360° LIVER FLUKE CONTROL
In 1379, Jean de Brie was the first to describe “liver rot” without directly attributing it to the liver fluke, although its presence was noted.

Since then, many researchers have studied this parasite whose biological description is well known but whose abilities to adapt to changes in cattle management and anthelmintic treatment is still surprising us today!

Even with effective drugs and knowing perfectly well how to identify danger areas and risk factors for infection, we still observe a prevalence of this parasite that is far too high.

This technical manual offers knowledge about this parasite: its significance in terms of health and economics, its lifecycle and the control methods adapted to the epidemiological situation faced by Australian farmers.
Liver fluke, *Fasciola hepatica*, is a major parasite of livestock in temperate regions throughout the world, including Australia. Liver flukes infect upwards of 300 million cattle and 250 million sheep worldwide, causing economic losses of $AUD 3 billion per year (Spithill et al., 1999). In Australia, it is estimated some 6 million cattle and 40 million sheep graze pastures in endemic liver fluke areas, costing producers in excess of $AUD 100 million per year in lost production and control (Boray 1999).

Fluke-infected cattle often demonstrate no clinical disease, but subclinical blood loss, tissue damage and impairment of appetite, which can lead to reductions in growth and weight gain, milk production and fertility. Animals that become heavily parasitised, however, can develop severe clinical disease and may die. Young animals are particularly vulnerable.

While liver flukes can have devastating effects on animal health and performance, they are relatively easily controlled. They have a complex lifecycle that is closely linked with particular habitats and heavily influenced by season. This means that we can design highly effective strategic control programs that suppress fluke numbers to levels with minimal economic impacts. The key to success is using the best products at the best times.

The FlukeKill™ program, a Virbac initiative, guides you through treatment timing and product choice. The program, which was designed with the assistance of Dr Joe Boray, the world’s leading authority on liver fluke, aims to limit the economic impact of the liver fluke in a highly effective and sustainable way.

**PARASITE OVERVIEW**

Liver fluke *Fasciola hepatica* is a parasitic flatworm that can live within a wide range of hosts including livestock (cattle, sheep, goats and horses), feral animals (rabbits and pigs), wildlife (kangaroos) and humans. Liver fluke is common in temperate areas including Europe and North America and was introduced to Australia through infected livestock imported in colonial times. A closely related species *Fasciola gigantica* is found in tropical regions throughout the world, but not Australia.
Liver fluke is found throughout south-eastern Australia, generally where annual rainfall is 600mm or more, or in drier areas where irrigation channels are accessible by livestock. This includes south-eastern Queensland, eastern New South Wales, most of Victoria and parts of Tasmania and south-eastern South Australia.

It is not unusual, however, for infected livestock to be found well outside of these well-known fluke areas since the parasite can survive for years within the host animal. For example, fluke-infected dairy cattle were detected in north Queensland, but when the origin of the infected individuals was traced back, they had all been imported from Victoria some years previously (Molloy and Anderson, 2006).

Western Australia is free of liver fluke and enforces strict quarantine procedures to maintain that status.

To confirm this distribution, Virbac Animal Health conducted a study in cattle across eastern Australia during 2004 (the largest survey of its kind to date). Overall, of the 700 plus properties tested, 55% were found to have liver fluke infections in their herds. Of the properties that tested positive, 66% had greater than half of the herd infected.
LIVER FLUKE LIFECYCLE

1. Adult flukes in the bile ducts produce eggs, which are passed out in manure and hatch when separated from faecal material in wet areas.

2. The first larvae or miracidia released invade the lymnaeid snails (intermediate host) living in wet areas.

3. The miracidia develop and multiply as sporocyst, rediae and cercariae.

4. The tadpole-like cercariae leave the snails.

5. The cercariae attach to vegetation, forming metacercariae. This is the infective stage of the fluke.

6. Cattle ingest the metacercariae. The young flukes hatch from the metacercariae in the small intestine and then penetrate the intestinal wall. The flukes are chemically attracted to the liver and begin their migration.

7. The young flukes penetrate the liver capsule and migrate through the liver tissue for six to eight weeks before entering the bile ducts where they become adult flukes.
The young flukes reach the liver within about a week of being ingested. They penetrate the liver capsule and migrate through the liver tissue, feeding on blood and growing rapidly. Young flukes from penetration to five weeks old are referred to as early immature flukes, while from five weeks old they are known as immature flukes.

About eight weeks after ingestion they leave the liver and enter the bile ducts to become adult flukes. They are generally about 2-3cm long when fully mature.

They begin producing eggs about 10-12 weeks after ingestion. While most flukes are eliminated within a year of infection, some have been known to survive several years in cattle and more than seven years in sheep.

The eggs travel with the bile from the gall bladder into the intestine and excreted in faeces. Eggs can accumulate in the gall bladder and may be released for weeks after the flukes have been killed.
FLUKE SNAILS

Only snails in the family Lymnaeidae are suitable as intermediate hosts for the liver fluke. This is a different family of snails from those that carry stomach flukes. Lymnaeid snails are characterised by having a shell with a clockwise spiral and fleshy, triangular tentacles. The main fluke snail in Australia [Austropeplea (Lymnaea) tomentosa] is a native species found in the wetter areas of south-eastern Australia, as per the fluke distribution in the map on page 4. Two introduced species (Austropeplea viridis and Pseudosuccinea columella) can also carry the parasite and have the potential to invade northern Australia.

Lymnaeid snails thrive in areas with very shallow, slow-flowing water. Ideal habitats include springs, small creeks, dam overflows and irrigation channels. When conditions are very dry, the snails can bury into the mud and become dormant, potentially surviving for many months in that state.
THE INFLUENCE OF LIVESTOCK FEEDING BEHAVIOUR

Cattle are particularly prone to liver fluke infections because they often feed in the wet areas that suit the snail intermediate host, which are therefore the areas with the highest level of contamination with metacercariae, the infective fluke stage. Sheep are less prone to infection because they usually avoid feeding in wet areas unless conditions are very dry and they are chasing green feed. During late summer and autumn, the most likely time for infection, pastures dry off in many regions and grazing stock will tend to look for green pick in the wet areas. Similarly, animals will tend to feed more in wet areas in times of drought. Unlike most parasites, infection levels of fluke can increase in dry conditions.

ENVIRONMENTAL INFLUENCES ON LIVER FLUKE POPULATIONS

While both the liver fluke and its snail intermediate host require a wet environment to complete their lifecycles, temperature plays more of a role in influencing liver fluke populations than rainfall does.

Both the flukes and the snails thrive over the warmer months of the year. Heading into winter, when the average daily temperature drops below 10°C, fluke eggs stop hatching, development of the larval flukes in the snails slows down and the snails become inactive. The infective larvae already on the pasture will die out over time and this will happen more quickly when there is very cold weather (e.g. a series of heavy frosts). This means that in colder areas the fluke lifecycle will effectively come to a halt over winter and the opportunity for cattle to pick up new infections diminishes. By the end of winter most of the flukes in the animal will be mature because they haven’t been acquired in the previous few months.

As temperatures become warmer in spring, the fluke snails become active again, potentially releasing parasites that they have carried through the winter. In addition, fluke eggs begin to hatch again, so that snails can quickly become infected if the livestock are carrying appreciable numbers of flukes. The fluke population builds up throughout the warmer months, with peak pasture contamination with metacercariae occurring in late summer/early autumn. This is often the time that clinical disease is observed.

In contrast, in warmer coastal areas where winter temperatures are mild, the fluke lifecycle can continue throughout the year and fluke numbers can continue to build up unless an effective control program is followed.
LIVER FLUKE DISEASE

While adult liver flukes impact on the health of livestock through their blood-feeding habits in the bile ducts, it is the immature and early immature stages in the liver that cause the most damage. The type of disease seen as a result of liver fluke infection is often divided into three categories based on the amount of liver damage caused by the young flukes. Those categories are acute, subacute and chronic.

ACUTE DISEASE

This form of the disease occurs where a large number of metacercariae are ingested over a short period of time. This results in the animal’s liver receiving many puncture wounds as the early immature flukes invade the liver. This damage can lead to the death of the animal through massive blood loss (bleeding into the body cavity) and the onset can be rapid, with the animal rarely showing signs of illness prior to its death. Deaths are generally seen 1-2 weeks after the animals have gained access to wet areas. Young animals are particularly prone to this form of the disease because even minor blood loss can have a major impact on them.

SUBACUTE DISEASE

The subacute form of the disease is seen where animals acquire a moderate number of flukes or a large number of flukes over an extended period of time. This means that there isn’t enough acute damage at any one point in time to cause the animal’s immediate death. There is, however, massive damage to the liver that can lead to the animal wasting away quickly. Deaths occasionally occur around eight weeks after first infection when the immature flukes are at their largest, particularly in young animals, but in most cases the issue will have been identified and treated before the animals deteriorate to that point. The scarring and fibrosis that result from the liver damage can lead to permanent damage and underperformance of the animal.

CHRONIC DISEASE

This form of the disease results from the ongoing acquisition of smaller numbers of flukes and is the form seen most commonly in adult cattle. Animals may waste away over an extended period of time, becoming emaciated, lethargic and anaemic as a result of tissue damage and blood loss. Other physiological responses include suppressed appetite and reduced feed conversion efficiency. They will often develop a distended abdomen and bottle jaw (indicators of a fluid imbalance associated with the loss of red blood cells). The majority of animals, however, will show no obvious signs of infection and will simply not perform as well as they should. A fluke burden of as few as 30 flukes is sufficient to retard an animal’s performance and an infection rate of 10% of the herd is considered to be the threshold where economic impacts become significant.
IMMUNITY TO LIVER FLUKE INFECTION

Can animals protect themselves from liver fluke?

There is little evidence that livestock can mount resistance to their first challenge from liver fluke. A form of resistance can develop over time but this is physiological and requires extensive prior damage to be caused to the liver, namely hardening and calcification of the bile ducts. Unfortunately, this type of resistance is not a protective immune response, having little ability to control immature flukes. Although fluke numbers can be suppressed, liver damage and consequently production loss will occur.

With the help of Virbac Animal Health, Professor Terry Spithill and his team at La Trobe University plan to develop a vaccine that allows livestock to develop a protective immune response to liver fluke. Professor Spithill, who has more than 30 years experience in parasite immunology, including investigating the genetics of triclabendazole-resistant fluke, says “A successful vaccine that provides protection will kill invading immature parasites before significant liver damage occurs, and consequently reduce production loss caused by liver fluke.”

However, with a vaccine for liver fluke some time away, all classes of animal still require an effective liver fluke control program. Professor Spithill says, “Not only do animals have little ability to mount a protective immune response to the first liver fluke infection, there is good evidence that fluke infection actually suppresses the animal’s immune system and immune responses to other diseases may be altered”.

Professor Terry Spithill is the co-director of The Centre for AgriBioscience at La Trobe University. His major area of research investigates host immune responses to parasites, parasite immune evasion mechanisms, drug resistance, and parasite proteomics with the aim to develop vaccines or drugs to control parasitic diseases.
ECONOMIC IMPACTS

The economic impacts of liver fluke infection include reduced growth rates and weight gains, reduced milk production, reduced fertility, liver condemnation, secondary bacterial infection, mortality, and increased drenching costs (Boray, 1985; Dargie, 1986).

LOWER GROWTH RATES AND WEIGHT GAINS

Studies have shown that even subclinical infections of as few as 30-40 flukes can reduce weight gains by 8-9%, while higher levels of infection have reduced weight gains by 28% (Ross, 1970; Hope Cawdery et al., 1977). While the greatest impact occurs in the first 16 weeks of infection, the performance of animals can be impaired for the rest of their lives, even after the flukes have been removed (Hope Cawdery et al., 1977). Young animals are particularly vulnerable and may never reach their genetic potential regardless of subsequent management.

IMPAIRED FEEDLOT PERFORMANCE

Several feedlot studies conducted in the USA have demonstrated that treatment of fluke-infected cattle with an effective flukicide at induction produces a positive cost-benefit result and improved productivity. The studies showed increases in weight gains between 5.9% and 9.5%, compared with animals carrying fluke burdens (Hicks et al., 1989; Malone et al., 1990).

LOWER CARCASS VALUE

In addition to reduced growth in the feedlot, abattoirs will condemn livers that show visible damage. Recent trials show that liver infection reduces cold carcass weight, carcass yield, marbling score and conformation (Brown & Lawerence, 2010; Sanchez-Vazquez & Lewis, 2012). The reduced value of carcasses through liver condemnation and quality downgrades alone exceed the cost of an effective treatment.

REDUCED MILK QUANTITY AND QUALITY

The effect of liver fluke infection on milk production is well documented and the parasite can be a significant impediment to dairy farming. A heavy infection can cost 0.7kg/cow per day in lost milk production and 0.06% reduction in milk protein (Charlier et al., 2007). While this has a direct impact on income for dairy farms, infection can also compromise growth rates in the offspring of infected beef cattle.

REDUCED FERTILITY

Liver fluke infection has been reported to have a negative impact on cow fertility. Infections have been shown to reduce conception rates in heifers by up to 50% and delay puberty by up to 39 days (Oakley et al., 1979). Managing fluke in heifers should be prioritised to limit production losses. In dairy cows, heavy fluke infection can also increase the inter-calving interval by 4.7 days (Charlier et al., 2007).

BLACK DISEASE

Black disease is a clostridial infection that occurs when Clostridium novyi proliferates within damaged liver tissue. Even light fluke infections can create enough damage in cattle to occur. While invariably fatal, the disease is rare these days because of the widespread use of effective clostridial vaccines such as Websters® 5-in-1 or Websters Clepto-7.
THE IMPORTANCE OF CONTROLLING YOUNG FLUKES

It is important to control the youngest stage of liver fluke possible. The longer the immature liver flukes are permitted to migrate through the liver tissue, the greater the damage and productivity losses they cause.

A study by Dr Joe Boray (1999) clearly demonstrated the economic advantage in removing early immature flukes. As shown in the figure opposite, animals that were treated to remove early immature flukes 1-2 weeks post-infection (PI) had greater weight gains than animals treated 4-6 weeks PI or 8-12 weeks PI. After 20 weeks, the average body weight of the early treated group was 8kg heavier than the group treated 4-6 week PI and 13kg heavier than the group treated to remove fluke after they had matured. Based on current stock prices, this could equate to as much as an additional $29 per head (Dargie, 1986).
DIAGNOSIS

As with any animal health issue, it is important to define the problem prior to implementing a control program. There is a range of tests available to detect liver fluke infections. We also now have the ability to determine prevalence of infection within dairy herds and to test the efficacy of treatments. It is important, however, to know the restrictions and capability of each test.

EGG COUNTS

Testing for liver fluke infection has traditionally been done by microscopic detection of fluke eggs in the faeces. While this test is highly reliable for detecting fluke infections in sheep, it is not very reliable for cattle. In cattle, liver flukes are irregular and intermittent egg layers and many flukes never reach the egg laying stage, despite developing and causing damage in the liver; so detection of eggs in the faeces is hit and miss (Vercruysse & Claerebout, 2001). Further, this test will only detect adult flukes, so it is a poor option for diagnosing acute and subacute forms of liver fluke disease.

BLOOD AND MILK ANTIBODY ELISA

The ELISA (Enzyme Linked Immuno-Sorbent Assay) is a test that detects the antibodies that cattle (and sheep) produce in response to liver fluke infection. The antibodies are found in the blood or milk of infected stock as quickly as 3 weeks after infection and the test is highly accurate (98%) for both types of sample (Cornelissen et al., 1999). It is an ideal test for dairy herds because a sample can be taken from the milk vat and the result will indicate the presence of infection across the milking herd. For beef cattle, blood samples are used for detection of fluke infection only i.e. not quantification. Blood samples are usually taken from a representative sample of ten animals, so numbers are insufficient to indicate the prevalence of infection. Antibody levels are not indicative of the number of flukes present in the animals, so they cannot be used to assess the intensity of infection. The drawbacks of this test are that blood samples are difficult to collect and the test cannot be used to assess the efficacy of a treatment because the antibodies take several months to degrade even after all of the flukes have been removed from the animal.

FAECAL ANTIGEN ELISA – RECENT DEVELOPMENT

A test that detects *F. hepatica* antigens (proteins released by the parasite) in the faeces of the host animal has recently been validated for use in Australia. This test is highly accurate and can detect even a few flukes in sheep or cattle, but the flukes are detected only once they leave the liver and move to the bile ducts. While there is an advantage associated with taking faecal samples rather than blood samples from beef cattle, the biggest advantage provided by this test is that it can be used as a post-treatment efficacy test. The antigens in the faeces disappear very soon (1-2 weeks) after the flukes have been removed, so a positive result 3-4 weeks after treatment indicates that flukes have survived the treatment and may be resistant to the chemical used.
POST-MORTEM EXAMINATION

Examination of the liver can be useful in a number of situations and used to determine how heavily animals are infected. Examination of the liver is the only way to determine if an animal has died from the acute form of liver fluke disease. Examination will reveal an otherwise healthy looking liver that is full of pinprick holes and leaking a lot of blood. The incidence and severity of the chronic form of the disease can also be gauged by examination of the livers of slaughtered animals. Abattoirs will often provide feedback on the rate of liver condemnations in a particular line of animals, but it is important to confirm the cause of those condemnations to ensure that it is liver fluke causing the problems. It is easy to determine the severity of fluke infection if animals are killed on-farm. Simply remove the liver and look for any signs of damage or scarring. Cut the liver and the bile ducts open and look for any flukes, which will be readily apparent (squeezing the liver may reveal flukes that were not obvious initially). Chronically infected cattle will generally have a brown tar-like deposit on the inside of the bile ducts and the wall of the duct will be thickened and calcified.

Top: Liver showing slight scarring, thickening of bile ducts and an adult fluke.

Right: Chronically infected liver showing thickened ducts, tar-like deposit and adult flukes.
CONTROL METHODS

Like all parasites of livestock, effective and sustainable control must be based on a sound understanding of the interaction between the parasite, its hosts, and the environment (Integrated Parasite Management). There are no chemicals currently registered in Australia for the control of snails, so fluke control measures must focus on limiting exposure of the livestock to infection, and treatment of the animals to remove any parasites they do acquire.

NON-CHEMICAL APPROACHES

Non-chemical control of liver fluke populations focuses on reducing the exposure of livestock to wet areas that harbour the snail intermediate host and the infective stage of the fluke. One approach is to modify the wet areas to make them an unsuitable snail habitat. This could include improving drainage, to dry areas out, or modifying water courses to improve water flow. Another option is to fence the wet areas off so that animals cannot graze in those areas. Unfortunately for many producers, neither of these options is feasible or economically viable as a complete solution. These approaches should not, however, be abandoned entirely. By reducing snail habitat and then fencing off the remaining wet areas, it is possible to manage those areas to minimise infection rates and the subsequent need for treatment of the animals. For instance, fluke-infested areas should not be used to graze young, highly susceptible stock. Where possible, those areas should only be grazed in late winter when the pasture contamination with infective metacercariae is likely to be at its lowest. It is also possible to identify and selectively treat only animals that have been grazing in the risky areas, reducing the amount of chemical treatment required.

CHEMICAL TREATMENT

The effective control of the liver fluke through chemical treatment relies on two key factors: choice of product and timing of treatment. It is only by using the right product at the right time that maximum effect will be achieved.

CHOICE OF ACTIVE INGREDIENTS

There is a wide range of single active and combination products available for liver fluke control and the level of control offered varies remarkably. In order to get an approved label claim, the product needs to be at least 90% effective against each stage of fluke identified on the label. Generally speaking, the younger the fluke is, the harder it is to kill, so while all flukicides will kill the adult flukes, few will kill the early immature flukes and only synergistic combination products reliably kill the 2-week-old early immature flukes.

Efficacy of Actives Against Flukes of Different Ages

<table>
<thead>
<tr>
<th>Active ingredients</th>
<th>Early Immature</th>
<th>Immature</th>
<th>Adult</th>
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<tbody>
<tr>
<td></td>
<td>2 weeks</td>
<td>4 weeks</td>
<td>6 weeks</td>
</tr>
<tr>
<td>Oxyclozanide</td>
<td>+</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Albendazole</td>
<td></td>
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<td>+</td>
</tr>
<tr>
<td>Clorsulon</td>
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<td>+</td>
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<tr>
<td>Nitroxynil</td>
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<td>+</td>
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<tr>
<td>Triclabendazole</td>
<td>+</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Triclabendazole + Oxendazole (Flukazole C)</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Nitroxynil + Clorsulon + Ivermectin (Nitromec)</td>
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</table>

± more effective in cattle than sheep.
Synergy is said to occur only where the combination of chemicals has a greater effect than that expected from the activity of the individual chemicals. In the case of flukicides, this can be seen where nitroxynil (kills adult and late immature flukes) and clorsulon (kills adult flukes only) are combined into one product (Nitromec® Injection). While it might be expected that, at best, the product will provide control of adult and late immature flukes, the synergy between the two chemicals actually gives control of all stages including early immature flukes as young as 2 weeks old. A similar synergistic effect can be seen where a combination of triclabendazole (tcbz) and oxfendazole (Flukazole® C) provides efficacy superior to triclabendazole alone.

Data from on-farm trial work has confirmed that the superior performance of the synergised combination translates to a productivity benefit for the producer.

**Liveweight Gain Following Treatment**

\[(n=20 \text{ per group, mean starting weight } = 273\text{kg})\]

<table>
<thead>
<tr>
<th>Days after treatment</th>
<th>Mean liveweight gain (kg)</th>
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<tbody>
<tr>
<td>40</td>
<td>13</td>
</tr>
<tr>
<td>70</td>
<td>13</td>
</tr>
<tr>
<td>106</td>
<td>21</td>
</tr>
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<td>135</td>
<td>25</td>
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Results from a field trial conducted on Angus weaner heifers on the Southern Tablelands of NSW.
DELIVERY METHOD – ORAL VS POUR-ON

Flukicides have historically been applied as oral (triclabendazole) or injectable (clorsulon, nitroxynil) products. In recent years, however, triclabendazole pour-ons have entered the market place. While clearly having the advantage of ease of application, there is considerable doubt surrounding the ability of these products to perform as well as comparable oral products.

In order for triclabendazole to achieve a high level of efficacy against the early immature and immature liver flukes, the drug must reach a high concentration in the liver. Triclabendazole given orally is absorbed from the gastrointestinal tract and quickly transported to the liver via the portal blood flow, achieving a high concentration of the drug quickly. In contrast, triclabendazole applied topically needs to penetrate through the skin and then travel through the entire vascular system before it reaches the liver. Triclabendazole is quite a large molecule, so this is a highly inefficient method of delivery.

The graph to the right shows the concentration of a marker for triclabendazole in the blood of cattle treated with Flukazole C (an oral triclabendazole + oxfendazole product) or a pour-on flukicide (triclabendazole at 2.5 times the oral dose + abamectin).
When the efficacy against 2-week-old and 4-week-old liver flukes was assessed for the two products, Flukazole C demonstrated superior control compared with the pour-on, as shown in the graphs above.

Further, absorption through the skin is highly variable depending on the coat and skin condition of the animal. A recent study (Sargent, et al., 2009) showed that treatment of cattle in winter with a pour-on flukicide could reduce the efficacy of the product.
Field data has shown that the lower efficacy offered by pour-on triclabendazole treatment translates into lost production.

**EFFICACY OF POUR-ON FLUKICIDES**

<table>
<thead>
<tr>
<th>Season</th>
<th>Winter</th>
<th>Spring</th>
<th>Summer</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Efficacy</td>
<td>60</td>
<td>80</td>
<td>100</td>
</tr>
</tbody>
</table>

**RESULTS FROM A FIELD TRIAL**

- **Efficacy of pour-on flukicides applied at different times of the year.**
- **Mean liveweight gain (kg)**
- **Days after treatment**
- **Mean liveweight gain (kg)**

**LIVEWEIGHT GAIN FOLLOWING TREATMENT**

(n = 22 per group, mean starting weight = 263kg)

- Triclabendazole/Abamectin Pour On
- Nitromec Injection
- Flukazole C plus Se + Cydectin Pour On
- Flukazole C plus Se + Cydectin LA Injection

**EFFICACY OF POUR-ON FLUKICIDES**

- Triclabendazole/Abamectin Pour On
- Nitromec Injection
- Flukazole C plus Se + Cydectin Pour On
- Flukazole C plus Se + Cydectin LA Injection

**TREATING FOR OTHER PARASITES**

Animals that are infected with liver flukes are often carrying other parasites as well, so it is important to consider the other parasite issues that are important at the time of fluke treatment. For instance, Brown stomach worm (Ostertagia ostertagi) is the most damaging roundworm of cattle and is found commonly in those areas where liver fluke is a problem. Other roundworm species are also common and can cause production losses in young animals. It therefore makes good sense in many cases to treat for roundworms at the same time as treating for the liver fluke. This can be done by either using a product that includes a broad spectrum endectocide as well as a flukicide (e.g. Nitromec Injection, Virbamec® Plus Injection) or by using another worming product at the same time as the flukicide. The second approach has the advantage of being able to incorporate a product with highly persistent activity against roundworms such as Cydectin® Long Acting Injection for Cattle, which can provide excellent productivity benefits (see figure above).
CHEMICAL RESISTANCE

Chemical resistance is the ability of a parasite to survive treatment at the normal dose. It occurs via random mutations in the genetic code of the parasites and then builds up within the population when we apply selection pressure in the form of chemical treatment (i.e. resistant worms survive the treatment and reproduce when susceptible worms do not, so the resistant worms become more prevalent within the parasite population).

Triclabendazole was introduced in the 1980s for the treatment of liver fluke infections in livestock. It has been the drug of choice for more than 30 years because it is the only chemical that, by itself, has activity against all three stages of the fluke (early immature, immature and adult). Repetitive use of a chemical for a long period is a high risk factor for the development of resistance and, unsurprisingly, resistance to triclabendazole has developed.

Resistance to triclabendazole was first reported in fluke in Australia in 1995 (Overend and Bowen, 1995) and since that time, has also been reported in several countries in Europe (Brennen et al., 2007). Recent work in Australia has detected resistance in widely spread areas including the southern and northern coasts of NSW, Gippsland, the Tallangatta Valley and the Riverina.

CASE STUDY

In December 2007, a 71-year-old sheep farmer in the Netherlands sought medical care with a 4-month history of intermittent upper body pain, night sweats, anorexia, and a 5kg weight loss. X-ray imaging of the liver showed several large lesions ranging in size from 1 to 4cm. An antibody ELISA was used to diagnose the patient with a liver fluke infection and the finding was confirmed with a faecal egg count. The patient was treated unsuccessfully with Fasinex® (triclabendazole) on 3 separate occasions over the next 2 years. Further attempts to treat the patient with experimental therapies proved unsuccessful, highlighting the serious nature of drug resistance in this parasite (Winkelhagen et al., 2012).
MINIMISING RESISTANCE ISSUES

Chemical resistance in parasites (and other pest species) has been an issue for decades and has been well studied. It is best to be proactive in managing resistance issues because once severe resistance to a particular chemical is established, the options for treatment are limited and control programs often become more complex and more expensive. There are a number of measures that can be taken to minimise the development of resistance. They include minimising chemical use, using the most potent products available, rotating different chemicals and monitoring treatment effectiveness.

MINIMISE CHEMICAL USE

Clearly, the more a chemical is used, the more likely it is that resistance will develop to that chemical. In any parasite control program, the main aim should be to use the minimum number of treatments required to get effective control of the parasite population. By implementing non-chemical strategies and optimising the timing of fluke treatments, the parasite population can be suppressed to a level that will not require additional treatments to overcome outbreaks of disease.

USE THE MOST POTENT PRODUCTS AVAILABLE

The more parasites that survive a treatment, the more likely it is that resistance will build up within the population. It is therefore essential to use the most potent products available for the treatment of any parasite. In the case of flukicides, the synergistic combination products (Flukazole C, Nitromec Injection) are the most potent products available for three stage fluke control. They are the only products on the market that have a claim for the control of 2-week-old early immature flukes.

ROTATION OF DIFFERENT CHEMICALS

Rotation of chemicals will ease the selection pressure placed on the parasite population. Until recently, only triclabendazole-based products could provide three stage fluke control. However, Nitromec Injection now provides an option for rotation away from triclabendazole that still provides control of all fluke stages.

MONITOR TREATMENT EFFECTIVENESS

Many producers discover that they have a parasite resistance issue only when they have an outbreak of disease. It is far better to be proactive in monitoring the effectiveness of the products used and make an informed decision about which active ingredients should be used. The faecal antigen ELISA now provides a simple test that can provide a good indicator of whether resistance issues are emerging and should be done routinely as a post-drench efficacy test every 2-3 years.
Nick Sangster is Professor of Veterinary Pathobiology and Head of the Animal and Veterinary Sciences School at Charles Sturt University. He is currently involved in research that has found triclabendazole-resistant liver fluke in multiple locations in Australia.

“We’ve been out to properties and found isolates where fluke have survived treatment with triclabendazole. We’ve encountered this on the NSW south coast, around Lismore and on the Murray River – in every area we’ve conducted research, we’ve found pockets of resistance.”

Professor Sangster says the best approach is to tackle resistance head on. This means first of all confirming liver fluke ahead of treatment and then introducing a parasiticide rotation program.

“It’s worth spending the money on proper diagnosis before investing in treatment, and when you are treating, rotation of products really is the best advice. It just makes sense that you’re less likely to see the development of resistance issues if you’re rotating products.”
LATE AUTUMN/EARLY WINTER TREATMENT

The autumn treatment is the most important treatment within the FlukeKill program. It is designed to clean out the flukes prior to animals facing the stresses of winter. For this treatment to be most effective, it should be administered following the onset of frosty weather when the opportunity for cattle to pick up new parasites starts to diminish. Once the average daily temperature drops below 10°C, the snails become inactive and the development of the larval flukes slows down, so fluke cercariae are no longer being released from the snails to contaminate the pasture. Further, many of the metacercariae already on the pasture will have been killed by the frost. It is therefore better to err towards treating late rather than treating too early and having the animals reinfected prior to winter.

Livestock can, at this time, harbour flukes of all ages, so it is important to use a product that will give the best control of all stages of the flukes, including the early immature stage. Flukazole C and Nitromec Injection are the most effective products available for use at these times.

Dr. Joe Boray is an internationally recognised expert on liver fluke and his life work underpins most of what we know about the treatment and control of fasciolosis.

"Control of fasciolosis is difficult and eradication is impossible in endemic areas without unsustainable expense. The fluke survives in the host, in the snails and in the environment for long periods under good or unfavourable conditions. Apart from sensible farm management, only a strategic treatment program, according to local climatic conditions, can keep the disease under sustainable control."

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Dr. Joe Boray
LATE WINTER/EARLY SPRING TREATMENT

The spring treatment is an essential preventative treatment that helps to break the fluke lifecycle by removing any flukes that have infected the animals throughout the winter. By preventing the contamination of the pastures with fluke eggs as temperatures warm up, the snail intermediate hosts do not immediately become infected as they become active. It is therefore essential that this treatment occurs prior to the spring break. It is better with this treatment to err towards treating early rather than waiting until too late and having fluke reproduction promoted early in the yearly cycle.

Fluke numbers in animals may be low at the end of winter, particularly if the pre-winter treatment was timed effectively, but even a few flukes can easily seed the environment with larvae (miracidia) that actively hunt out snail hosts. The spring treatment is therefore immensely important in suppressing the early expansion of the fluke population, which has a flow on effect throughout the rest of the fluke season, reducing overall fluke numbers and minimising productivity losses. The spring treatment is even more important if timing for the late autumn/early winter treatment was too early or the winter was mild so that substantial numbers of flukes infected the animals following the pre-winter treatment.

Winters are sufficiently cold in most fluke areas that little reinfection occurs in the later stages of winter. Therefore, the flukes within the animals will have had the required time to mature into the adult stage. This means that an adulticide such as Virbamec Plus will be an excellent option for treatment. However, where treatment has been delayed until after the spring break or in warmer coastal areas where snails have not gone dormant and reinfection has occurred throughout the winter period, it is essential that a product that controls all stages of the flukes (Flukazole C or Nitromec Injection) should be used.

The summer treatment for liver fluke can be very important in certain cases. The most important is in April/May. Some properties also need an August treatment. But on heavily infected properties, or after a series of good seasons, a summer treatment for fluke could be important, to reduce pasture contamination and to avoid fluke disease.

“We have just come out of 2-3 La Niña years, years with above average rainfall. This favoured a build up of liver fluke and their intermediate host snails. Although spring has been dry in places, conditions overall favour increasing snail and fluke numbers from spring right through to autumn, even with average rainfall. Some properties, even those that had an August fluke drench, could have large numbers of infective fluke larvae (metacercariae) in wet areas. This means high infection rates in livestock over summer. If administering a summer treatment, use a flukicide effective against early immature stages, as many of the fluke in affected animals will be from new infections.”

DR. STEPHEN LOVE
SUMMER/EARLY AUTUMN TREATMENT

In our coldest areas, the warmer period of the year is quite short, so fluke numbers rarely exceed levels that require control beyond the two core treatments outlined earlier. In most fluke areas, however, the extended period of warm conditions allows fluke numbers to build up to damaging levels well before the late spring/early winter treatment occurs. Young stock are particularly at risk. In these cases an additional treatment in January or February is recommended to suppress fluke numbers. Summer treatments should utilise products that provide control of the maximum range of fluke ages, particularly the early immature flukes (Flukazole C or Nitromec Injection).

MID-WINTER TREATMENT

In some areas fluke infection can continue throughout the year, even in winter. This can occur in warm coastal areas where the fluke lifecycle continues unabated all year. It can also occur in areas where there is extensive snail habitat and heavy fluke challenge so that many metacercariae survive through at least the early part of winter. Areas where this may occur include irrigation flats and country that has a high number of springs and small streams. In these cases a mid-winter treatment may also be required. Highly effective all stage treatments (Flukazole C or Nitromec Injection) should be used for all mid-winter treatments.

TYPICAL FLUKE CHALLENGE IN ONE YEAR

Typical fluke challenge depending on treatment program.

FlukeKill™ Liver Fluke Control Manual
The following charts provide examples of where these four treatments may be utilised.

**Liver Fluke Control Chart – Corryong, Vic (Upper Murray Valley)**

- **T** Treatment
- **S** Snails active
- **WM** Winter Metac.
- **SM** Summer Metac.

Total annual mean rainfall: 783mm

(Source: Boray, 2002)

**Liver Fluke Control Chart – Orbost South-East, Vic (Snowy River)**

- **T** Treatment
- **S** Snails active
- **WM** Winter Metac.

Total annual mean rainfall: 851.9mm

(Source: Boray, 2002)
LIVER FLUKE CONTROL CHART – KEMPSEY, NSW (NORTH COAST)

Av. monthly rainfall (mm) and Av. daily temp (°C) for Kempsey, NSW (North Coast).

Total annual mean rainfall: 783mm (Source: Boray, 2002)

LIVER FLUKE CONTROL CHART – GOULBURN, NSW (SOUTHERN TABLELANDS)

Av. monthly rainfall (mm) and Av. daily temp (°C) for Goulburn, NSW (Southern Tablelands).

Total annual mean rainfall: 1201mm (Source: Boray, 2002)

Symbols:
- T: Treatment
- T*: Optional treatment
- S: Snails active
- SM: Summer Metac.
- WM: Winter Metac.
PRODUCER TESTIMONIAL

Using a more effective fluke treatment in your cattle can save thousands of dollars according to a recent trial conducted in NSW. After participating in the trial, Hugh Brown from Newbridge, near Blayney, has completely changed his weaner treatment programs.

“We run Angus and Angus cross breeders in the central tablelands of NSW, retaining about 100 heifers as replacements each year. We weren’t suffering in a major way from liver fluke, but we’re always looking at ways we can improve our program.”

The most interesting finding of the trial was the difference in weight gains between animals treated with straight triclabendazole plus Cydectin Pour-On and Flukazole C plus Cydectin Pour-On. The Flukazole C-treated group gained an additional 18% (8kg) liveweight over 135 days compared to the straight triclabendazole group. This difference was the direct result of controlling liver fluke down to 2-weeks of age (Flukazole C) versus 4-weeks of age (straight triclabendazole).

However, the most significant and impressive weight gains came from combining Flukazole C and Cydectin Long Acting Injection. Heifers treated with this combination were 44% (20kg) heavier after 135 days compared to heifers treated with a commonly used pour-on flukicide. Furthermore, the fluke pour-on failed to reduce fluke egg output to zero for the duration of the trial.

With the property turning off 450 young cattle a year, the 20kg/per annual in extra weight gain delivered by this treatment combination would result in an extra $18,000 in profit when the cattle are sold to feedlots.

1. Based on sale price of $2.00/kg LWT
DAIRY PROGRAMS

The limited availability of flukicides that can be used for the treatment of lactating dairy cattle can make it difficult for many dairy farmers to follow the programs outlined above. In most cases, the most practical approach is to use Flukazole C at drying off, followed by a number of treatments with Virbamec Plus during lactation. A late autumn or winter dry off treatment with Flukazole C followed by an early spring treatment with Virbamec Plus and 1-2 treatments with Virbamec Plus during summer-early autumn is the best option available. Dairy heifers should be treated with Flukazole C prior to having their first calf to ensure they are not carrying flukes into their first lactation.

TREATING OTHER LIVESTOCK

It must be remembered that liver flukes infect other animals on our farms. While it is not possible to treat wildlife and feral animals, it is possible to treat any sheep that also have access to the fluke-infested paddocks on the property. It is essential that they be treated using the same program as used for the cattle. A range of different active ingredients that provide all stage and adulticide treatment options is available for sheep.

FEEDLOT INDUCTION/QUARANTINE TREATMENT

It is important that all animals sourced from fluke areas are effectively treated to clean the flukes out. Animals may be carrying early immature and immature flukes that will continue to cause liver damage and productivity losses for up to two months even when no new parasites are acquired. Further, liver flukes can survive and cause damage for several years once established in the bile ducts. If using triclabendazole as the induction treatment, only the high potency, synergised form (Flukazole C) should be used. Nitromec offers an effective option for a quarantine treatment because it can also control triclabendazole resistant flukes.
REFERENCES


1. Based on sale price of $2.00/kg LWT
FlukeKill™ Liver Fluke Control Manual

For more information on sustainable and effective liver fluke control, contact Virbac Animal Health on 1800 242 100 or talk to your local Virbac Animal Health Area Sales Manager.

virbac.com.au

Flukazole C
- Synergised formulation of triclabendazole and oxfendazole
- Ideal late autumn/early winter or summer treatment
- Controls damaging 2-week-old early immature flukes
- Broad spectrum control of internal parasites

Nitromec Injection
- Synergised formulation of nitroxynil and clorsulon
- Ideal late autumn/early winter or summer treatment
- Controls triclabendazole resistant flukes
- Controls damaging 2-week-old early immature flukes
- Also contains ivermectin, providing broad spectrum control of internal and external parasites

Virbamec Plus
- Contains clorsulon and ivermectin
- Ideal late winter/early spring treatment
- Can be used during lactation
- Non-triclabendazole based
- Broad spectrum control of internal and external parasites

Flukazole, Nitromec, Virbamec, Cydectin and Websters are registered trademarks of Virbac (Australia) Pty Ltd.

Autumn
Optimal time for an autumn treatment is April/May. The autumn treatment must control early immature, immature and adult flukes.

Late winter/spring
Optimal time for the late winter/spring treatment is August/September. This is important to remove remaining flukes and stop pasture contamination with fluke eggs.

1. Cold winter: Virbamec Plus
2. Warm winter: Nitromec Injection or Flukazole C plus Selenium

Use Nitromec Injection or Flukazole C Plus Selenium.

Summer
An optional mid summer treatment may be required for heavily infected properties.

Use Nitromec Injection or Flukazole C Plus Selenium.