the case where lungworm and fluke are also involved.

The general control principles employed are either to dose first year calves at the onset of disease (metaphylaxis), or to administer wormers preventatively in the early part of the grazing season (prophylaxis). These strategies are intended to limit pasture contamination and subsequent exposure to infective larvae later in the season. Increasingly, control measures are now also being applied to cattle in their second grazing season and even in high-performing adult cows.

One of the major constraints with strategic single-dose treatments are the labour costs involved in gathering and handling cattle. As a consequence there has been significant development of products with persistent action, particularly with the macrocyclic lactone (MLs) anthelmintics. The appearance of pour-on products for ease of use and convenience is now so widespread that pour-on ML products now dominate the cattle anthelmintic market. One of the other developments over the last few decades has been the introduction of controlled release devices (boluses) which deliver anthelmintic either continuously or at targeted times throughout the grazing season. This offers the possibility of a single dose treatment at turnout without re-course to further treatment if grazing is managed correctly.

2. The parasites

2.1. Nematode parasites of cattle in the UK

Cattle can be parasitised by over 18 species of gastrointestinal nematodes, and these infections are referred to hereafter as parasitic gastroenteritis (PGE), of which the most economically important species is *Ostertagia ostertagi. Cooperia oncophora,* a small intestinal species, is commonly found in young cattle in their first grazing season and is often the main contributor to parasite faecal egg counts. Other species of nematodes found in the gastrointestinal tract of cattle are generally of lesser importance.

The lungworm, *Dictyocaulus viviparus*, is another important pathogenic nematode in cattle. The liver fluke, *Fasciola hepatica,* and the rumen fluke *Paramphistomum spp* (both trematodes) are discussed in Section 7. The tapeworm, *Moniezia benedeni* is only briefly mentioned in this manual.

Table 2.1. Nematode parasites of cattle

Site	Species	Features	Pathogenicity (H/M/L)
Abomasum			
	Ostertagia ostertagi	Main cause of PGE	H
	Ostertagia leptospicularis	*Deer parasite. Pathogenesis* similar to *O. ostertagi*	M
	Haemonchus placei	*Sporadic. or H. contortus*	H
	Trichostrongylus axei	Heavy infections may produce clinical signs of PGE	M
Small intestine			
	Cooperia oncophora	Very common in young cattle in their first grazing season and main contributor to FEC	L
	Cooperia pectinata	Pathogenic but less common in UK cattle	M
	Cooperia punctata	'Bankrupt' worm. Pathogenic but less common in UK cattle	M
	Cooperia surnabada	Similar to *C. oncophora. Syn C. mcmasteri*	L
	Trichostrongylus colubriformis	Mainly sheep parasite. Pathogenicity low in cattle	L
	Trichostrongylus longispicularis	Uncommon in UK cattle	L
	Nematodirus helvetianus	Occasional and potentially pathogenic	M
	Bunostomum phlebotomum	Occasionally reported in UK. Can cause anaemia	M
	Strongyloides papillosus	Relatively common but only very young calves may rarely show signs of disease	L
	Toxocara vitulorum	Rare. Few recent reported cases in parts of GB. Possible zoonosis	L
	Capillaria bovis	Common but little significance	L
Large intestine			
	Oesophagostomum radiatum	Common but little significance	M
	Trichuris globulosa	Common but little significance	L
Lungs			
	Dictyocaulus viviparus	Highly pathogenic; increasingly reported and distributed	H

2.2. Life cycles of the gastrointestinal nematodes

The typical life cycle

The life cycles of the gastrointestinal nematodes (Fig. 2.1.) are all very similar, with one or two minor exceptions. The following description applies particularly to *Ostertagia*: Eggs are passed in the faeces and, under optimal conditions, develop within the faecal pat to the infective third stage within two weeks. When moist conditions prevail the L3 migrate from the faeces on to the herbage. After ingestion the L3 exsheaths in the rumen and further development then takes place in the lumen of an abomasal gland. Two parasitic moults occur before the L5 emerges from the gland around 18 days after infection, becoming sexually mature on the mucosal surface. The entire parasitic life cycle usually takes three weeks, but under certain circumstances many of the ingested L3 become arrested in development at the early fourth larval stage (EL4) for periods of up to six months (also referred to as hypobiosis).

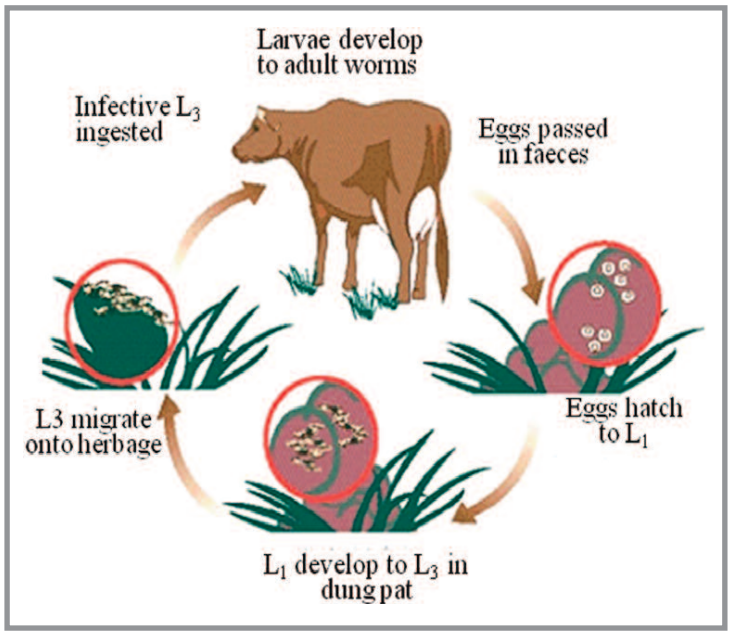


Figure 2.1. The basic life cycle of the nematode parasites of cattle

2.3. Important variations on the basic life cycle

2.3.1. *Toxocara vitulorum*

The most important source of infection is the milk of the dam, in which larvae are present for up to 3-4 weeks after parturition. There is no tissue migration in the calf following milk-borne infection and eggs may be present in the faeces 18-21 days post infection. The ingestion of larvated eggs by calves over six months old seldom results in patencyas the larvae migrate to various tissues where they remain dormant. In female animals, resumption of larval development in late pregnancy allows further trans-mammary transmission.

2.3.2. *Bunostomum phlebotomum*

Infection with the L3 may be percutaneous or oral. After skin penetration, the larvae travel to the lungs and moult to 4th stage larvae before re-entering the gastrointestinal tract after approximately 11 days. Ingested larvae usually develop without a migration. Further development continues in the gut.

2.3.3. *Capillaria bovis*

The infective L1 develops within the egg in about 3-4 weeks. Infection of the final host is through ingestion of this embryonated infective stage. Development to the adult stage occurs without a migration phase. The prepatent period (PPP) is 3–4 weeks.

2.3.4. *Nematodirus helvetianus*

Development to the L3 takes place within the eggshell. *N. helvetianus* does not have the same critical hatching requirements as *N. battus* in sheep and so the larvae often appear on the pasture within 2-3 weeks of the eggs being excreted in the faeces. More than one annual generation is therefore possible. The prepatent period is around 3 weeks.

2.3.5. *Strongyloides papillosus*

This parasite is unique among parasitic nematodes, having both parasitic and free-living life cycles. The parasitic phase is composed entirely of female worms in the small intestine that produce larvated eggs by parthenogenesis. After hatching on pasture, larvae may develop through to free-living male and female worms, but under certain circumstances (possibly related to moisture and temperature) the L3 can become parasitic, infecting the host by skin penetration or ingestion. The L3 then migrate via the blood, through the lungs and trachea, to develop into adult female worms in the small intestine. Calves may become infected soon after birth via somatic larvae excreted in the milk.

2.3.6. *Dictyocaulus viviparus (Parasitic bronchitis)*

The adult female worms in the lungs are ovo-viviparous, producing eggs containing fully developed larvae that hatch almost immediately. The L1 migrate up the trachea, are swallowed, and pass out in the faeces. The larvae are unique in that they are present in fresh faeces, are characteristically sluggish, and their intestinal cells are filled with dark brown food granules. In consequence the pre-parasitic stages do not need to feed. Under optimal conditions the L3 stage is reached within five days, but usually takes longer in the field. The L3 leave the faecal pat to reach the herbage either through their own movements or by windborne spread utilising the *Pilobolus fungus*, which grows on faecal pats.

After ingestion the L3 penetrate the intestinal mucosa and pass to the mesenteric lymph nodes where they moult. The L4 then travel via the lymph and blood to the lungs and break out of the capillaries into the alveoli about one week after infection. The final moult occurs in the bronchioles a few days later and the young adults then move up the bronchi and mature.

2.4. *Epidemiology of parasitic gastroenteritis*

This description applies primarily to infections with *O. ostertagi,* but is similar for other cattle nematode species. A considerable number of L3 can survive the winter on pasture and in soil. Sometimes the numbers are sufficient to precipitate disease in weaned calves 3–4 weeks after they are turned out to graze in the spring (Type I disease). However, this is unusual and the role of the surviving L3 is rather to infect calves at a level, which produces patent sub-clinical infection and ensures contamination of the pasture for the rest of the grazing season.

A high mortality of overwintered L3 on the pasture occurs in spring and only negligible numbers can usually be detected by June. This mortality combined with the dilution effect of the rapidly growing herbage renders most pastures not grazed in the spring safe for grazing after mid-summer. However, some L3 may survive in the soil for at least another year and can subsequently migrate onto the herbage.

Eggs deposited in the spring develop slowly to L3; this rate of development becomes more rapid towards mid-summer as temperatures increase and, as a result, the majority of eggs deposited during April to June all reach the infective stage from around mid-July onwards. If sufficient numbers of these L3 are ingested then Type I disease occurs at any time from July until October. Development from egg to L3 slows during the autumn.

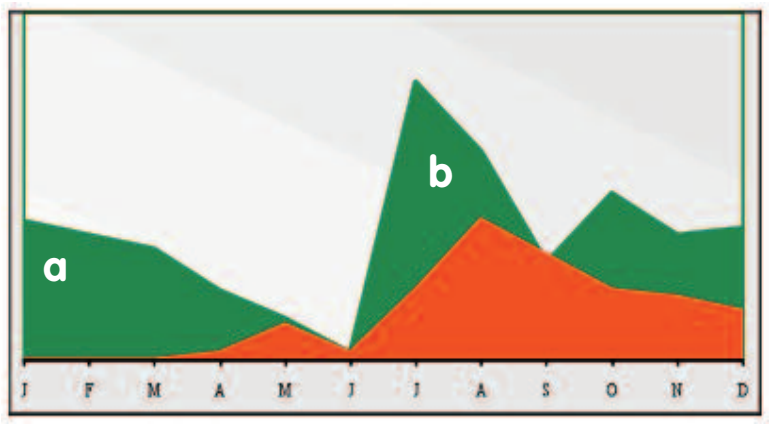


Figure 2.2. The epidemiology of nematode parasitism in calves at pasture

Calves turned out onto pasture carrying overwintering infective larvae (green [a]) contaminate the pasture with parasite eggs (red). Eggs undergo development, leading to the build up of infective larvae from mid-summer onwards (green [b])

As autumn progresses and temperatures decline, an increasing proportion (up to 80%) of the L3 ingested become inhibited at the early fourth larval stage (EL4). In late autumn calves can therefore harbour many thousands of these EL4 but few developing forms or adults. These infections are generally asymptomatic until maturation of the EL4 takes place during winter and early spring when Type II disease may materialize. Where maturation is not synchronous, clinical signs may not occur but the adult worm burdens which develop can play a significant epidemiological role by contributing to pasture contamination in the spring.

Two factors, one management and one climatic, appear to increase the prevalence of Type II ostertagiosis in dairy calves.

- Firstly, the practice of grazing calves from May until late July on permanent pasture, then moving them to hay or silage aftermath for two to three months before returning them to the original grazing in late autumn. The permanent pasture will still contain many L3 and when ingested they will become arrested.

- Secondly, in dry summers the L3 are retained within the crusted faecal pat and cannot migrate onto the pasture until sufficient rainfall occurs. If rainfall is delayed until late autumn many of the larvae liberated onto pasture will become arrested following ingestion and so increase the chance of Type II disease.

Although primarily a disease of young dairy cattle, ostertagiosis can nevertheless affect groups of older cattle in the herd, particularly if these have had little previous exposure to the parasite. Acquired immunity is slow to develop and calves do not achieve a significant level of immunity until the end of their first grazing season. Housing over the winter allows the immunity to wane by the following spring and yearlings turned out at that time are partially susceptible to re-infection, subsequently contaminating the pasture with small numbers of eggs. However, immunity is rapidly re-established and any clinical signs which occur are usually of a transient nature. By the second and third year of grazing, adult stock in endemic areas are usually highly immune to re-infection and of little significance in the epidemiology of the disease. However, around the periparturient period when immunity wanes there are reports of clinical disease following calving, particularly in heifers. Burdens of adult *Ostertagia spp.* in dairy cows are usually low and routine treatment of herds at calving should not be required.

Although the basic epidemiology in beef herds is similar to dairy herds, the influence of immune adult animals grazing alongside susceptible calves has to be considered. In beef herds where calving takes place in the spring, ostertagiosis is uncommon since egg production by immune adults is low, and the spring mortality of the overwintered L3 occurs prior to the suckling calves ingesting significant quantities of grass. Consequently, only low numbers of L3 become available on the pasture later in the year. However, where calving takes place in the autumn or winter, ostertagiosis can be a problem in calves during the following grazing season once they are weaned, the epidemiology then being similar to that seen in dairy calves.

2.5. Epidemiology of parasitic bronchitis

Parasitic bronchitis (Husk, Hoose), caused by the lungworm *Dictyocaulus viviparus*, is seen mainly in young grazing animals in late summer or early autumn although over the past few years it has been increasingly reported in older animals including adult cattle. As with many other parasitic nematodes, infection is acquired by the ingestion of infective larvae from the pasture, however, the epidemiology is complex and the occurrence of the disease is often unpredictable.

Parasitic bronchitis is predominantly a problem in areas that have a mild climate, high rainfall and abundant permanent grass. Outbreaks of disease occur from June until November, but are most common from July until September. It is not clear why the disease is usually not apparent until calves turned out to graze in the spring have been at grass for 2–5 months. One explanation is that the initial infection, acquired from the ingestion of overwintered larvae, involves so few worms that neither clinical signs nor immunity are produced; however, sufficient numbers of larvae are then seeded on to the pasture so that by July the numbers of L3 are sufficient to produce clinical disease. Young calves added to such a grazing herd in July may therefore develop clinical disease within 2–3 weeks. An alternative explanation is that the L3 overwinter in the soil and possibly only migrate on to pasture at some point between June and October.

Although dairy or dairy-cross calves are most commonly affected, autumn-born single-suckled beef calves are just as susceptible when turned out to grass in early summer. Spring-born suckled beef calves grazed with their dams until housed or sold do not usually develop clinical signs, although coughing due to a mild infection is common. However, the typical disease may occur in weaned calves grazed until late autumn.

The dispersal of larvae from the faecal pat appears to be effected by a fungus rather than by simple migration, as the infective larvae are relatively inactive. This fungus, *Pilobolus*, is commonly found growing on the surface of bovine faecal pats about one week after deposition. The larvae of *D. viviparus* migrate in large numbers up the stalks of the fungi on to, and even inside, the sporangium or seed capsule. When the sporangium is discharged it is projected a distance of up to 3 metres in still air to land on the surrounding herbage. Another factor that plays a part in the epidemiology of parasitic bronchitis is the role of carrier animals, whereby small numbers of adult worms can persist in the bronchi, particularly in yearlings, until the next grazing season.

Parasitic bronchitis may be seen in adult cattle under two circumstances.

1. As a herd phenomenon, or in a particular age group within a herd, if animals have failed to acquire immunity through natural challenge in earlier years. Such animals may develop the disease if exposed to heavy larval challenge as might occur on pasture recently vacated by calves suffering from clinical husk.

2. Disease is occasionally seen where an individual adult is penned in a heavily contaminated calf paddock.

The disease is most commonly encountered in the patent phase although the other forms have been recognised. In addition to coughing and tachypnoea, a reduction in milk yield in cows is a common presenting sign. Normally the natural challenge of adult cattle, yearlings or calves which have acquired immunity to *D. viviparus*, whether by natural exposure or by vaccination, is not associated with clinical signs. Occasionally, however, clinical signs do occur to produce the 're-infection syndrome' which is usually mild, but sometimes severe. It arises when an immune animal is suddenly exposed to a massive larval challenge that reaches the lungs and migrates to the bronchioles where the larvae are killed by the immune response. It can be difficult to differentiate this syndrome from the early stages of a severe primary infection and the only course of action is treatment with anthelmintics and a change of pasture.

3. Disease caused by parasitic nematodes

3.1. *Ostertagia ostertagi*

Ostertagia ostertagi infections generally predominate in the second half of the grazing season. Immunity to disease takes longer to develop than to *Cooperia* (see 3.2.) and cattle are not normally considered to be immune until they have experienced two complete grazing seasons. The immunity is not sterile (does not remove infection totally) and adult cattle can frequently harbour high *O. ostertagi* burdens, which in some individuals may result in clinical disease.

Disease is usually seen in calves grazed intensively during their first grazing season, as the result of larvae ingested 3–4 weeks previously; in the northern hemisphere this normally occurs from mid-July onwards (Type I disease). With Type I infections, morbidity is usually high, often exceeding 75%, but mortality is rare provided treatment is instituted early.

Type II disease occurs in yearlings, usually in late winter or spring following their first grazing season, and results from the maturation of larvae ingested during the previous autumn that subsequently become arrested in their development at the EL4 stage. In Type II the prevalence of clinical disease is comparatively low and often only a proportion of animals in the group are affected; mortality in such animals can be high unless early treatment with an anthelmintic effective against both arrested and developing larval stages is instituted.

The main clinical sign in both Type I and Type II disease is profuse watery diarrhoea and in Type I, where calves are at grass, this is usually persistent and has a characteristic bright green colour. In contrast, in the majority of animals with Type II the diarrhoea is often intermittent and anorexia and thirst are usually present. Hypoalbuminaemia is marked, often leading to submandibular oedema. In both forms of the disease, the loss of body weight is considerable during the clinical phase and may reach 20% in 7–10 days.

3.2. *Cooperia spp.*

The main species found in Britain is *C. oncophora*, which is generally considered to be a mild pathogen in calves, although in some studies it has been associated with loss of appetite and poor weight gain. Occasionally a heavy infection can induce intermittent diarrhoea. *C. oncophora* is particularly common in young cattle during their first grazing season and is the main contributor to FECs. Cattle appear to mount a rapid immune response to this parasite and associated FECs tend to decline towards the end of the first grazing season and remain low in subsequent years.

Other species of *Cooperia (C. pectinata, C. punctata, C. surnabada)*, which are less commonly found in Britain, may cause catarrhal enteritis with loss of appetite, poor weight gain, diarrhoea and, in some cases, submandibular oedema.

3.3. *Trichostrongylus spp.*

In heavy abomasal infections of *T. axei* there may be weight loss and diarrhoea. At lower levels of infection inappetence and poor growth rates, sometimes accompanied by softening of the faeces, can occur. Intestinal species of *Trichostrongylus* found in cattle are rarely associated with clinical signs of disease.

3.4. *Nematodirus helvetianus*

N. helvetianus has been incriminated in outbreaks of bovine parasitic gastroenteritis but experimental attempts to reproduce the disease have been unsuccessful. Low to moderate infections may produce no obvious clinical manifestations, however in severe infections diarrhoea can occur during the pre-patent period and young animals may become dehydrated.

3.5. *Haemonchus spp.*

Haemonchosis caused by *H. placei* (or *H. contortus*) presents either as severe anaemia and weakness, or in more chronic infections as weight loss, weakness, lethargy and submandibular oedema.

3.6. *Strongyloides papillosus*

Generally considered to be non-pathogenic in cattle in the UK, despite numerous larvated eggs often being present in the faeces. In warmer climates, large numbers of infective larvae may accumulate in the environment and cause

problems in housed calves. Erythematous reactions may occur in the inter-digital cleft caused by the skin-penetrating L3. Passage of larvae in large numbers through the lungs may cause haemorrhage and large numbers of adult worms in the small intestine may cause catarrhal enteritis.

3.7. Lungworm *(Dictyocaulus viviparus)*

Lungworm infection is characterised by bronchitis and pneumonia and typically affects young cattle during their first grazing season on permanent or semi-permanent pastures.

Within any affected group differing degrees of clinical severity are usually apparent. Mildly affected animals cough intermittently, particularly when exercised, while moderately affected animals have frequent bouts of coughing at rest accompanied by tachypnoea and hyperpnoea. Severely affected animals frequently adopt the classic 'air-hunger' position of mouth breathing with the head and neck outstretched. Calves may show clinical signs during the pre-patent period and occasionally a massive infection can cause severe dyspnoea of sudden onset often followed by death in 24–48 hours.

Most animals gradually recover although complete return to normality may take weeks or months. However, a proportion of convalescing calves suddenly develop severe respiratory signs, which usually terminates fatally 1–4 days later (post-patent parasitic bronchitis).

3.8. Numbers of worms associated with disease

If gastrointestinal parasitism is suspected as the cause of an outbreak of disease in a herd, a post-mortem examination and worm count should be performed wherever possible. Inspection of the abomasal mucosa, for example, may reveal the typical "morocco leather" appearance of the hyperplastic gastric glands associated with *O. ostertagi* infections. It is not sufficient to attempt a visual estimation of the number of worms in the abomasum or small intestine because such estimations are difficult and ignore developing and arrested worm burdens. This is particularly important with inhibited and hypobioitic stages which may be present in the mucosa.
Worm estimations should be undertaken at a specialist parasitological laboratory using appropriate worm recovery and counting techniques. The numbers and species of worms present provide definitive evidence to support the diagnosis of parasitic gastroenteritis.

The following table is presented only as a guide to the interpretation of adult worm burdens in cattle. Worm numbers may vary greatly between individuals. Numbers of developing, or inhibited larvae are generally much higher (where undertaken).

	Estimated worm numbers		
Worm Species	**Light**	**Moderate**	**Heavy**
Total Abomasum	<1000	5000	10,000+
Ostertagia ostertagi	<1000	1000-2000	2,000+
Trichostrongylus axei	1-10,000	10,000-30,000	30,000+
Haemonchus placei	1-500	500-1000	5000+
Total Small Intestine	<5000	15,000	30,000+
Trichostrongylus spp	<5000	5,000-20,000	20,000+
Cooperia spp.	1-5000	5,000-10,000	10,000+
Bunostomum phlebotomum	1-50	50-200	200+
Total Large Intestine	Rarely estimated		
Oesophagostomum radiatum	1-100	100-1000	1000+

3.9. Immunity (acquired resistance) to gastrointestinal nematodes

Following repeated exposure, cattle generate an acquired immunity to gastrointestinal nematodes. Cattle exposed to *C. oncophora* infections appear to mount a rapid immune response to this parasite after about 8-12 months of exposure. Immunity to *O. ostertagi* is slower to develop and cattle are not normally considered to be immune until they have been exposed to infective larvae over two grazing seasons. The response is to some extent genetically controlled and individual animals vary in their ability to mount an immune response. Using FEC as an indicator, it has been shown that about 25% of calves have an innate resistance to worm infections, 50% generate an acquired immunity during their first grazing season, whilst 25% have an inadequate response, fail to show a reduction in FEC and may still carry relatively high worm burdens at the end of the first grazing season.

3.10. Development of immunity to lungworm

Calves exposed to *Dictyocaulus viviparus* quite rapidly acquire patent infections, readily recognisable by the clinical signs. After a period of a few weeks, immunity develops and the adult worm burdens are expelled. On subsequent exposure in succeeding years such animals are highly resistant to challenge, although if this is heavy then clinical signs associated with the re-infection syndrome may be seen. However, this is an acquired immunity that is dependent on sufficient exposure to the parasites, and at this age is not as strong and effective as in adult animals.

3.11. Resistance and resilience

Parasites typically have an aggregated distribution within their hosts- a small percentage of animals (~20%) carry the bulk of the parasite population and the remainder (~80%) carry small burdens. This pattern may in part be due to genetically determined differences in host susceptibility. The relationship between parasite burdens and performance can vary and leads to the concepts of "resistance" and "resilience". Resistance describes individuals that carry lower burdens of parasites whilst resilience indicates individuals that may still carry higher parasite burdens but whose performance is largely unaffected by their presence. As a general rule, resistant animals can alter parasite epidemiology by reducing contamination, transmission and exposure within a system. Resilience would not be expected to alter parasite abundance in the same way or to the same extent.

There have been a number of attempts to select for animals that possess innately greater resistance to parasites using indicator markers such as FECs, but it may be possible to identify markers in the host genome that could markedly increase the accuracy and speed of selection. Some early attempts in sheep, with selection based on FECs were less successful because various performance parameters suffered. However this can be overcome by co-selecting for traits such as growth rate as well as low FECs. There are now a number of sheep flocks that have been selected in this way but such studies have yet to be conducted in cattle.

3.12. Immunity and nutrition

Parasitism typically has adverse effects on the host's nutritional status and productivity. Studies have shown that protein supplementation can reduce FECs and worm burdens in growing animals by improving host immunity, thereby compensating for some of the negative effects of gastrointestinal parasitism.

4. Anthelmintics used against gastrointestinal nematodes

A wide range of cattle worming products are available in the UK. Most "wormers" are marketed for the control of PGE and are used for both treatment and prevention.

4.1. Broad-spectrum anthelmintics

The broad-spectrum anthelmintics can be divided into three groups on the basis of chemical structure and mode of action (Table 4.1.). These groups are:

- **Group 1 - BZ, Benzimidazoles (BZ) ('white' drenches)**

All products in this group are effective against nematodes and are ovicidal, although individual generic products may vary in efficacy against some nematode species. Most are efficacious against tapeworms. After administration the BZ passes into the rumen, which acts as a reservoir allowing gradual release into the bloodstream. BZs act by inhibiting tubulin activity in intestinal cells of nematodes or tegumental cells of cestodes, preventing uptake of glucose. The longer the time it stays in the animal the more effective it is. *There is one BZ anthelmintic (triclabendazole), which is narrow spectrum (liver fluke only) and differs from all the other BZs in many respects but is classed with them because of its chemical structure.*

- **Group 2 - LV, Levamisoles (LV) ('yellow' drenches)**

This group includes the imidazothiazoles (levamisole) and tetrahydropyrimidines (morantel and pyrantel). These drugs are rapidly absorbed and excreted, and most of the dose is lost from the system within 24 hours. Therefore, it is not essential to maintain high concentrations in cattle for protracted periods. LVs act on the nerve ganglion of the parasite causing paralysis. They are not ovicidal. The therapeutic safety index, compared to other anthelmintics, is low. Animals given levamisole may be hyperactive for a few minutes. Toxic signs, due to a stimulant effect on nerve ganglia, may manifest as salivation, bradycardia and muscular tremors, and in extreme cases death from respiratory failure. Injectable levamisole may cause inflammation at the site of injection. Morantel is no longer available for use in cattle in Britain.

- **Group 3 -ML, Macrocyclic lactones (ML) ('clear' drenches)**

The macrocyclic lactones include the avermectins (ivermectin/doramectin/eprinomectin) and the milbemycins (moxidectin). These compounds are highly lipophilic and following administration are stored in fat tissue from where they are slowly released. They act on glutamate-gated Cl- channels and -aminobutyric acid (GABA) neurotransmission sites in nematodes, blocking interneuronal stimulation of inhibitory motor neurones leading to a flaccid paralysis.

4.2. Narrow spectrum anthelmintics

The substituted phenol (nitroxynil) and the salicylanilides (oxyclozanide, closantel) are narrow spectrum anthelmintics. They are effective only against trematodes and some blood sucking nematodes (e.g *Haemonchus, Bunostomum*). They act by uncoupling oxidative phosphorylation at the mitochondrial level, reducing the availability of ATP, NADH and NADPH. In the host they bind to plasma protein, which increases the duration of activity against blood sucking parasites.

Clorsulon (a benzenesulphonamide) is active against immature liver flukes over eight weeks of age and adult liver fluke. It inhibits enzymes in the glycolytic pathway by blocking the oxidation of glucose to acetate and proprionate, leading to a gradual suppression of motility and paralysis.

The fasciolicides are discussed in greater detail in Section 7.

Table 4.1. Anthelmintic preparations for cattle

Compound	Spectrum of Activity	Activity against				Comments
		Ostertagia Cooperia Tricho'gylus	Lungworm	Tapeworm	Fluke*	
Group 1 BZ, Benzimidazoles ('white' drenches)						
Albendazole	Broad	+	+	+	+ >10wks	50% higher dose rate required for fluke
Fenbendazole	Broad	+	+	+	-	Some activity against tapeworm segments
Oxfendazole	Broad	+	+	+	-	
Triclabendazole	Narrow	-	-	-	+ >2days	
Group 2 – LV, Levamisole ('yellow' drenches)						
Levamisole	Broad	+	+	-	-	Injectable and oral formulations. Incomplete activity against inhibited L_4
Group 3 - ML, Macrocyclic Lactones ('clear' drenches)						
Ivermectin	Broad	+	+	-	-	Endectocidal activity. Injectable and Pour-on
Doramectin	Broad	+	+	-	-	Endectocidal activity. Injectable and Pour-on
Eprinomectin	Broad	+	+	-	-	Endectocidal activity. Pour-on only
Moxidectin	Broad	+	+	-	-	Endectocidal activity. Injectable and Pour-on
Flukicides						
Nitroxynil	Narrow	-	-	-	+ >7wks	Injectable only
Oxyclozanide	Narrow	-	-	-	+>10 wks	Oral only in combination with levamisole
Closantel	Narrow	-	-	-	+>6wks	Pour-on only in combination with ivermectin
Clorsulon	Narrow	-	-	-	+>8 wks	Injectable only in combination with ivermectin

* Age of fluke killed, also refer to Table 7.2

4.3. Activity against hypobiotic larvae

For treatment of type II ostertagiosis, or for treating animals at housing, it is advisable to use a product with high activity against hypobiotic (arrested) fourth-stage larvae. Use of an anthelmintic that lacks such efficacy may necessitate repeated treatment as it will only remove adult worms and developing larvae, leaving hypobiotic larvae to resume development and cause damage to the abomasal wall. There is some variability in efficacy between products and evidence suggests that at recommended dose rates, the Group1-BZ (albendazole, fenbendazole, oxfendazole) and Group3-ML anthelmintics (doramectin, eprinomectin, ivermectin and moxidectin) are more active against arrested fourth-stage larvae than products containing levamisole (Group2-LV).

4.4. Injectable and pour-on formulations of MLs

Doramectin, ivermectin and moxidectin are available in injectable and pour-on formulations, while eprinomectin is only available as a pour-on product. All have variable persistent anthelmintic activity against abomasal nematodes, some intestinal nematode species, lungworms and some ectoparasites. Their persistent activity means that they can be used at extended treatment intervals in strategic dosing strategies. The recommendation for ivermectin products is a 3-8-13 week early season dosing strategy and a 0-8 strategy is recommended for doramectin products. A long acting injectable preparation of moxidectin has persistent activity of between 90 and 150 days for various parasite species. The persistent activities of the various generic ML compounds, based on methods of administration, are summarised in Table 4.2. on the previous page.

4.5. Boluses

Bolus devices are a popular labour-saving means of administering wormers to cattle. Only two shapes and designs now remain, each being administered by use of specially designed dosing guns. Care is required when administering boluses and it is important to ensure that the bolus is administered correctly and has been swallowed.

Boluses fall into two categories either sustained-release (SRB) where anthelmintic is released constantly over a period of time, or pulse-release (PRB) where the drug is released at intervals. Boluses are normally administered at the start of the grazing season, although some can be given later in the season. The only SRB bolus now on the market is the Panacur SR Bolus™, which is a cylindrical bolus consisting of 10 flat-faced tablets in two magnesium alloy tubes joined and enclosed by alloy rings. The bolus is designed to release fenbendazole by galvanic erosion over a period of 140 days and can be administered to first year animals either at turnout, or later in the grazing season.

The PRB bolus (Autoworm™) consists of either five or seven annular tablets of oxfendazole, mounted on a central metal core with a weighted end, which retains the bolus in the rumen/reticulum. Drug release is determined by the corrosion rate of the central core. The first dose of oxfendazole is released approximately three weeks after administration with the remaining doses released at regular intervals thereafter (approximately 21 days) giving the boluses active lives of 15-21 weeks depending on the release profile. The boluses are designed primarily for first year grazing animals at turnout but can be given for cattle already at grass or for use in the second grazing season.

4.6. Activity against parasitic bronchitis *(Dictyocaulus)*

All available anthelmintics are all highly effective against developing fourth-stage larvae and adult *Dictyocaulus viviparus.*

Some degree of control of parasitic bronchitis in calves can be achieved by early season suppression of pasture contamination in much the same way as for the control of gastrointestinal nematodes. Periods of persistent activity of the ML compounds against *D. viviparus* are given in Table 4.2. However, the epidemiology of lungworm infection is complex and still not fully understood, and vaccination of calves with an irradiated larval vaccine (Huskvac™) is the most reliable form of prevention in endemic or high-risk areas of the country. For spring calving and all-year-round calving herds there may be practicality issues for use.

4.7. Activity against cestodes (Tapeworms)

Adult stages of tapeworms affecting cattle (*Moniezia*) are usually of little consequence. Several of the benzimidazoles used in the treatment of nematodes are also effective against cestodes. Some flukicidal drugs also have cestocidal activity (See Table 7.2.). Larval stages of cestodes affecting cattle, most notably the metacestode stage of the human tapeworm *Taenia saginata (Cysticercus bovis)*, are generally refractory (not readily responsive) to treatment with anthelmintics. The BZs have some activity against *Moniezia* infections in cattle. None of the other anthelmintics available for cattle have activity against tapeworms.

Table 4.2. Persistence of ML products against endoparasites and ectoparasites in cattle (days) (Datasheet Data)

		Stomach Worms			Small Intestine Worms		Large Intestine Worms		Lungworm	Mites	Lice			Flies
											Chewing	Sucking		
Active	**Route**	*O. ostertagi*	*T. axei*	*H. placei*	*Cooperia spp*	*N. helve*	*Oes*	*Bun*	*D. vivparus*	*P. bovis*	*B. povis*	*Linog-nathus*	*Selenop otes*	*H. irritans*
Doramectin	Injection	35	28	28	21	-	21	22	35	42	-	28	-	-
	Pour-on	35	28	-	28	-	21	-	42	-	-	49	35	<42
Eprinomectin	Pour-on	<28	<21	<14	<28	<14	<28	-	<28	-	-	-	-	-
Ivermectin	Injection	<21	<14	<14	<14	-	<21	-	<28	-	-	-	-	-
	Pour-on	<21	<14	<14	<14	-	<21	-	<28	-	-	-	-	<35
Moxidectin	Injection 1%	35	-	-	-	-	-	-	42	-	-	-	-	-
	Injection 10%	120	90	90	-	-	-	-	120	-	-	-	133	-
	Pour-on	35	-	-	-	-	-	-	42	-	-	-	-	-

- = no information

< = activity up to

4.8. Activity against ectoparasites

It is not the intention of this technical manual to cover ectoparasitic infections of cattle in any detail, however it is important to bear in mind that ML products also have some activity against a number of cattle ectoparasites.

Activity of ML compounds is variable between individual products and is dependent on the active molecule, the product formulation and the method of application. Periods of persistence against ectoparasites are summarised in Table 4.2. In general, pour-on products are more effective against sucking lice (*Lignonathus, Haematopinus*) and to some extent chewing lice (*Bovicola*) as well as headfly (*Haematobia*) infestations on cattle when compared with equivalent compounds administered by injection. The MLs are also extremely effective against warble fly larvae (*Hypoderma spp*) present in the oesophagus (*H. lineatum*) or epidural fat (*H. bovis*) during their resting phases over the winter months, and third stage larvae present in their subcutaneous site in the spring.

5. Anthelmintic resistance (AR)

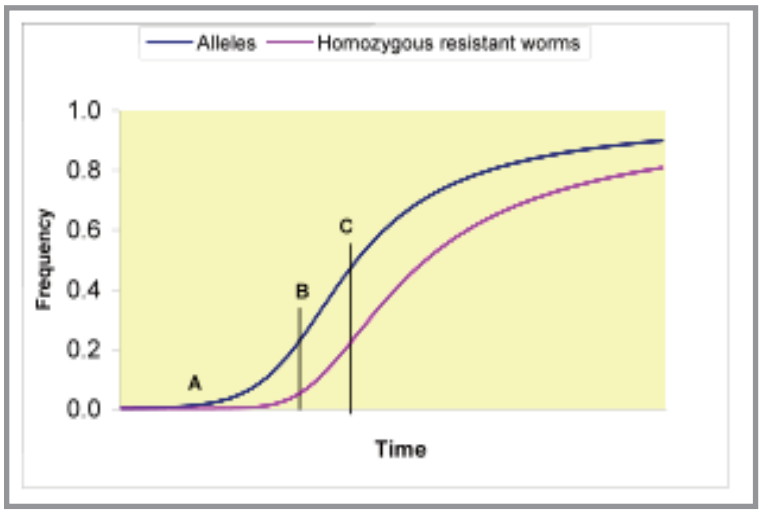
5.1. What is resistance

Resistance is the heritable ability of a parasite to tolerate a normally effective dose of an anthelmintic. The parasite is considered resistant if it survives exposure to the standard recommended dose of the anthelmintic and the ability to survive is passed on to its offspring. Resistance can be viewed as drug tolerance, since 'resistant' parasites can often be removed by exposure to higher dose rates of anthelmintic up to the maximum dose tolerated by the host. Anthelmintic resistance in cattle can be measured in several ways. These include field tests, such as a simple Wormer Test (WT) as an indication of treatment efficacy, or the more often used Faecal Egg Count Reduction Test (FECRT). (Section 8. has details of these techniques). A fully effective anthelmintic is expected to reduce the FEC to zero after administration. If the reduction is 95% or less, then this is interpreted as the presence of resistance genotypes. (Point B in Fig. 5.1.)

Under field conditions however, anthelmintics may continue to give clinical responses in parasitised cattle when the reduction in faecal egg count (FEC) is < 95%. Consequently, farmers remain unaware that resistance to an anthelmintic is present until the reduction reaches approximately 80% or less (point C in Fig. 5.1.). Beyond this point there may be production losses from poor worm control and the severity of the resistance will increase rapidly if the anthelmintic remains in use.

This distinction between the detection of resistance using FECRTs, at the 95% level and farmers seeing apparent failure at approximately the 80% level is vital to the slowing of the development of anthelmintic resistance. By detecting resistance at an early stage, cattle farmers can employ the COWS recommendations to prolong the time taken for the worm population on their farm to move from point B to point C (Fig. 5.1.). This means the activity of the wormer group(s) concerned can be maintained for longer.

Figure 5.1. The rate at which AR appears in a herd



Point A, resistance alleles are at very low levels; B, resistance detectable in tests (95%); C, resistance apparent as a clinical problem (<80%)

5.2. Worldwide AR situation

Although widely reported in sheep, AR appears less of a problem in cattle. This may be a reflection of the relative frequency of treatment and the differences in parasite population dynamics between the two hosts. It may also reflect the prolonged survivability of free-living larval stages within the bovine faecal pat, thus ensuring a supply of susceptible worms.

BZ-resistance has been described in *Cooperia spp., Haemonchus spp., Ostertagia ostertagi* and *Trichostrongylus axei* in Australia, New Zealand, USA, South Africa and parts of Europe. Reports of ML-resistance in cattle nematodes have

been less common but have been described, mainly in *Cooperia oncophora,* but also *Haemonchus spp.*, *Trichostrongylus longispicularis* in several of these countries, and more recently in *O. ostertagi*, in the USA. There have been a small number of reports from the USA, New Zealand and South America of cattle nematodes resistant to multiple anthelmintics.

Most reports of ML resistance in cattle have been reported in *Cooperia* species following the identification of positive FEC or FECRT after use of pour-on treatments. Poor absorption of pour-on ML anthelmintics and subsequent reduced efficacy against *Cooperia* species, which are the dose-limiting species for the ML group (Vercruysse and Rew 2002), provides a more likely explanation for positive post-treatment FEC than acquired resistance (McKenna 1995). However, in the longer term, shedding of *Cooperia spp*. eggs during the prepatent period following treatment with topical ML anthelmintics has been shown experimentally to select for AR (Van Zeveren and others 2007) and may lead to increasing AR reports in these species.

5.3. The UK situation

Reports of AR in cattle nematodes in the UK are still rare. There has only been one published report of ML resistance in *Cooperia oncophora* in the SW England (Stafford and Coles 1999) plus one report of inefficacy with an ML pour-on in Highland cattle in Scotland (Sargison and others 2009). To what extent these, and other anecdotal reports, are attributable to true AR rather than treatment failure is not always clear. The presence of AR nematodes needs to be clearly differentiated from treatment failures, which may occur for a variety of reasons.

In a survey of parasite control methods on 72 beef farms in south-west England, topical treatment (predominantly using ML pour-ons) was shown to be the most common method of anthelmintic administration (Barton and others 2006), and this was also observed in a recent EBLEX-funded study conducted by FERA in conjunction with several pharmaceutical companies. Where apparent treatment failures occurred, these were predominantly following use of ML pour-on products, with *Cooperia spp*. most commonly found in post-treatment FEC.

5.4. Side resistance

Anthelmintics within the same class share the same mode of action. When resistance appears to one anthelmintic in a class, other anthelmintics in the same class will also be affected. Thus worms that are resistant to oxfendazole, for example, are also resistant to other BZ anthelmintics such as fenbendazole and albendazole. Worms that are resistant to ivermectin will also show side-resistance to doramectin, eprinomectin and moxidectin.

5.5. Resistance selection mechanisms

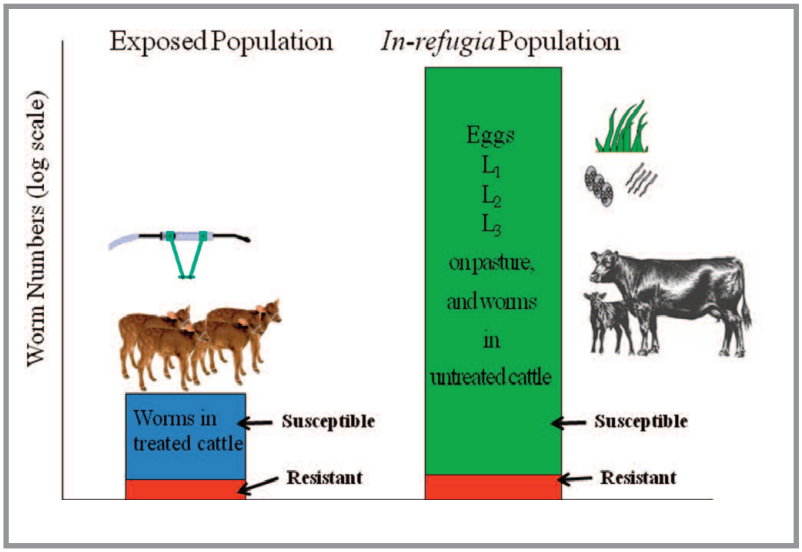
5.5.1. Anthelmintic resistance may be inevitable but can be delayed

The genes, or alleles, which allow parasites to become resistant to anthelmintics are believed to be in existence in unselected worm populations (see the text box for Fig. 5.3. for a detailed description). Consequently, for all anthelmintics that have been developed to date, it appears that the development of AR is an inevitable consequence of their use but its development can be delayed. There are several factors that have been shown to influence the rate at which AR appears in a worm population, and they are discussed below. It is our improved understanding of these factors that has led to the development of these guidelines for anthelmintic use, which are discussed in Section 6. Knowledge of the resistance status - to which drugs, with what species, and when - can greatly influence the advice given to maintain effective control and manage resistance development.

5.5.2. The size of *in-refugia* populations

In any parasite ecosystem, there are two sub-populations of worms; the parasitic and the free-living. It is only the parasitic sub-population (the parasites within the host) that can be exposed to any anthelmintic treatment. Worms that are in the free-living sub-population (eggs, L_1, L_2, L_3 - see Section 2.) are not exposed to the anthelmintic and are said to be *in-refugia* (Fig. 5.2.). Any worms in cattle that are not treated also contribute to the *in-refugia* sub-population. One of the important factors influencing the rate at which resistance develops in a worm population is the relative size of the exposed population and the unexposed or *in-refugia* population. In general, the larger the *in-refugia* population in comparison to the exposed population, the more slowly resistance will develop. As previously alluded to, the cattle *in-refugia* population is comparatively large reflecting the pro-longed survivability of free-living larval stages within bovine faecal pats.

Figure 5.2. The exposed and *in-refugia* worm populations



The worms inside the dosed cattle are exposed to the anthelmintic. Worms that are free-living on pasture, or exist as adults or larvae in untreated animals, are *in-refugia*. The *in-refugia* population is typically much larger than the exposed population and the relative sizes of these two populations influence how rapidly AR develops. There are resistant and susceptible worms in both populations but only the susceptible worms in the exposed population (in blue) are removed by treatment.

5.5.3. Frequency and duration of treatment

The more frequently treatments are given the faster AR develops. The underlying principle of selection for AR is that treatment gives the resistant worms a reproductive advantage over the susceptible worms. For two or three weeks after dosing (in addition to the anthelmintic's persistency period - see Table 4.2.), before newly ingested L3 have become egg-laying adults, the only eggs being passed in the faeces of dosed cattle are from worms that survived treatment. When the interval between dosing becomes shorter, and approaches the pre-patent period of the worm, the susceptible worms have less and less opportunity to produce eggs and most, or all, pasture contamination occurs with eggs from resistant parasites. If this strategy is continued the susceptible population is progressively replaced with a resistant one.

Frequency of dosing does not exert its effect on AR development in isolation from other factors that contribute to AR. For example, if the *in-refugia* population is small, replacement happens faster and AR may appear after relatively few treatments. Similarly, persistent products (long acting injectables with sustained activity) and sustained release boluses, may select for resistance towards the end of their period of activity if drug concentration levels decline slowly to sub-optimal levels (the "tail" effect). The indications are that not all high-frequency dosing strategies are equally bad, and that just seeking to reduce dose frequency may not be enough to slow the development of AR.

5.5.4. Re-infection after dosing

After dosing, any surviving resistant parasites in cattle enjoy a period of reproductive advantage over the susceptible parasites, the extent of which depends on how quickly the cattle become re-infected with L3 from the unselected population on pasture. If the pasture is highly infective, and the cattle are highly susceptible, re-infection occurs quickly and selection for resistance is minimised. An adult worm burden derived from the unselected population of larvae *in-refugia* is re-established within 3-4 weeks.

If re-infection is delayed, the resistant survivors will enjoy a longer period of reproductive advantage. Re-infection could be delayed if the pasture has a low level of contamination, if climatic conditions do not favour the movement of L3 onto pasture (too dry, for example), if the cattle have a relatively strong acquired resistance or if they have been treated with a persistent anthelmintic.

5.5.5. Anthelmintic dose rates

Under-dosing of cattle with anthelmintics is probably common-place, either because the weight of the animal was under-estimated, instructions for dose calculation were misleading, dosing equipment was faulty, or, for some pour-on products, adverse weather conditions were present at the time of treatment. Underdosing is now recognised as a very significant factor in the development of resistance. The reasons why dose rates are important are discussed in more detail in the text box for Fig. 5.3.

5.6. Reversion to susceptibility

Reversion, by definition, is the return towards susceptibility of a resistant nematode population in the absence of the selecting drug. It will occur only if there is active selection (natural or otherwise) against resistance alleles.

Normally, in unselected populations of worms, resistance alleles are either absent or are present at very low frequencies and it could be assumed that these alleles have a selective disadvantage for fitness. If anthelmintics are used and any resistance alleles are present, they will increase in frequency. If anthelmintic use is discontinued, natural selection might be expected to reduce the prevalence of resistance alleles in favour of the fitter, fully susceptible parasites and the population would, theoretically, revert towards full susceptibility.

If anthelmintic use continues however, further genetic selection in favour of the resistant parasites tends to make the resistance alleles less deleterious to survival. This process of 'learning to live' with the new alleles is called co-adaptation. In parasite populations where co-adaptation to resistance alleles has occurred, the resistant worms are no longer less fit to survive or reproduce than susceptible parasites. If anthelmintic use is discontinued at this stage, reversion to susceptibility does not occur. As reports of resistance in cattle nematodes are relatively uncommon, there is little or no supportive data on the occurrence of reversion in the field.

5.7. Rotation of anthelmintics

It has been a recommendation in the past, particularly with sheep worm control practices, that there should be a slow rotation between anthelmintics of different classes, changing classes every one to two years. Thus, a BZ anthelmintic could be used for worm control in year 1, a LM in year 2 and a ML in year 3. This strategy was intended to prolong the effective life of each anthelmintic by allowing reversion to susceptibility to occur when the anthelmintic was not in use. This was only expected to occur if AR was in the early phase of resistance development and co-adaptation had not occurred – long before AR was detectable in the worm population on the farm – and when natural selection might reduce the prevalence of parasites containing resistance alleles (point A in Fig. 5.1.). Given the widespread use of ML products on UK cattle farms, in practice this becomes an increasingly difficult recommendation to follow. Where it is introduced, it is not important which alternate drug is used as long as it comes from a different anthelmintic class, because it is natural selection rather than selection with anthelmintics that is expected to reduce the prevalence of resistant worms.

5.8. Spread of AR between farms

Previous discussions have assumed that resistance alleles occur in worms on all farms albeit at a very low frequency. It is possible that on some farms 'closed' populations of nematodes exist that have no alleles for resistance. On such farms, the greatest risk for the appearance of AR may be the importation of resistance alleles in worms in cattle from other herds where resistance occurs.

To prevent the introduction of resistant worms effective quarantine treatments are critical. The details of approaches to quarantine treatments are provided in Section 6.

5.9. The genetic basis for anthelmintics resistance

Alleles, loci and genes

The different forms of a gene, at a specific position on a chromosome, are called alleles. The position at which it occurs is called a locus (Latin for 'place'). The word gene can refer to either the locus or the allele. Generally, it is acceptable to substitute the word gene for allele. Worms are diploid creatures – meaning they have paired chromosomes. When both alleles at the same locus on each pair of chromosomes are the same, the worm is homozygous for that gene. When they are different (e.g. one allele for resistance to anthelmintic, and the other for susceptibility), the worm is heterozygous.

Resistance alleles pre-exist in worm populations

Anthelmintic resistance is now accepted as a pre-adaptive phenomenon, in that the allele or alleles that confer resistance already exist within the worm population before it has ever been exposed to the anthelmintic in question. In the absence of the anthelmintic, natural selection keeps the resistance alleles at a very low frequency because, presumably, the resistance alleles make the worms carrying them less fit for survival than fully susceptible worms.

The introduction and continued use of an anthelmintic, however, confers a survival advantage on the resistant worms. This allows them to reproduce at higher rates than susceptible worms, and their frequency within the population increases. Eventually the frequency of worms with a resistant phenotype becomes so high that anthelmintic resistance is said to have 'appeared' or to have 'developed' in the herd. This is likely to be the time at which resistance to anthelmintics is first detected in field tests, or when the anthelmintic fails to cure clinically-affected cattle. In fact, by that time, AR has already been present in the population for a substantial period, as the current methods of detection are relatively insensitive (Fig. 5.1.).

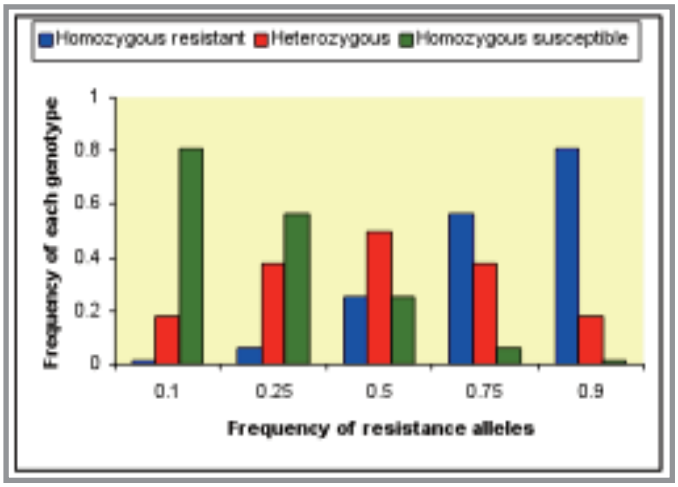
When anthelmintic resistance in worms behaves as a recessive trait, only homozygous worms survive a full dose of anthelmintic. Heterozygous parasites are killed by the anthelmintic. Low doses of anthelmintic, however, may allow the heterozygotes to survive. It could be said that low dose rates enable the trait to behave as a dominant trait, rather than a recessive one.

Dose rates

When AR alleles are rare, homozygous AR parasites are very rare and most resistant alleles will be in heterozygous parasites (Fig. 5.3.). Full dose rates of anthelmintics reduce the rate at which AR develops, compared to low dose rates, because they kill the heterozygotes and thereby remove most of the resistant alleles from the worm population. For example, when the resistant-allele frequency is 1 in 104, 99.99% of the resistant alleles in the worm population are in heterozygous worms. When anthelmintics are administered in this phase of AR development (point A on Fig. 5.1.), full doses (killing all heterozygotes and all homozygous susceptibles) are expected to significantly delay the emergence of AR compared to low doses (which allow heterozygotes to survive, but kill homozygous susceptibles).

As resistance alleles become more prevalent in the worm population, homozygotes become relatively more common (Fig. 5.3.). Once resistance alleles are no longer rare, a point is reached where there is little difference in the rate at which AR continues to develop between full doses and low doses (where only homozygous susceptibles are killed).

Figure 5.3. Frequency of resistance alleles by genotype



When resistance alleles are rare, most of the resistance alleles are in heterozygous parasites and very few in homozygous-resistant parasites. For this reason, low dose rates are likely to select more heavily for AR than full dose rates when AR is in the very early phase of development.

5.10. Anthelmintic efficacy

Anthelmintic resistance is not the only reason that anthelmintics sometimes appear to fail to control worm parasites. Other reasons for anthelmintic inefficacy include:

- **Dosing with insufficient anthelmintic due to:**
  - underestimation of the animal's weight;
  - poorly maintained dosing equipment.

- Failure to follow the manufacturer's instructions:
  - not storing the products correctly;
  - using products beyond their use-by date;
  - applying products incorrectly, or under adverse weather conditions (pour-ons);
  - mixing anthelmintics with other products.

- Rapid re-infection of animals after treatment from highly infective pastures;

- Use of the incorrect drug for the target worms.

6. Anthelmintic resistance – new guidelines

Due to the limited number of reports of AR in cattle, specific recommendations for controlling AR in cattle nematodes have not been adequately or previously addressed. It therefore seems sensible and appropriate that recommendations aimed at limiting the development of resistance in sheep nematodes (SCOPS guidelines) should be adopted and followed wherever possible. The ultimate choice of anthelmintic product, when considered as part of a worm control programme designed to delay the onset of resistance, may be influenced by a number of factors of which group type and ease of application become the overriding factors.

Table 6.1. The guidelines for anthelmintic use and worm control in cattle (based on SCOPS principles for sheep)

Guideline	Comment
1. Work out a control strategy with your veterinarian or advisor	• Specialist consultation as part of herd health planning is an increasing requirement on farms. Worm control programmes for cattle will require on-going consultations
2. Use effective quarantine strategies to prevent the importation of resistant worms in introduced cattle	• Bought in cattle can be a potential route of introducing resistance alleles into a non-closed herd
3. Test for anthelmintic efficacy on your farm	• Whilst resistance is still rare in cattle nematodes, treatment failures do occur. It is important to monitor continued efficacy as underdosing can select for AR
4. Administer anthelmintics effectively	• Administer the right dose in the correct way by following manufacturers' instructions
5. Use anthelmintics only when necessary	• Understand the trade-off between tolerating some level of parasitism and minimising selection for AR. FEC monitoring has an important role
6. Select the appropriate anthelmintic for the task	• Target treatment according to parasites (and their stages) present, based on time of year
7. Adopt strategies to preserve susceptible worms on the farm	• Aim to reduce selection for AR when treating adult cattle, immune older animals or when dosing on low contamination pastures
8. Reduce dependence on anthelmintics	• Alternative control measures include grazing management using sheep or older immune animals

6.1. Work out a control strategy with your veterinarian or advisor

Developing a cost effective, reliable and sustainable strategy in terms of AR management for worm control is not straightforward. On-going consultations between farmers, their veterinarians and advisors will be needed to combine an expert knowledge of worm parasites with a practical and detailed understanding of the individual farm, its livestock and the practicalities for handling and treatment. This relationship needs to evolve so that the farmer makes tactical decisions within the context of an agreed strategy. This will need to be updated by advice and interpretation of analyses, such as Wormer Tests (WT) and FECs (see sections 8.1. and 8.2.), which give up to date information on the status of the herd and effectiveness of wormer treatments.

6.2. Avoid introducing resistant worms – use quarantine treatments

The objective of quarantine treatments is to reduce the probability of any AR worms being introduced onto the farm. If any resistant worms do survive the quarantine treatment, then their numbers should be so low that the emergence of AR is greatly delayed. Quarantine should be applied to cattle purchased from other herds, and cattle which have been grazing on other farms where the resistance status is unknown.

There are three steps in the recommended quarantine protocols:

Step 1 - Treatment

All cattle brought onto the farm should be treated with anthelmintics likely to remove all worms – both resistant and susceptible genotypes.

Reports of resistance are relatively uncommon in cattle, so specific recommendations are much less clear when compared with those given for sheep. As reported suspect resistance has been mainly with ML products involving *Cooperia spp.*, it would seem appropriate to give an oral BZ anthelmintic (albendazole or fenbendazole) or an LV product, given either subcutaneously or by pour-on. Best practice is considered sequential treatment with both.

The two treatments should be given sequentially not simultaneously. If both products are given orally they should not be mixed before administration. There is no specific recommendation for a time interval between administrations of the two products.

Step 2 - Holding

Hold cattle off pasture for 24-48 hours, until any worm eggs present in the gut have passed out in the faeces.
After cattle have been treated they should be held away from pasture for 24, or preferably, 48 hours. This time period allows eggs produced by worms before treatment to pass out in the faeces. After these time periods most worm eggs will have gone. Cattle should have access to feed and water throughout the period that they are held off pasture.
Faeces passed in the 24 to 48 hours post-treatment should not be applied to pastures that will subsequently be grazed by cattle.

Step 3 - Turnout onto contaminated pasture

Cattle should be turned out to pasture contaminated with worm eggs and larvae, to minimise the impact of any worms that survive treatment on the farm's AR status.
After the period of confinement off pasture, treated cattle should ideally be turned out to pastures with levels of worm eggs and larvae representative of the worm population of the farm. This is to ensure that any eggs produced by worms before treatment and passed in the faeces will be diluted by the pre-existent free-living stages on the contaminated pasture. This will have the effect of (a) keeping the introduced resistant genes at a low frequency in the free-living population, and (b) encouraging rapid re-infection of introduced cattle with indigenous worm populations, shortening the period when introduced worms are dominant.

The efficacy of the quarantine treatment should be assessed by sampling treated cattle for FEC 14 days post treatment. If FECs are more than zero, treatment should be repeated until 14-day post-treatment FECs are zero. At that point, the cattle can be released onto other farm pastures.

6.3. Test for anthelmintic efficacy

Whilst AR is still relatively uncommon in cattle nematodes there may still be a need to test for anthelmintic efficacy. This would appear to be particularly true with pour-on products where sub-optimal dosing can lead to failure to control post-treatment FECs (see section 5.10.) and subsequently to suspicion of AR. Early detection of reduced efficacy means that efforts can be concentrated on reducing selection pressures to help maintain anthelmintic efficacy for longer. Consideration should also be given to the species of nematode concerned since results will vary according to the species present. As previously discussed, the dose-limiting species *Cooperia oncophora* is not-infrequently reported in post ML-treatment faecal egg counts. The methods for determining anthelmintic efficacy are described in Section 8.

6.4. Administer anthelmintics effectively

6.4.1. Dose at the rate recommended for the heaviest in the group
All cattle should be dosed at the rate recommended for the heaviest animal in the group. Scales should be used to weigh two or three of the biggest animals. If the weight range is such that the lightest animal might receive more than a double dose, divide the group into two and then calculate a dose rate for each of the two sub-groups based on the heaviest in each.

Where two anthelmintics are being administered e.g. for quarantine treatment, the full dose rate for each drug must be used.

6.4.2. Check the dosing gun, syringe or pour-on applicator
Dosing guns/syringes/pour on applicators should be checked regularly to ensure that they are delivering the required dose. For both drenches and pour-ons, this can be done by delivering two or more 'doses' into a graduated measuring device, immediately before treatment commences. Use the product, not water, because the higher viscosity of the actual product will be a better 'test' for the equipment.

6.4.3. Dosing technique
Oral drenching guns are designed to deliver over the back of the tongue so that the entire dose is swallowed into the rumen. If anthelmintic is administered into the buccal cavity and then swallowed, some or the entire dose may by-pass the rumen and go direct to the abomasum because of the action of the oesophageal groove. Anthelmintic that enters the abomasum is absorbed and metabolised very rapidly. This means that the parasites may have insufficient exposure to the anthelmintic to provide the expected level of efficacy.

Boluses should be administered with the correct applicator to ensure that the bolus fits correctly. It is important to follow the manufacturer's guidelines on the correct way to insert the bolus into the applicator. This should then be inserted from the front of the mouth over the back of the tongue with no more than gentle firm pressure, taking care not to insert the gun too far into the throat. As the animal begins to swallow, passage into the throat becomes easier and once in the throat the plunger is pressed ejecting the bolus. The applicator should then be carefully removed at the same time checking that the bolus has been swallowed.

Injections should be given subcutaneously at the recommended site of injection, following manufacturer's instructions. For subcutaneous injections raise a fold of skin at the injection site recommended by the product manufacturer and inject carefully. After the injection briefly massage the site. It is important to use the correct-sized needle according to the size of the animal and site of injection. If a large dose is to be delivered it may be advisable to split the dose between two injection sites. It is worth noting that for injectable, long-acting moxidectin the site of subcutaneous injection is the base of the ear.

Pour-on products should be applied along the length of the flattest part of the animal's back, from the withers to the tail head. The anthelmintic is formulated in a vehicle that transports the drug either through the skin or down the shafts of the hair and through the hair follicles. In general, animals should not be treated when the hair is wet or if rain is anticipated within two hours of treatment. However, some products are waterproof and can be used on wet animals. Areas of damaged skin should be avoided, as should areas contaminated with mud or manure.

6.4.4. Do not mix
Anthelmintics must not be mixed with any other products prior to administration.

6.5. Use anthelmintics only when necessary

6.5.1. Dosing of adult cows
Adult cows, following exposure to gastrointestinal nematodes during their first two seasons at grass, have usually developed a strong acquired immunity. Immune animals exposed to larval challenge when at grass may carry small worm burdens in adulthood and have a very low FEC (<20epg). Therefore, anthelmintic treatments to adult cows are

not usually necessary although several studies have suggested that treatment can result in improved milk production, and improved reproductive performance through better conception rates and reduced calving intervals. Occasionally, adult cows may develop signs of Parasitic Bronchitis through either reduced exposure and lack of immunity (see section 2.5.) or heavy larval challenge (re-infection syndrome), and require appropriate anthelmintic treatment. It should be borne in mind that, with the exception of eprinomectin which has a zero milk withdrawal period, ML products can only be given during the dry period but not within 60 days of calving.

6.5.2. Dosing of calves at turnout
Calves born and raised indoors are usually worm-free at turnout and should not require anthelmintic treatment at this time. The exception is if there is an anticipated high level of pasture infectivity and risk of disease, when administration of a ML product with persistent activity (see 4.4.), or a bolus, can be used to prevent both disease and further pasture contamination.

6.5.3. Treatment of calves at grass
Strategies for the control of parasitic nematode infections of cattle are generally targeted at first-year grazing calves. On farms where new leys or aftermaths are available, worming and grazing management can be integrated as a means of worm control. In this respect, "clean grazing" systems can be designed and function well for control of PGE. These should be encouraged, but offer little protection for the control of lungworm disease because of its unpredictable nature.

By providing "low risk" grazing (see 8.8.1.) at the start of the grazing season in the form of new leys, or grass previously grazed by sheep, anthelmintic treatments can generally be avoided. Where only "medium" or "high" risk pastures exist then anthelmintic treatment(s) will be required at some point during the grazing season. These could be avoided by moving calves to "low risk" pasture in the form of aftermaths (hay or silage fields) from mid July onwards.

The so called "dose and move" strategy is now generally considered to be highly selective for AR and consideration should be given to use of targeted selective treatments of cattle to be moved (see 6.7.1.).

On many farms where provision of low or medium risk grazing is impracticable, worm control can be achieved by worming in the early part of the grazing season (sometimes referred to as "poor man's clean grazing systems"). Examples of this include the 3-8-13 strategy for ivermectin (Ivomec), the 0, 8 dosing strategy for doramectin (Dectomax), or the use of boluses (see 4.4. and 4.5.). Calves dosed strategically in this manner should remain set-stocked on the same fields for maximum benefits. Alternatively, calves should be moved to "low risk" pasture when these become available allowing sufficient time after the "dose" to reduce selection pressure for AR.

6.5.4. FEC monitoring to optimize the timing of anthelmintics use
FEC monitoring provides information about the worm status of a herd of cattle and can help in the decision about the need for treatment with anthelmintics. If grazing calves have high FECs, and the faecal samples have been collected appropriately, it can be assumed that worm burdens are high and that treatment is justified. Unfortunately the corollary is not always true and low FECs require careful interpretation. See Section 8. for details on performing and interpreting FECs.

6.6. Selecting the appropriate anthelmintics

6.6.1. Use narrow spectrum anthelmintics where possible
Unnecessary exposure of worms to an anthelmintic can lead to increased selection pressure for AR without providing any improvement in worm control. For calves at grass the use of a levamisole (LV) product, for example, instead of a more-broader spectrum ML product may be equally effective against *Ostertagia or Cooperia* species.

6.6.2. Avoid off-target (inadvertent) use in combination products
The use of combination products (flukicide plus broad-spectrum wormer) active against liver fluke and nematodes should be avoided when only liver fluke is the target for control. Instead, the narrow-spectrum flukicide should be used alone.

6.6.3. Use of larval culture with FEC

Consider the use of larval culture and larval identification in conjunction with FEC to identify and target pathogenic nematode species, particularly *Ostertagia ostertagi*. Baermannisation of faecal samples and identification of L1 larvae is required for the detection of lungworm infections due to *D. viviparus*. See Section 8. for details.

6.6.4. Rotate anthelmintics where appropriate

As discussed in Section 5., reversion is unlikely to occur once resistance has been detected in a worm population. Although there is no strong evidence that rotating anthelmintic classes is an effective strategy to delay the appearance of AR, it is possible that rotation could delay the appearance of ML resistance on farms where the gene for resistance is either absent, or at very low levels. It makes sense, therefore, to continue to advise rotation between a ML and other effective anthelmintics where practically possible.

The intention to rotate between anthelmintic classes should not be allowed to take precedence over other more important decisions about selection of anthelmintics. In particular, the quarantine strategies for introduced animals described earlier in this section should be applied regardless of the current anthelmintic in the rotation.

6.6.5. Using boluses and anthelmintics with persistent action

All ML products given by injection or pour-on have persistent but variable anthelmintic activity against abomasal nematodes, some small intestinal species and against lungworms (see Table 4.2.).

In terms of worm control, long acting preparations and boluses offer the ability to prevent larval infection and the development of patent worm infections, which thus minimises egg output for a prolonged period, and hence reduces pasture contamination. However, this also means a long period of exposure to the chemical and in theory this may influence selection pressure for AR, particularly towards the end of the period of activity when sub-optimal levels of chemical may occur (the so called "tail-off" effect). Prolonged activity may also delay the development of immunity leaving treated animals susceptible to infection once activity has ceased.

6.7. Preserve susceptible worms on the farm

The 'dose and move' strategy has been widely recommended in the past, and is a successful, cost-effective method of achieving good worm control. When pastures with low levels of worm eggs and larvae become available for grazing, best use is made of them by treating animals with anthelmintics before placing them on the field. This ensures pasture contamination remains low for an extended period providing a period of productivity uninhibited by parasite infection, without the need for repeated anthelmintic treatment.

Unfortunately, the strategy has the potential to select for AR because any worms surviving treatment will enjoy an extended period of reproductive advantage over unselected parasites. For the period that cattle remain free from re-infection from the low contamination pasture, any surviving worms are resistant and contaminate the pasture with their eggs. Without the dilution effect of a heavily contaminated pasture the frequency of resistant genes in the free-living population can increase quickly, and in theory, the cleaner the pasture the faster the resistant-gene frequency increases.

The benefit of the low contamination pasture may persist for weeks or months. At the end of that period, the pasture will be more heavily contaminated, but now with a more-resistant population of parasites than was present earlier in the season. Young calves grazing the pasture subsequently will be infected with a selected population of parasites, with a higher resistant-gene frequency than before treatment. The repetition of such events around the farm over several years may lead ultimately to a highly resistant population of parasites, despite the farmer having 'enjoyed' the benefits of good worm control in the meantime.

6.7.1. Targeted selective treatments (TSTs)

Anthelmintic treatments should ideally be targeted, and based on appropriate whole herd FEC monitoring programmes (see section 8.2.). In theory, some calves in a group can be left untreated, allowing a pool of unselected parasites to produce eggs that are passed out on to the low-contamination pasture. It has been suggested that leaving a percentage of a group untreated before such a move, will be sufficient to provide a large enough dilution

effect to delay the development of AR. Only a few TST studies in calves have been conducted, under the PARASOL research program, and it is perhaps too early to draw any conclusions at this stage as to whether this is an achievable strategy for limiting the development of AR.

6.7.2. Delay the 'move' after the dose

Whilst suggested for lambs, a delayed dose and move, is practically more difficult with calves because of the variations in persistence in activity between ML products and the timing between treatment intervals. The intention is to allow any treated calves to become 'lightly' re-infected with susceptible worms before allowing them access to the 'low risk' pasture. This will ensure that soon after the move, contamination of the 'clean' pasture with eggs from susceptible worms will recommence and reduce the reproductive advantage offered to any resistant parasites surviving treatment. It should however, be possible to plan the availability of aftermaths with turnout and the need for strategic early season worming plans as part of farm health planning initiatives.

6.8. Reduce dependence on anthelmintics

6.8.1. Use grazing management

Control of pasture-borne nematode infections can be achieved through the use of various grazing management strategies. The objective of these management strategies is to minimise the reliance on and use of anthelmintics by avoiding exposure to parasite burdens that would lead to clinical disease and loss of production. At the same time, management needs to allow the calves to build up immunity to the parasites if they are to remain on the farm beyond the first grazing season.

To achieve these objectives, it is necessary to understand the basic principles of risk assessment for pastures, cattle management systems and to be able to relate these to the management and monitoring tools available to the farmer. Grazing strategies can be categorised as preventative, evasive and diluting, with a common aim being to generate low risk pastures and/or avoid highly infective pastures. This can be achieved by avoiding the development of heavily infected pastures, by moving young susceptible stock to less infected pastures, or by mixing these animals with older immune stock or with other livestock species that are refractory to infection with cattle nematodes (See Section 8. for guidelines).

6.8.2. Bioactive forages

Grazing on bioactive forages, such as chicory, has been shown to reduce the negative effects of parasitism in sheep. Little work has been done with these forages in grazing cattle and it is not clear at this stage if they can be used in practical cattle production systems.

7. Trematodes (flukes)

7.1. Liver fluke

Disease due to liver fluke (Fasciolosis) is caused by the trematode parasite *Fasciola hepatica*. Disease can result from the migration of large numbers of immature flukes through the liver, or from the presence of adult flukes in the bile ducts, or both. Liver fluke can infect all grazing animals (and man) but mainly affects sheep and cattle. It is less pathogenic in cattle.

7.1.2. Life cycle

Compared to other helminths the life cycle is complex, involving an intermediate host, the mud snail *Galba (Lymnaea) truncatula*, and several free-living stages. The role of the snail, which prefers muddy, slightly acidic conditions often associated with poor drainage, means that the incidence of liver fluke is far greater in the wetter areas of the country and in years when there is high summer rainfall. With the capacity of the snail to multiply rapidly (100,000 offspring in 3–4 months) along with the multiplication of the parasite within the snail, there is potential for very large numbers of parasites on the pasture.

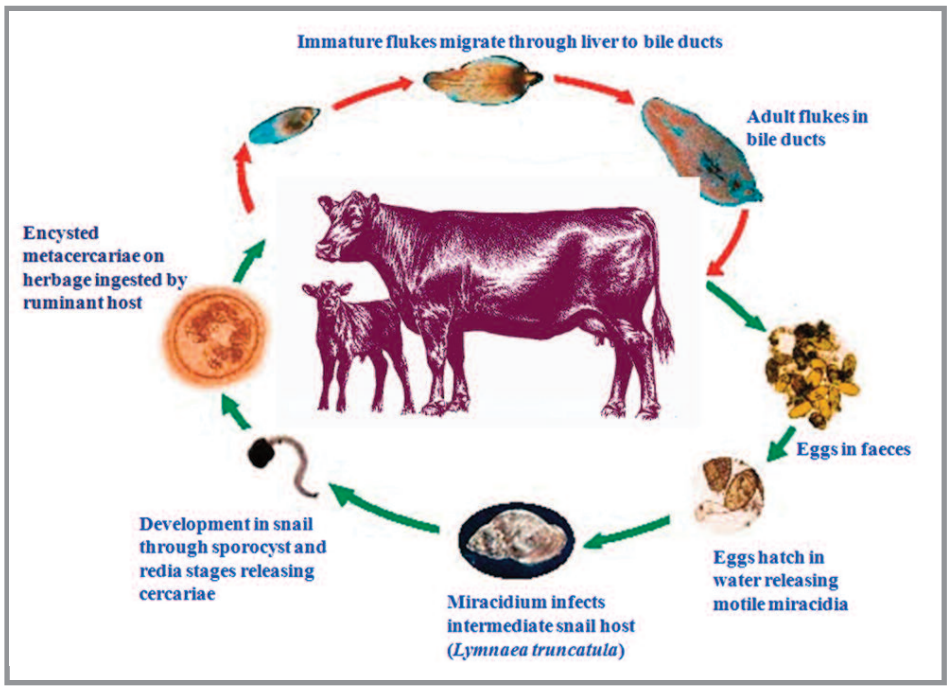


Figure 7.1. Life cycle of the liver fluke, *Fasciola hepatica*.

Adult fluke lay eggs that are passed out onto pasture in the faeces. At suitable temperatures, a miracidium develops within the egg, hatches and migrates in thin films of moisture, actively seeking the snail host. Miracidia can only survive for a few hours outside the snail. Within the snail they undergo two further developmental stages, including multiplication, eventually becoming infective cercariae which emerge from the snail when the temperature and moisture levels are suitable. The cercariae migrate onto wet herbage encysting as metacercariae, the highly resilient infective stage of the liver fluke. Following ingestion the young flukes migrate to the liver, through which they tunnel, causing considerable tissue damage. The infection is patent about 10–12 weeks after the metacercariae are ingested. The whole cycle takes 18-20 weeks.

7.1.3. Epidemiology

The hatching of fluke eggs and the multiplication of snails depend on adequate moisture and temperatures greater than 10°C. Such conditions normally occur from May–October in the UK. The incidence of Fasciolosis is highest in years when rainfall is above average during May–July. The epidemiology of liver fluke is often viewed as the result of two distinct cycles of snail infection and pasture contamination.

- **Summer infection of snails**

In wet summers, snail populations multiply rapidly and snails are invaded by hatching miracidia from May–July. If wet weather continues, the snails shed massive numbers of cercariae onto pasture during July–October. Conversely, if the climate in May–July is dry or cold, fewer snails appear, fewer fluke eggs hatch and levels of contamination in the autumn are much lower. Clinical fasciolosis resulting from summer infection of snails arises usually from ingestion of large numbers of metacercariae over a short period of time in July–October.

- **Winter infection of snails**

Less commonly, snails can become infected in late summer or early autumn and development within infected snails is delayed as the snails become dormant and hibernate. The cercariae are then not shed onto the pasture until the following spring. This can produce an initial and significant infection in herds or flocks in the spring.

7.1.4. Liver fluke disease

The pathogenesis of fluke infections varies according to the number of metacercariae ingested and the phase of parasitic development in the liver. Essentially, the pathogenesis is two-fold: The first phase occurs during migration in the liver parenchyma and is associated with liver damage and haemorrhage. The second occurs when the parasite is in the bile ducts, and results from the blood feeding activity of the adult flukes and from damage to the biliary mucosa by their cuticular spines. Although acute and subacute disease may occur occasionally in cattle under conditions of heavy challenge, especially in young calves, the chronic form of the disease is by far the most important and is seen in the late winter/early spring.

The pathogenesis is similar to that seen in sheep but has the added features of calcification of the bile ducts and enlargement of the gallbladder. The calcified bile ducts often protrude from the liver surface, giving rise to the term 'pipe-stem liver'.

Aberrant migration of the flukes is more common in cattle and encapsulated parasites are often seen in the lungs. On re-infection of adult cows, migration to the foetus has been recorded resulting in prenatal infection. There is some experimental evidence that Fasciolosis increases the susceptibility of cattle to infection with *Salmonella dublin*.

In heavy infections, where anaemia and hypoalbuminaemia are severe, submandibular oedema occurs frequently. With smaller fluke burdens, the clinical effect is minimal and the loss of productivity is difficult to differentiate from inadequate nutrition. Diarrhoea is not a feature of bovine Fasciolosis unless it is complicated by the presence of *Ostertagia spp*.

Fasciola infections may cause a loss of production in milking cows during winter. Clinically, these are difficult to detect since the fluke burdens are usually low and anaemia is not apparent. The main effects are a reduction in milk yield and quality, particularly of the solids-not-fat component. Serological and a bulk milk tank ELISAs are available for fluke surveillance (See sections 8.5.3. and 8.6.3.).

7.1.5. Treatment and control

Control programmes must take into account the farm history, topography, geographical location and the prevailing weather. Most programmes rely heavily on flukicidal treatments. The choice of product and frequency of use will depend on the level of fluke challenge, the time of year, and the management and husbandry systems on the farm.
Fluke burdens can be monitored in cattle herds by post-mortem examinations when the opportunity arises, with FECs and by use of serological assays or a bulk tank milk ELISA (see Sections 8.5.3. and 8.6.3.). Herds should be monitored before a flukicide is used unless there is a history of fluke infection on the farm. Continued monitoring can help determine the need for repeated treatments. Grazing cattle in winter can be treated with any of the flukicides effective against both adult and immature stages. In-wintered cattle need to be treated after housing, the timing of treatment depending on the flukicide used and its activity against immature stages. Those products effective against immature fluke less than 6 weeks old can be used to treat cattle on housing; other products should be used 4–6 weeks post housing. Dairy cows can be treated at drying-off. In high-risk years, outwintered cattle should also be treated in spring to remove fluke burdens and reduce contamination of pastures with fluke eggs. Flukicides with adult activity only can be used at this time thus reducing the selection pressure associated with products containing triclabendazole.

Combination fluke and worm products should only be used when both groups of parasites are present, as their use could potentially lead to off-target selection for resistance.

Where fluke infection is present, identification and exclusion of snail habitats from livestock offers some measure of control. Drainage eliminates the snail and offers an effective means of control, but the proliferation of environmental schemes to protect wetland areas has reduced the opportunities for this to be implemented. Simply keeping stock off the wettest fields in the autumn and the winter, when the incidence of disease is at its highest, can reduce the risk from fluke.

Table 7.2. Efficacy of flukicides available for use in cattle in the UK

Chemical Group	Anthelmintic	Fluke Activity			Comments
		Adult	6-12 wks	1-6 wks	
Salicylanilides	Closantel	+	+	-	Some activity against tapeworm segments
	Oxyclozanide	+	-	-	
Substituted phenols	Nitroxynil	+	+	-	Also active against blood nematodes
Benzimidazoles	Albendazole	+	-	-	Also active against nematodes and tapeworms
	Triclabendazole	+	+	+	
Sulphonamide	Clorsulon	+	±	-	

7.1.6. Resistance to flukicides

The widespread use of triclabendazole (TCB) in sheep, because of its activity against immature fluke, has led to the development of TCB-resistant fluke in several countries including the UK. An EU funded project DELIVER has evaluated an FECRT for fluke resistance investigations in sheep and the methods developed may be applicable to cattle, although this is further complicated because of the much lower FECs seen in cattle. The possibility of other reasons for flukicide failure should always be considered, particularly if animals are in poor condition or may be suffering from liver damage.

Where resistance is suspected to a particular product, then an alternative flukicide listed in Table 7.2. should be considered, taking into account the variations in activity against immature fluke between products.

7.1.7. Preventing the development of resistance

Rotational use of triclabendazole, with oxyclozanide, closantel and nitroxynil, or clorsulon should be considered where flukicides are used strategically, although additional treatments may be required in years when triclabendazole is not used. Opportunities to avoid the use of triclabendazole should be exploited whenever alternate drugs will give satisfactory levels of control, such as spring treatment of chronic infections.

7.1.8. Quarantine

Quarantine treatment strategies for liver fluke in introduced cattle, sheep or goats should be considered using a 'risk-based' approach and developed for farms considered 'at risk' in conjunction with a veterinarian or advisor. The three principal reasons for treatment are:

1. Infected animals may be introduced onto a farm that has no known snail habitat and, therefore, no history of fluke infection. The risk of introduced fluke establishing on the farm is very small (or zero, if there is no snail habitat) and treatment in this case is intended to remove any fluke in the cattle for the sake of their health. Following treatment with a flukicide, FEC monitoring in subsequent months is advised to detect any small

residual burden. The consequences of introducing small numbers of fluke, or resistant fluke, are not serious in the long-term.

2. The farm may have areas considered to be a suitable habitat for snails but no history of fluke infection. The risk of introduced fluke establishing on the farm is considered to be significant so treatment is aimed at removing all fluke, including any possible resistant fluke.

3. Liver fluke may be endemic on the farm so introducing small numbers of fluke will not be serious, particularly if wildlife reservoirs exist. However, if the endemic fluke are fully flukicide-susceptible, the consequences of introducing resistant fluke are potentially serious.

Choosing a treatment strategy

The following factors should be considered when choosing a quarantine treatment strategy.

- Fluke resistance to triclabendazole has not been reported in cattle in the UK and, in most cases, treatment with this drug should remove a very high proportion of susceptible flukes of all stages.
- Treatment with products containing nitroxynil or closantel is expected to prevent the output of fluke eggs for 6-8 weeks; and for 4-6 weeks with clorsulon, provided the fluke are susceptible to the drug used. Treatment with other products containing albendazole or oxyclozanide which are only active against adult fluke may only prevent the output of fluke eggs for up to 3 weeks. If the introduced cattle are infected with young immature fluke, treatment will have to be repeated after the immatures are old enough to be killed by these products (see Table 7.2.). In this context, it may be worth considering the use of two doses given 4-6 weeks apart depending on the product used.
- Resistance to closantel and to nitroxynil has not been reported in cattle.
- Treatment with more than one product with activity against immature flukes (triclabendazole, nitroxynil, closantel) will reduce the risk of introducing fluke with resistance to any one product. It is not recommended, however, that two products be used at the same time, and it is important to check with the manufacturer if there are any compatability issues.
- As infected animals can pass fluke eggs for up to 3 weeks after adult fluke are killed, it is advised that treated cattle be kept on quarantine pastures or pastures with no fluke habitat for at least 4 weeks after treatment.
- FEC monitoring can be used to determine the need for treatments subsequent to the initial one.
- Any sheep brought onto the farm should also be treated following SCOPS guidelines as these may be an important source of resistant fluke to all grazing animals.

7.2. Rumen fluke

Rumen fluke of the genus *Paramphistomum* have a worldwide distribution and are considered to be important parasites of a number of ruminant species, particularly in tropical and subtropical areas. They are approximately 1 cm long and may be found in large numbers feeding on the wall of the rumen and reticulum. Generally, mature flukes do not cause clinical disease (Taylor and others, 2007). Their large operculate eggs are similar in appearance to those of the liver fluke, *Fasciola hepatica*, except that they are clear rather than yellow. The intermediate stage involves water snails and infection is usually associated with access to flooded pasture. Immature fluke attach and feed for up to six weeks on the mucosa of the duodenum. They may also be found in the ileum, jejunum and abomasum before moving into the fore stomachs. Heavy infections with immature parasites may lead to enteritis with diarrhoea, anorexia, dehydration and increased thirst.This is sometimes associated with high mortality in young stock. Despite the worldwide distribution of rumen flukes they are rarely seen on British farms.

Since June 2007, several reports of rumen fluke have been made in parts of England and Wales (Foster et al. 2008). Infection levels reported have been low, not associated with clinical disease, and identified initially on FEC, or on post mortem. Therefore, detection may be a consequence of the more frequent requests for fluke diagnoses in cattle, and the use of more sensitive trematode FEC detection methods capable of detecting low levels of infection. Alternatively, it may be that conditions conducive to the survival of fluke have led to increased exposure of cattle to rumen fluke originating from deer or buffalo.

8. Techniques

8.1. Detecting anthelmintic resistance

The presence of AR is dynamic, although not reversible, such that its detection on a farm will be seasonably variable depending on the species and strains present at the time of any applied test, and the test's specificity and sensitivity in detecting resistant alleles within the worm populations. The lack of appropriately validated and standardised methods for AR detection is the subject on ongoing research.

The presence of AR can be investigated in herds in a number of ways.

8.1.1. Post-dosing faecal egg counts ("wormer tests")

A quick indication of the efficacy of an anthelmintic can be gauged by laboratory testing of faecal samples from 10 cattle following treatment. The time of sampling post treatment depends on the anthelmintic used and its persistency against parasite species; the general recommendations are **7 days after LV, 10-14 after BZ and 14-16 days after a ML.** In practice, this means checking 7 days for LV, or 14 days post treatment, for BZ and ML products. Due to variability in persistence of ML products additional post-treatment sampling times may be required. The WT is merely an indicator of anthelmintic inefficacy and not necessarily anthelmintic resistance per se, as many other factors can influence test results. The utility of this test is improved if faecal samples from 10 cattle in the treated group are collected and submitted on the day of dosing to provide a rough estimate of the reduction in FEC achieved. The advice about faecal collection in Section 8.2. should be followed.

8.1.2. Faecal egg count reduction tests (FECRT)

A more structured on-farm test can be conducted in which a number of different anthelmintics are tested against a control group of animals. In practice this is much more difficult in cattle than with sheep because of the numbers of calves normally present on the farm. Where possible, groups of 10 calves are allocated to control or treatment groups, which might include a BZ, LV, and ML. In practice, given the now almost extensive use of MLs, it is most likely this will be an ML group, a control group and then ideally either a BZ or LV group. FECs are performed prior to treatment on individual samples taken from animals in all groups, then from all animals in the control and ML groups at 14 days post treatment. If a BZ group is also used then these should be also be sampled 14 days post treatment. Where an LV is included then these should be sampled at 7 days post treatment with corresponding samples also taken from the control group at the same time.

AR is suspected if the percentage reduction in FEC of a test group compared with the treatment control group is < 95%. Results may differ according to whether arithmetic or geometric means are used in the calculations, and where necessary the advice of an expert should be sought with interpretation of the results.

***NB. Animals that have not been dosed for 10 weeks, or are known to have had zero egg counts after their last dosing, should be used and a mean FEC of 200 epg or more is recommended before starting the trial.*

8.1.3. *In vitro* tests

Whilst a range of *in-vitro* tests has been developed for use in testing for resistance in sheep nematodes, there is a lack of validated methods for investigating resistance in cattle nematodes. Molecular-based techniques have been reported but have, as yet, to be tested under field conditions.

8.2. Faecal egg count monitoring

FECs can be monitored using a suitably equipped and trained veterinary practice, a commercial service or by adopting a DIY approach using the FECPAK system.

8.2.1. Guidelines for collection of faeces

These guidelines are for the estimation of the mean FEC of a group of cattle. A 'group' in this context refers to a group of animals of the same age and sex grazing together in the same field and with the same anthelmintic-treatment history.

- At least 10 cattle in the group should be sampled. The wide variation in FEC between animals grazing together in the same field means that random sampling effects have a significant impact on the confidence limits surrounding the estimate of the group mean FEC. Even if 10 animals are sampled, the confidence limits are wide. This number is generally considered to be an acceptable compromise between repeatability and cost (Fig. 8.1.).
- The animals should be healthy and have had full access to pasture and/or feed before sampling because counts are reported as eggs per gram (epg) of faeces and variation in faecal output will affect the count. If cattle have been held off feed for more than a few hours before sampling, or if any animals included in the sample are i nappetant due to illness, the FEC will be difficult or impossible to interpret. A high count may be incorrectly assumed to reflect a high worm burden. For this reason, FECs should not be used as a diagnostic aid when PGE is suspected in cases where cattle are profoundly ill. A worm count as part of a post-mortem examination is a much more appropriate way to estimate worm burden in such cases.

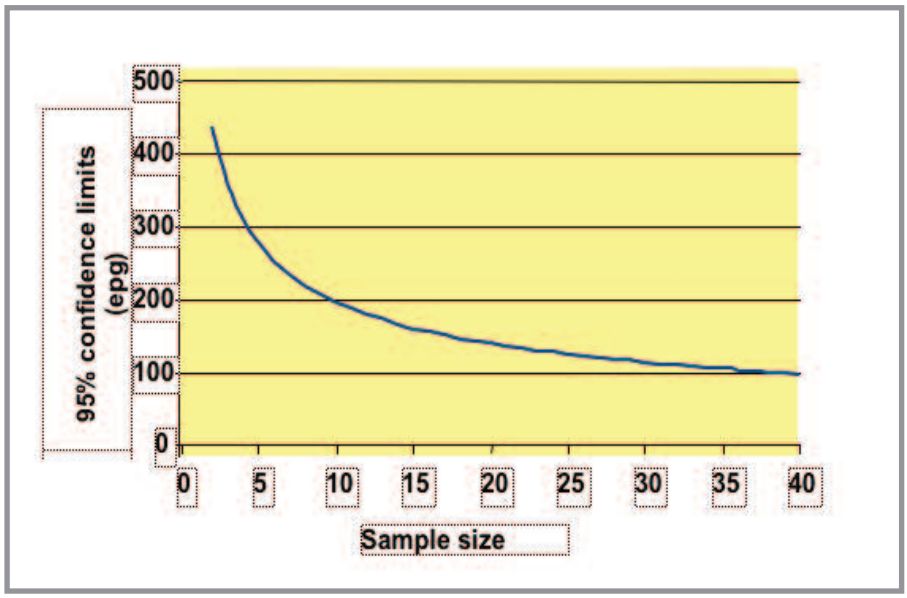


Figure 8.1. Confidence limits around an estimate of mean FEC become narrower as the sample size increases.

- Samples should be fresh when collected (less than one hour old) and kept cool (not frozen) in an airtight container or plastic bag, before delivery to the laboratory within 48 hours. If the faeces are too old some eggs will have hatched and the reported egg count will be an underestimate.
- Some laboratories pool the 10 samples and report the average of the 10 animals as a single count. This is acceptable and can substantially reduce the cost, but the faecal samples should still be kept separate until they arrive at the laboratory. The technicians can then ensure the pooled sample is prepared with equal amounts of faeces from each individual animal.

8.2.2. Larval culture and differentiation

FECs are reported as counts of worm eggs per gram of faeces. Eggs of most strongyle genera of interest (*Ostertagia, Cooperia, Trichostrongylus, Haemonchus, Oesophagostomum, Chabertia, Bunostomum*) cannot be differentiated except those of *Nematodirus,* which are very much larger than eggs of the other strongyles. *Trichuris, Capillaria and Strongyloides* eggs are also readily differentiated.

It is often useful to know whether worms of one particular genus dominate FECs or not. If so, larval culture and differentiation can be performed, usually using the faeces left over from the FEC. This technique takes a further 7 to 10 days.

Larval differentiation involves hatching the eggs in the sample and identifying the larvae. Usually 50 or 100 larvae are counted, and the percentage of each genus reported. However, the eggs of each genus may not hatch equally because the temperature at which the culture is performed may favour the hatching rates of one genus over others. It is safer, therefore, to use the larval culture results as a general indication of the worm genera present, rather than a precise determination of the proportion of the FEC contributed by each genus.

8.2.3. Interpretation of FECs

FECs have some limitations and should be viewed as 'additional diagnostic information' to be considered with history and clinical signs. Careful interpretation is particularly important where the FEC is low.

- *Nematode genera* and species vary in their fecundity and pathogenicity:
  - With some genera (eg *Nematodirus*) egg production is not strongly related to the size of the worm burden so pathogenic levels of infection may have low egg counts;
  - *Cooperia oncophora* is highly fecund and makes a significant contribution to FEC but is not that pathogenic.
- As cattle grow older they develop an immunity that reduces worm fecundity, so egg count becomes a less reliable indicator of the size of a worm burden;
- Faecal egg production per worm varies with the time of year, particularly those present in fit, healthy animals in good body condition and with a strong immunity. Generally, egg production is highest when larval intake is lowest;
- During the winter months high levels of arrested worm burdens may be present but the FEC is zero.

Despite these limitations, FECs can be used to help decide if anthelmintic treatment is necessary, or can be safely delayed or omitted. On some farms, FEC monitoring may allow anthelmintics to be better timed, and therefore used more efficiently rather than less frequently. On other farms where anthelmintics are used excessively, FEC monitoring may provide a farmer with the necessary additional information to reduce anthelmintic frequency, while continuing to manage the risk of disease outbreaks or lost productivity.

The following table is presented only as a guide to the interpretation of faecal egg counts in cattle. Egg numbers may vary greatly between individuals.

Worm Species	Faecal Egg Counts (FEC)		
	Low	Medium	High
Mixed Infection	100	200-700	700 +
Ostertagia ostertagi	150	200-500	500 +
Trichostrongylus spp.	50	50-300	300 +
Cooperia spp.	500	500-3000	3,000

8.3. Baermann's test for lungworm larvae

The Baermann's apparatus is used to identify the first stage larvae of *D. viviparus* present in faeces. The apparatus consists of a sieve, with either gauze or filter paper, placed in glass funnel connected to a rubber tube and held in a retort stand. Faeces are placed on the gauze and the funnel is slowly filled with water until the faeces are immersed. The apparatus is left overnight at room temperature during which the larvae migrate out of the faeces and through the sieve to sediment in the neck of the funnel. A clip on the rubber is then removed and the water in the neck of the funnel collected in a small beaker for subsequent microscopic examination.

8.4. Serum enzyme assays

8.4.1. Serum pepsinogen

Large populations of *O. ostertagi* can induce extensive pathological and biochemical changes and these are maximal when the parasites are emerging from the gastric glands (about 18 days after infection), but may be delayed for several months when arrested larval development occurs. In heavy infections of 40,000 or more adult worms, the principal effect of these changes is a reduction in the acidity of the abomasal fluid (the pH increasing from 2.0 up to 7.0) resulting in failure to activate pepsinogen to pepsin. The subsequent leakage of pepsinogen into the circulation leads to elevated plasma pepsinogen concentrations and the loss of plasma proteins into the gut lumen, eventually

leading to hypoalbuminaemia. In clinically affected calves up to two years old, plasma pepsinogen levels are usually in excess of 3.0 i.u. tyrosine (normal levels are 1.0 i.u. in non-parasitised calves). The test is less reliable in older cattle where high values are not necessarily correlated with large adult worm burdens but instead may reflect plasma leakage from a hypersensitive mucosa under heavy larval challenge. Elevated pepsinogen values can be observed in clinically healthy cows and there appears to be some correlation between serum pepsinogen and *O. ostertagi*-specific antibody levels in adult cows, suggesting that adult cows with elevated serum pepsinogen levels may suffer some production losses.

8.4.2. Serum gastrin

Serum gastrin has been proposed as a potential diagnostic tool for ostertagiosis. However, a very high infection dose (>100,000 L3) is required to provoke a significant gastrin release in parasite-naïve calves. The technique is expensive and serum gastrin has a weak stability over time. Therefore, gastrin determination is not considered as a useful tool for routine monitoring of *Ostertagia* infections.

8.5. Serological assays

8.5.1. *Ostertagia* ELISA

An *Ostertagia* ELISA has been developed that can be used to detect worm infections in adult milking cattle and potential effects on milk production (Sanchez et al, 2002, Charlier el al 2005). A number of potential disadvantages exist with such ELISAs that are based on crude worm extracts as cross-reactions with other helminths may occur. Some cross-reaction with *Cooperia spp*. occurs but this is not considered as a disadvantage if the aim is to estimate the overall burdens. However, cross-reactions with *Dictyocaulus viviparus and Fasciola hepatica* can pose difficulties where these co-infections co-exist. The test may require further standardisation and repeatability before it can be used in the field to determine the need for worm treatment of adult milking cows.

8.5.2. Lungworm ELISA

Several lungworm ELISAs have been developed to detect lungworm-specific antibodies. Most are based on the use of native lungworm antigen but more recently recombinant proteins have be developed for use in commercialised "dipstick" ELISAs such as the *Ceditest*™ Lungworm ELISA (Cedi-Diagnostics Lelystad, The Netherlands). The presence of antibody indicates exposure but not necessarily active infection or immunity to the disease. This means that ELISA results used to diagnose infection in individual animals must be interpreted with care and it is more appropriate to submit a representative number of blood samples from a suspect herd.

With the lungworm ELISA available through the VLA for example, individual results are reported as either positive or negative, and therefore give no indication of the level of infection, nor if the infection is active. A number of positive results, however, do provide an indication of herd exposure and the need for further investigations and/or possible treatment.

8.5.3. Fluke ELISA

Diagnosis of liver fluke infections in cattle is normally based on *Fasciola* eggs in faeces, however, this is not possible during the prepatent period and FEC suffers from poor sensitivity during the patent period due to the relatively low number of eggs shed in cattle faeces. To improve diagnosis during both early and chronic phases of infection, several ELISA techniques have been described. Some of these tests rely on antibody detection using crude somatic extracts or excretory/secretory (E/S) products of *F. hepatica*. The specificity of antibody responses to *F. hepatica* varies during the course of infection and as a result, several antigens have been identified for use in serological tests. Whilst ELISA antibody tests can identify animals with prepatent infections, a disadvantage with these tests is that a positive result does not necessarily indicate a current infection, but rather a history of exposure. It has been shown for example, that antibodies persist in fluke-infected cattle after treatment with triclabendazole for up to 7 months.

As with the lungworm ELISA, results used to diagnose infection in individual animals must be interpreted with care.

8.6. Bulk milk tank ELISA

Monitoring worm infections in adult cattle can be used to evaluate the effectiveness of worm control measures and to target anthelmintic treatments where required. In dairy cows, research has focused on the detection of parasite antibody levels in individual or bulk tank milk, because this medium is less costly to sample than blood samples and therefore potentially more suitable for monitoring.

8.6.1. *Ostertagia* milk ELISA

Factors such as milk yield, age of the cow, stage of lactation and the level of mastitis in a herd can all influence milk antibody levels. The ELISA has a reported good repeatability and results suggest that the ELISA can be used to assess whether GI-nematode infections are potentially affecting milk yield in a herd. However, monitoring worm infections in adult cattle by this means has not been routinely adopted yet. Reasons for this may be incomplete knowledge on the effects of GI nematodes on milk yield, the fact that *O. ostertagi* ELISA has only recently become available, or that subsequent evaluation in the field has only recently been initiated in some countries.

8.6.2. Lungworm milk ELISA

An ELISA for the detection of antibodies against the bovine lungworm, *Dictyocaulus viviparus*, in milk has been reported but is not available for use in the UK. The reported test specificity and sensitivity were 100% and 97.5% respectively, and the test offers the potential for routine veterinary diagnosis of lungworm exposure using milk samples instead of sera.

8.6.3. Fluke milk ELISA

The milk ELISA has been reported as an effective alternative to the serum ELISA for diagnostic and surveillance purposes. The test may be more cost-effective since veterinarians are not required to collect milk samples and farmers can submit samples. It has been adapted and validated from the serum ELISA for use with samples of bulk tank milk. The reported sensitivity is 96 % with a specificity of 80% which is comparable to the serum test in terms of its diagnostic sensitivity and specificity.

9. Strategies

9.1. Risk management for pastures

	HIGH	MEDIUM	LOW
SPRING	Grazed by first year calves in the previous year	Grazed only by adult or yearling cattle the previous year Grazed by beef cows (with or without calves at foot) the previous year	New leys / seeds or forage crops Sheep or conservation only in the previous year
FROM MID JULY	Grazed by first year calves in the spring	Adult cattle or conservation in the spring Pasture clean at the start of the year and grazed by parasite-naïve calves	Grazed by sheep or conservation only in the first half of the grazing season Forage crops or arable by-products

9.2. Mixed grazing

Pasture contamination and infectivity levels can be reduced by grazing sheep and cattle together. This effectively reduces the stocking density of the host species but can make pasture utilisation more difficult. In single-suckled beef production systems, the grazing of immune cows with their calves acts in a similar way by reducing pasture infectivity levels for the susceptible calves.

9.3. Additional risk factors

9.3.1. Rainfall and temperature

In dry years, the levels of infective larvae on the pasture are lower, but once it rains, there tends to be a huge increase in infectivity as the L3 larvae emerge from the dung. It is common, therefore, to see heavy worm burdens in the autumn and winter following a dry summer. This is particularly true for lungworm infections in calves in their first grazing season.

9.3.2. Previous exposure

Calves will not normally develop immunity to re-infection with *Ostertagia spp.* until they have been exposed to constant re-infection for an entire grazing season. With lungworm infections calves exposed to *Dictyocaulus viviparus* quite rapidly acquire patent infections, readily recognisable by the clinical signs. After a period of a few weeks, immunity develops and the adult worm burdens are expelled. On subsequent exposure in succeeding years such animals are highly resistant to challenge, although if this is heavy, clinical signs associated with the re-infection syndrome may be seen. However, this is an acquired immunity that is dependent on sufficient exposure to the parasites, and at this age is not as strong and effective as in adult animals.

Indoor calves turned out late in the season, or reared indoors and turned out as yearlings may be parasite-naïve and succumb to PGE when subsequently exposed, irrespective of their age. This can be an issue in yearling calves reared indoors in their first year of life and turned out to grass as yearlings for finishing at grass, or with lungworm infections in dairy heifers or cows that have had little previous exposure to lungworm infections at pasture.

9.3.3. Concurrent disease

The ability of cattle to withstand a challenge from these parasites may be impaired by concurrent disease. Conversely, infection with parasitic disease may predispose animals to other infectious diseases. Thus, for example, liver fluke may

increase the susceptibility of cattle to infection with *Salmonella Dublin* or predispose infected animals to *"Black Disease" (Clostridium novyi)*.

9.4. Systems of production

The UK cattle industry can be divided into two distinct farming systems of production. In beef herds, cows generally calve in spring or the autumn. Dairy herds can also follow a similar seasonal pattern of calving although in many dairy herds calving occurs all year round with only minor seasonal peaks. On dairy farms, calves are removed from their dams at or soon after birth, while on beef breeding farms the calves typically remain with their dams until weaning, when calves are generally 6-8 months of age. For both systems, young stock can typically be considered as either first year or second year grazing animals with exposure to parasitic worms dependent on the month of birth and subsequent management.

Approaches to parasite control in dairy herds reflects the management of the calves, which are removed from the dam soon after birth and raised indoors, independent of their dams, on milk substitute and concentrates until weaning. Many dairy farms will cull their male calves or sell them for beef production, hence young stock remaining on the farm comprises mainly heifer replacements. Age at turnout and time of turnout will therefore depend on month of birth and availability of pasture.

Spring-calving herds aim to produce the bulk of milk from grass, and calving typically occurs in late winter/early spring. Weaned calves may therefore be turned out onto grass as early as two months of age in April or May. If the calving season is more protracted, calves may be kept inside until after weaning and turned out from mid-summer onwards. The risk period for calves from parasitic infections in their first grazing season may vary from just a few months to the whole grazing season.

Calves turned out in spring follow the classic sequence of events of acquiring infection from over-wintering infection and subsequent pasture contamination. Depending on rainfall and temperature conditions, this results in a build up of pasture infectivity from mid July onwards and a high risk of disease and production losses.
Calves turned out mid season onto pasture that has been grazed by older calves could be exposed to high levels of pasture larval challenge and be at risk to disease. If pasture is available in the form of aftermaths then infections could be low and the risk of disease less.
Calves from all year round breeding herds may be born in any month of the year and in such systems their first grazing season could last from a few months to the whole grazing season. Calves born late in the summer or autumn and may not graze until the following year, entering their second year as relatively parasite-naïve animals.

In spring calving beef herds, cows are typically immune and suckling calves are not exposed to pasture-derived parasitic infections until weaning at about 6 months of age. Thereafter, higher worm burdens may be acquired depending on levels of pasture infectivity. More often, because of the limited exposure to worm infections, these calves may fail to acquire protective immunity and suffer production losses in their second grazing season. Under both these systems of production appropriate monitoring and control strategies need to be applied during the animals' second grazing season.

Autumn-born suckled beef calves, particularly if housed over the winter, will have little or no exposure to worm infections until turn out in the spring when they will be consuming a high proportion of grass in their diet. As a consequence they are more prone to worm infections earlier in the grazing season. Exposure will be dependent on the numbers of over-wintering infective larvae but cycling of infection can occur leading to build up of infective larvae on pasture from mid July onwards. There is therefore potentially high risk of clinical disease and production losses similar to that seen in dairy calves in their first grazing season.

On non-breeding farms, animals destined for beef production are purchased either from beef breeding herds or dairy herds for fattening. Cattle may be purchased either as calves at just a few weeks of age from dairy herds, or as weaned beef calves typically 6-9 months of age, or older. On these farms the approaches to parasite control depend on several factors including the previous grazing histories, the intended weight and age at which calves are to be sold, the time of year, the type of farm and the availability of pasture.

Summary of endoparasite control issues and implications in beef and dairy cattle

System	Features / risks	Implications for Control
Spring Calving Dairy Herds	Adult cows usually immune but may be sub-clinical production effects on high-producing animals Calves turned out in spring may experience high overwintering infections and show clinical signs of disease. Calves grazing the same pastures become exposed to higher worm burdens from mid-July onwards.	Monitor and treat with eprinomectin during lactation if considered necessary Turnout calves onto safe pasture. Treat calves in early part of grazing season to minimise pasture contamination using bolus or timed treatments with ML. Lungworm vaccine prior to turnout in lungworm high risk areas. FEC monitoring and treatment where necessary. Alternatively, move to safer pastures mid July onwards.
Autumn Calving Dairy Herds	Housed calves may acquire significant infection early in the next spring. Calves grazing the same pastures become exposed to higher worm burdens from mid-July onwards.	Turnout calves onto safe pasture. Treat calves in early part of grazing season to minimise pasture contamination using bolus or timed treatments with ML. Lungworm vaccine prior to turnout in lungworm high risk areas. FEC monitoring and treatment where necessary. Alternatively, move to safer pastures mid July onwards. Treatment for arrested worms on housing,
All Year Round Calving herds	Calving may occur in any month of the year. Calves born in spring may be turned out at 2-3 months of age or as yearlings the following spring Calves born in late summer or autumn may not graze until the following spring.	FEC monitoring and preventative control measures where necessary. Graze low or moderate risk pastures in spring. FEC monitoring and preventative control measures where necessary. Graze low or moderate risk pastures in spring.
Spring Calving Beef Herds	Cows are typically immune and excrete low numbers of worm eggs in faeces. Spring Calving Beef Herds Calves are susceptible to infection but mainly milk feeding until weaning at about 6 months of age and thus acquire only modest worm burdens. High worm burdens may be acquired post-weaning depending on pasture larval levels and management thereafter. If exposure is low, beef calves may fail to acquire protective immunity and suffer reduced growth rates in their second season at grass.	Treatment unnecessary. Treatment for fluke and ectoparasites may be required on housing. Treatment unnecessary FEC monitoring and treatment where necessary. Move to safer pastures after weaning. FEC monitoring and preventative control measures where necessary. Graze low or moderate risk pastures in spring. Housing treatment for arrested worms, Fluke and ectoparasite treatment may be required.
Autumn Calving Beef Herds	Autumn-born suckled calves, particularly if housed, may acquire significant infection early in the next spring. High worm burdens may be acquired post-weaning depending on pasture larval levels and management thereafter.	FEC monitoring and preventative control measures where necessary. FEC monitoring and preventative control measures where necessary. Housing treatment for arrested worms. Fluke and ectoparasite treatments may be required.
Non-Breeding Herds	Purchased animals from beef or dairy herds for fattening	Varies depending on age at purchase and management system. FEC can be used to determine the need to treat.

10. Bibliography

General

Cattle Book (2008) Defra Website https://statistics.defra.gov.uk/esg/cattlelp.htm

Charlier, J., Claerebout, E., Duchateau, L., Vercruysse, J. (2005). A survey to determine relationships between bulk tank milk antibodies against *Ostertagia ostertagi* and milk production parameters. *Vetinary Parasitology 129, 67–75*.

Sanchez J., Dohoo I., Leslie K., Keefe G., Markham F., Sithole F. (2005). The use of an indirect *Ostertagia ostertagi* ELISA to predict milk production response after anthelmintic treatment in confined and semi-confined dairy herds. *Veterinary Parasitology* 130, 115-124

Taylor M.A. Coop R.L., Wall R.L. (2007) Veterinary Parasitology 3rd Edition, Chapter 3: Parasites of Sheep and Goats. Blackwell Publishing, Oxford

Taylor M.A. (1996). Bovine Anthelmintics: an overview of current thinking. *Veterinary Practice* 28, 7-8

Taylor M.A. (1999) Anthelmintics for cattle: a review. *Cattle Practice* 7, (2) 157-167

Taylor M.A. (2000). Use of Anthelmintics in Cattle. *In Practice*, 22, 290–304

Taylor M.A. (2004). Bovine Antiparasitics. In: Bovine Medicine, Diseases and Husbandry of Cattle, Blackwell Scientific Publications, 2nd edition (Ed A H Andrews).

Vercruysse and Rew (2003). Macrocyclic Lactones in Antiparasitic Therapy, CABI Publishing, Oxford, p187

Anthelmintic resistance

Barton C.H.J., Dale E.F.,Dixon C., Coles G.C. (2006). Survey of parasite control on beef farms in south-west England. Veterinary Record 159, 682-883

Coles G C and Taylor M A (1990). Animal Production and the Problem of Anthelmintic Resistant Nematodes. *State Veterinary Journal* 144 (124), 40-53

Coles G C, Bauer C, Borgsteede F H M, Geerts S, Klei T R, Taylor M A and Waller P J (1992). World Association for the Advancement of Veterinary Parasitology (WAAVP) Guidelines for Detecting Anthelmintic Resistant Strongylid Nematodes of Ruminants, Horses and Pigs. *Veterinary Parasitology* 44, 35-44

Coles,G.C., Jackson F; Pomroy,W.E., Prichard,R.K., Samson-Himmelstjerna,G., Silvestre,A., Taylor,M.A., Vercruysse,J. (2005). The detection of anthelmintic resistance in nematodes of veterinary importance. *Veterinary Parasitology* 136, 167 – 185

Fiel C.A., Saumell C.A., Steffan P.E., Rodriguez E.M. (2001). Resistance of *Cooperia* to ivermectin treatments in grazing cattle of the Humid Pampa, Argentina. *Veterinary Parasitology* 97, 213-219.

Mason, P.C., McKay, C.H. (2006) Field studies investigating anthelmintic resistance in young cattle on five farms in New Zealand. *New Zealand Veterinary Journal* 54 (6) 318-322.

McKenna P.B. (1991). Resistance to benzimidazole anthelmintics in cattle in New Zealand. *New Zealand Veterinary Journal* 39, 154-155.

Stafford, K., Coles, G. (1999) Nematode control practices and anthelmintic resistance in dairy calves in the south west of England. *Veterinary Record* 144 659-661.

Suarez, V.H., Cristel, S.L. (2006) Anthelmintic resistance in cattle nematode in the western Pampeana Region of Argentina. *Veterinary Parsitology* 144, (1-2) 111-117.

Sargison N., Wilson D., Scott P. (2009). Relative inefficacy of pour-on macrocyclic lactone anthelmintics treatments against *Cooperia* species in Highland calves. *Veterinary Record* 164, 603

Taylor M.A. (1992). Anthelmintic Resistance in Helminth Parasites of Domestic Animals. *Agricultural Zoology Reviews* 5, 1-50

Taylor MA, Hunt KR and Goodyear KL (2002) Anthelmintic resistance detection methods. *Veterinary Parasitology* 103, 183-194

Vermunt J.J., West D.M., Pomroy W.E. (1995). Multiple resistance to ivermectin and oxfendazole in Cooperia species of cattle in *New Zealand. Veterinary Record* 137, 43-45

Vermunt J.J., West D.M., Pomroy W.E. (1996). Inefficacy of moxidectin and doramectin against ivermectin-resistant Cooperia spp. of cattle in New Zealand oxfendazole in *Cooperia* species of cattle in *New Zealand. New Zealand Veterinary Journal* 44, 188-193

Waghorn, T.S, Leathwick, D.M., Rhodes, A.P., Jackson, R., Pomroy, W.E., West, D.M., Moffat, J.R. (2006) Prevalence of anthelmintic resistance on 62 beef cattle farms in the North Island of New Zealand. *New Zealand Veterinary Journal* 54, 278-282

Liver and rumen flukes

Foster A.P., Otter A., O'Sullivan T., Cranwell M.P., Twomey D.F., Millar M.F. and Taylor M.A. (2008). Rumen fluke (paramphistomosis) in Britain Cattle. *Veterinary Record* 162, 528

Taylor M A (1987). Update: Liver fluke treatment. *In Practice*, 9, 163-166.

Mitchell GBB (2007) Liver fluke. In: *Diseases of sheep*. ID Aitken (Ed), 4th ed. Blackwell Sciences Ltd, Oxford, 195-204.

Fairweather I and Boray JC (1999) Fasciolicides: Efficacy, actions, resistance and its management. *Veterinary Journal* 158, 81-112.

Lungworm

David G.P. (1997). Survey on lungworm in adult cattle, *Veterinary. Record* 141, pp. 343–344.

Duncan J.L., Armour J., Bairden K., Urquhart G.M. and Jorgensen R.J. (1979). Studies on the epidemiology of bovine parasitic bronchitis, *Veterinary. Record* 104, pp. 274–278

Leaflets

EBLEX (2010). The BRP Beef and Sheep Parasite Control Guide. A comprehensive list of products for the control of internal and external parasites in beef cattle and sheep. Website: www.eblex.org.uk

11. GLOSSARY

Acquired immunity	immunity acquired following exposure to parasite antigens as opposed to innate immunity which is natural resistance to an organism
Anthelmintic	a compound ("wormer") used to treat or control parasitic worms at some stage in their life cycle
Asymptomatic	no symptoms
Bionomics	the influence of environment (particularly temperature and humidity) on the development of free-living life cycle stages.
Biotic potential	the ability of an organism to increase in numbers; for parasites, this is largely determined by the numbers of off-spring produced by sexual and asexual phases of reproduction, and the generation time.
Bradycardia	decrease in heart rate
Carrier animals	animals infected but showing no clinical signs
Catarrhal enteritis	inflammation of the intestinal mucosa with excessive production of mucous
Definitive (final) host	the host in which sexual reproduction (of the parasite) takes place.
Direct life cycle	there is no intermediate host in the life cycle.
Dose limiting species	the species of parasite least susceptible to a wormed product at the recommended dose rate
Dyspnoea	difficulty in breathing
Ectoparasites	parasites that live on the surface of the host or embed themselves into the skin.
Endoparasites	parasites that live within the body of the host.
Epidemiology (epizootiology)	factors governing the spread of infection and disease through host populations.
Erythematous	redness caused by congestion of capillaries, occurs with inflammation
Generation time	time taken for one generation to complete its life cycle. This can be from a few days (e.g. coccidia) to several years (e.g. the sheep tick) and may be dependent on climate.
Helminth	a parasitic worm including the class types nematode (roundworm), cestode (tapeworm) or trematode (fluke)
Horizontal transmission	transmission of the parasite through the host population.

Host specificity	some parasites have a wide host range, others a narrow host range, whilst still others are highly specific.
Hyperpnoea	abnormal increase in depth and rate of respiration but not laboured
Hypobiosis	development of parasite ceases at a particular stage in the life cycle and metabolic rate slows considerably (**arrested** or **arrestation**); duration probably predetermined genetically and triggered by environmental factors or stimuli such as temperature or light intensity.
Hypobiotic	inhibited or "arrested" development of worm larvae within the animal brought about by external stimulii
Indirect life cycle	an intermediate host is involved in the life cycle.
Intermediate host	a host (other than the final host) in which development (sometimes including asexual reproduction) of the parasite takes place - usually an essential part of the life cycle.
Nematode	a worm in the Class Nematoda, these are round worms
Obligatory parasite	has to be parasitic for at least part of its life cycle.
Operculate	refers to eggs with a hinged 'lid'
Ovicidal	having activity against parasite egg stages
Parasitic zoonosis	parasitic infection transmitted from vertebrate hosts to man.
Parasitism	two species living together, one (the parasite) at the expense of the other (the host).
Paratenic host	the parasite enters host tissues but no development or growth takes place (often, the parasite is waiting for its paratenic host to be eaten by its next intermediate or final host, eg *Toxocara cati* in a mouse).
Patency	presence of adult egg-laying parasites as detected by faecal egg counting methods
Parthenogensis	asexual reproduction in which eggs are produced and develop without fertilisation and requiring only the female of the species
Pathogenesis	the sequential development of pathological changes that take place within the host during a disease process.
Percutaneous	through the skin
Periparturient period	the period around the time of birth including late gestation and the first few weeks after parturition

Predilection site	most parasites establish at a particular anatomical site or in a particular tissue.
Prepatent period	the time from infection of the host to the appearance of eggs or larvae in faeces or blood.
Prevalence and incidence	the prevalence of infection is the proportion of an animal population harbouring the parasite; the incidence of the associated disease is the number of new cases per unit time. Thus the prevalence of liver fluke in a herd of cattle in an endemic area is likely to be 100% but the incidence of fasciolosis in that herd will probably be much lower.
In-refugia	term used to describe the free-living stages of parasitic worms present on pasture either as eggs or larvae
Reservoir host	an infected definitive host, which can act as a source of infection for other animals.
Somatic larvae	Larvae found within the muscles
Sporangium or seed capsule	reproductive part of fungus where spores develop
Tachypnoea	rapid respiration
Therapeutic safety index	the index or range which within treatment is safe
Transport host	a loose association in which the parasite "hitches a lift", i.e. is merely carried. This may be a means of geographical dispersal or of enhancing opportunity for infecting a host.
Vertical transmission	transmission of the parasite from one host generation to the next; for example, prenatally or via (e.g. *Toxocara vitulorum*)

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